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# Obstetrical brachial plexus palsy: an analysis of 105 cases

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Obstetrical brachial plexus palsy (OBPP) remains a dramatic consequence after complicated childbirth. An increasing number of methods are being developed for the physical therapy and the early repair of the nerve lesions in OBPP, including neuroma excision and nerve grafting, neurolysis and neurotization. Secondary deformities of the shoulder, forearm, and hand can be reconstructed using soft tissue and skeletal procedures. In this article we analyze our approach to 105 patients to obtain optimal functional outcome in patients with OBPP.

*Key words: obstetrical brachial plexus palsy, Horner's sign, C7 lesion, tendon transfer.*

The brachial plexus, which originates from C5 to T1 spinal segments, is formed by the exchange of motor and sensory nerve fascicles between the spinal cord and the nerves innervating the shoulder girdle and the upper extremity. Autonomic innervation of the head and neck is also partly supplied by the cervical sympathetic nervous system.

Obstetrical brachial plexus palsy (OBPP) is described as partial or total severance of the brachial plexus during delivery, and it is a dramatic disability, particularly following a difficult labor. The traction applied to the baby's arm has been known as the causative factor since Smillie's treatise in 1764. Duchenne[1], Klumpke, Sever[2], Lauwers[3] and later Erb[4] have expounded further on this condition. It has a higher incidence in comparison to clavicular and humeral fractures and fetal death[5].

Enthusiasm over surgical repair in the early period of this century diminished as a result of serious complications, but there were expectations for decades that a better cure would be found[6]. Until the 1970s, the dogma that nerve repair was futile remained unquestioned. The studies of Gjorup[7], Narakas[8], Tassin[9], and Gilbert[10,11] led to a remarkable growth of interest among peripheral nerve surgeons in the clinical evaluation of and optimal treatment options in OBPP. Marked improvements in microsurgical reconstruction techniques, progress in late rehabilitative surgery techniques, recent developments in physical therapy renewed interest in obstetrical brachial plexus surgery. Gilbert and Tassin[12] concluded that if biceps and deltoid contraction had not started by three months of age, ultimate function was likely to be poor, although that was later debated by several authors[13-15]. Valid indications for early primary surgical intervention remain a controversial issue.

In this study we review the physical treatment, surgical indications, and results of these treatment modalities.

## Material and Methods

During the period between May 1995 and December 1998, 136 patients with OBPP were seen at the outpatient clinics. A detailed physical examination was performed by the surgeon (GL) and by the physiotherapist (NT). Observations of shoulder, elbow, and hand functions were recorded. Clinical examinations were repeated at four weekly intervals. Seventy-seven of these patients were treated solely with a guided home exercise program. Twenty-eight patients were treated surgically: 17 patients had

primary brachial plexus exploration and microneural reconstruction, and 11 patients had secondary reconstructive procedures including tendon transfers, arthrolyses, and humeral external rotation osteotomies. In 11 of the patients who later had brachial plexus surgery, a home therapy program was applied for a short period, and six patients were elected for surgical intervention at the first consultation. These patients were included in Group II. Thirteen infants are currently undergoing a home physiotherapy program. Seven patients aged between five and 24 months, who were previously treated conservatively elsewhere for OBPP, are candidates for secondary reconstructive procedures. Eleven patients were lost to follow-up. The patients who were lost to follow-up, were currently having their home physical therapy program, and were candidates for secondary reconstruction were excluded from this study, and 105 patients were analyzed.

### Clinical Evaluation

The babies were examined as soon as possible after birth. Any problems during the course of the pregnancy were ascertained. Medical records of the delivery were obtained for babies born in hospital. The number and the problems of previous pregnancies and birth weights of the infants were recorded. General examination of the musculoskeletal system, specifically physical examination of the hip joint, the spine, the clavicles, and the extremities was an essential first step in our clinical examination. Further investigations were performed if any pathologic finding was observed.

The babies were first examined by having the parents hold the baby upright, with deltoid and supraspinatus function looked at and palpated. In a prone position on a specific examination table, serratus anterior, trapezius, and rhomboidei activity was examined. In a supine position muscle activity in the shoulder girdle was looked for. Distal functions, including thumb movements in three planes, finger flexion and extension, wrist flexion and extension, and biceps and triceps function provoked by several stroking and movement maneuvers were recorded. When turning the baby from supine to lateral decubitus position, the arm was kept in a neutral or extension position on the normal side by the activities of the posterior part of the deltoid and triceps, which are affected in proximal brachial plexus lesions. The appearance of the skin, the existence of perspiration and nail growth in the involved extremity were noted. Horner's sign was searched for and photographed using a Sigma 1/150 mm objective from a standard distance of 50 cm under a standard illumination. The babies with Horner's sign were examined preoperatively and postoperatively at the Outpatient Clinic of the Department of Ophthalmology. This examination included exophthalmometric measurements, phenylephrine test, and assessment of the function of the Müller muscle.

### Home Physiotherapy Program

All the parents were instructed by our senior physiotherapist (NT). A physiotherapy program essentially consisting of the method described by Clarke and Curtis[16] with slight modifications was employed. During the first three weeks, the shoulder, arm, forearm, and hand were kept in neutral position. Passive range of motion exercises were started with stretching four weeks after birth. The parents were shown how to abduct and externally rotate the involved shoulder by stabilizing the contralateral shoulder. Elbow and wrist ROM exercises were also demonstrated. Special emphasis was given to external shoulder rotation and forearm supination. Active-assisted and active exercises were begun if there was enough muscle power. Natural play activities were specifically helpful in planning home therapy. The parents were also educated regarding tricky movements during washing, skin care, and carrying. The patients and their parents were seen regularly at monthly intervals during the first 12 months. Although the regular outpatient controls were done only up to the age of 12 months, the parents were advised to continue those exercises as long as possible.

### Decision Making

It is essential that the same surgeon perform serial and careful clinical examinations. Discussion of the clinical findings with the parents was the most important aspect in guiding the surgeon in the decision-making process. We do not routinely employ electromyography (EMG) studies due to the unnecessary technical difficulties encountered during electrodiagnostic examinations. Preoperative computerized tomography (CT) myelograms were performed only in two cases, mainly for medico-legal concern. Magnetic resonance imaging (MRI)

investigations were performed in severe cases, and in all cases in whom an operative intervention was scheduled.

The main indication for surgery was the absence of deltoid and/or biceps function by the end of the 4th month. Acceptance by the parents of the fact that no further progress in shoulder and elbow function was expected was the essential prerequisite for surgery; none of the patients in this series was operated without the parents', observation that no further improvement was taking place.

The aims of surgery were clearly explained to the parents, and a written consent, including permission for the possible harvesting of the sural nerve(s), was obtained.

## Surgical Technique

### *Group II*

Following the induction of general anesthesia using halothane (0.7-1%), $N_2O$, and a short-acting neuromuscular blocking agent (succinylcholine 1.5-2 mg/kg), no further neuromuscular blocking agents were used until the completion of brachial plexus exploration, since electrical stimulation is used in intraoperative monitoring. Legs were prepared and draped following tourniquet application for sural nerve autograft harvesting. A small silastic rubber cushion under the upper thorax, and a slight beach chair position made the exposure easier. The head was turned gently to the contralateral side. A full brachial plexus exposure was obtained if necessary using the classic incision following the sternocleidomastoid, the clavicle, the coracoid and the deltopectoral groove. The supraclavicular fibrofatty tissue was moved superolaterally, and the omohyoid muscle was sutured medially and laterally and divided. Superficial and deep cervical vessels were coagulated and very carefully divided. The phrenic and spinal accessory nerves were identified and protected. The elements of the brachial plexus were identified, including the roots, divisions, trunks, cords, and the dorsal scapular, suprascapular, axillary, musculocutaneous, median, ulnar, and the lateral and medial pectoral nerves. During this exposure division of the clavicle was frequently necessary. If all the roots could be observed up to the levels of the foramens, electrical stimulation was applied. If a good motor response was provoked, and the appearance of the root was satisfactory, an external neurolysis was performed. If there was minimal or no motor response, and the appearance of the root was not satisfactory, extensile extra and intraneural neurolyses were performed. If there was extensive fibrotic changes and neuroma formation, it was apparent that grafting was indicated. A sural nerve was harvested from the contralateral side using "neural strippers" and/or open techniques. In routing the "Axonal donors", priority was given to the lower trunk. The musculocutaneous and the axillary nerves were grafted next. The most frequently performed procedure in this study group was the C5-C6 to upper cord grafting. In severe cases with limited proximal supply, 3rd, 4th, 5th, and 6th intercostal nerves were used. In cases with internal rotation contracture of the shoulder, subscapularis release was also applied in addition to the brachial plexus surgery. Following microreconstruction, the clavicle was reduced and fixed with 1/0 vicryl sutures passing through the bone. The subcutaneous tissue and the skin were closed with interrupted sutures. The upper extremity was immobilized over the thorax with an elastic bandage. The sutures were removed without removing the elastic, and immobilization was continued for four weeks postoperatively. Following this period the regular physical therapy protocol was adhered. No splint of any kind was used. Exercises and play provoking awareness of the involved limb were encouraged. The patients were seen at monthly intervals after the operation.

### *Group III*

Significant internal rotation contractures of two cases (ZT, MMA) were treated with combined latissimus dorsi and teres major transfer defined by Richards[17], provided the latissimus dorsi had full strength. Humeral derotation osteotomy[18] was performed for patients with an internal rotational contracture and glenohumeral deformity. In patients with persistent internal rotation contracture despite the physical therapy, subscapularis release was performed. Tendon transfers in forearm and hand were performed as imposed by the deformity and functional loss. For optimal positioning and stabilization in patients with severe wrist involvement, arthrodesis was applied with standard plates using the technique described by Weiss and Hastings[19].

## Findings and Results

### *Associated Anomalies and Injuries*

Three of the cases were found to have acetabular dysplasia and were treated with abduction

splints. In one case, brought to us at the age of 37 months, there was a right unilateral facet dislocation with a rotatory subluxation of C4 over C5. Posterior spinal fusion for spinal instability was performed, and a secondary reconstructive procedure for shoulder internal rotation contracture is planned in this child. In another case there was a severe spinal stenosis due to bilateral facet dislocation and C5-C6 subluxation leading to paraparesis in addition to right-sided OBPP. This baby had a laminoplasty recently. In one case there was right mild OBPP, in addition to fractures of the occiput, the right clavicle, and the right humerus. All these injuries were treated conservatively with a satisfactory outcome. In one baby there was a supracondylar humerus fracture which was treated conservatively. In three cases isolated clavicular fractures were found and treated conservatively. In a patient in Group III wrist arthrodesis was performed because of instability. The result of the operation was satisfactory in terms of wrist stabilization, but an increase in fingertip ulcerations was observed. The child has a habit of biting his fingertips for which psychiatric examination/treatment were arranged.

In one patient in Group II (EK), a transient contralateral upper brachial plexus lesion developed postoperatively, and resolved spontaneously. This was probably related to improper "hand up" positioning for fluid transfusion and noninvasive monitoring[20]. This was the only case in this series with bilateral brachial plexus findings.

*Group I: Home Physiotherapy Group*

The mean age of the 77 infants who completed a planned physical therapy program with satisfactory clinical results was 3.2 months at the time of the first clinical visit. There were 47 (61%) males and 30 (39%) females in this group. In 43 cases the left side, and in 34 the right side was affected. The mean birth weight was 4,117 g. There were 65 vertex, 7 breech presentations, and 5 cesarean sections. Twenty-three of these children were the first, 33 were the second, 15 were the third, 5 were the fourth, and 1 was the fifth living child in their families. Maternal diabetes was diagnosed in two of the cases. In 35 patients (45%) there was upper plexus involvement, and in 42 patients (55%) there was total plexus involvement. There were no cases of isolated lower plexus paralysis. In three cases a transient ptosis at the affected side was observed. The mean age of this group at the time of the completion of the conservative treatment was 17 months, and the mean follow-up was 14.3 months. At the end of the follow-up period, no functional impairment was recognizable by the parents, and no motor, reflex or sensory abnormalities were detectable in any of the patients examined.

Brachial plexus lesions in three infants delivered by caserean section were of intermediate type with paresis of the latissimus dorsi and triceps and paralysis of the wrist and finger extensors. Shoulder abduction, elbow flexion, and forearm supination were not affected in these infants, and the typical waiter's tip position was not observed. In all infants, the neural dysfunctions were noticed by the pediatricians during routine postnatal controls. All of these infants recovered within six weeks.

*Group II: Brachial Plexus Exploration and Microneural Reconstruction Group*

The mean age of the 17 infants who had brachial plexus exploration and microneural reconstruction was 17 months. There were 11 males and six females in this group. There were one (6%) left-sided and 16 (94%) right-sided lesions. There were 13 vertex and four breech presentations. The mean birth weight of this group was 4,150 g. The birth weights of the infants in Group I and in Group II were not different statistically. The mean age at the time of surgery was 17.3 months. If the four cases that were operated over the age of 35 months were excluded, the corrected mean age in the primary surgery group was 10.3 months. The mean postoperative follow-up of this group was 21 months. The mean age of this group at the time of the last outpatient visit was 38 months. The findings and surgical procedures performed in this group are listed in Table I. The mean operative blood loss was 30 cc, and no transfusions were needed. No infection or clavicular healing problems were seen. Shoulder function was assessed using modified Mallet classification[21]. Impairment of elbow and hand functions was assessed using Gilbert's criteria[22,23].

*Group III: Late Reconstruction Group*

The mean age of the 11 patients in whom secondary reconstructive procedures were performed, such as humeral rotational osteotomies and tendon transfers, was 10.9 years

at the time of the first outpatient visit. There were nine males and two females in this group. Two (18%) of the lesions were left-sided and nine (82%) were right-sided. The mean follow-up was 14.7 months. The surgical procedures performed in this group are listed in Table II.

Table I. Surgical Procedures in Group II

| Patient | Age (m) | Surgical procedure | Results |
|---|---|---|---|
| MÖ (male, L) | 7 | Neurolysis (C5-C6, C7, upper trunk) | Shoulder: Mallet V; Elbow: Gilbert 3/2/0 Hand: Gilbert V |
| NK (female, R) | 41 | Neuroloysis (C5-C6, C7, C8-T1; 2, 3, 4 intercostal routing to axillaris and lateral cord) | Shoulder: Mallet II Elbow: Gilbert 2/1/-1 Hand: Gilbert III |
| ÖB (male, R) | 19 | Neurolysis (C5-C6; C7; nerve grafting to the lateral cord) | Shoulder: Mallet IV Elbow: Gilbert 2/2/0; Hand: Gilbert V |
| Ek (female, R) | 38 | Neurolysis (C5-C6, C7, C8-T1; 2, 3, 4 intercostal routing to axillaris; C6 to musculocutaneous grafting) | Shoulder Mallet II Elbow: Gilbert 2/1/-1 Hand: Gilbert IV |
| HB (female, R) | 35 | Neurolysis (C5-C6, C7, C8-T1; C5 and C6 to uper trunk grafting) | Shoulder: Mallet IV Elbow: Gilbert 3/2/0; Hand: Gilbert IV |
| BY (male, R) | 8 | Neurolysis (C5-C6, C7, C8-T1) | Shoulder: Mallet IV; Elbow: Gilbert 3/1/0 Hand: Gilbert III still recovering |
| OK (male, R) | 6 | Neurolysis (C5-C6, C7, C8-T1) | Shoulder: Mallet IV; Elbow: Gilbert 3/1/0 Hand: Gilbert III still recovering |
| MG (female, R) | 6 | Neurolysis (C5-C6, C7) | Shoulder: Mallet II; Elbow: Gilbert 1/0-2 Hand: Gilbert IV |
| EB (male, R) | 11 | Neurolysis (C5-C6, C7, C8-T1) | Shoulder: Mallet IV; Elbow: Gilbert 3/2/0 Hand: Gilbert III still recovering 14 months postoperative |
| TK (female, R) | 38 | Neurolysis (C5-C6, C7, C8-T1; C5 to axillaris, C6 to lateral cord grafting) | Shoulder: Mallet III Elbow: Gilbert 2/1/-1; Hand: Gilbert IV |
| MK (male, R) | 8 | Neurolysis (C5-C6, C7) | Shoulder: Mallett III; Elbow: 3/1/-1 Hand: Gilbert III still recovering 12 months postoperative |
| SG (female, R) | 21 | Neurolysis (C5-C6, C7, C8-T1) | Shoulder: Mallet II; Elbow: Gilbert 2/1/-1 Hand: Gilbert V |
| NK (male, R) | 13 | Neurolysis (C5-C6, C7, C8-T1) | Shoulder: Mallet IV; Elbow: Gilbert 3/2/0 Hand: Gilbert V |
| CE (male, R) | 8 | Neurolysis (C5-C6, C7; C5-C6 to lateral cord grafting) | Shoulder: Mallet V Elbow: Gilbert 2/1/0; Hand: Gilbert III still recovering 10 months postoperative |
| AÜ (male, R) | 11 | Neurolysis (C5-C6, C7, C8-T1; C5-C6 to upper trunk, C7 to posterior cord grafting) | Shoulder: Mallet II Elbow: Gilbert 2/1/0 Hand: Gilbert III still recovering 6 months postoperative |
| SE (male, R) | 7 | Neurolysis (C5-C6, C7) | Shoulder: Mallet V; Elbow: Gilbert 2/2/0 Hand: Gilbert III han began to improve 4 months postoperative |
| GCS (male, R) | 9 | Neurolysis (C5-C6, C7) | Shoulder: Mallet V; Elbow: Gilbert 3/2/0 Hand: Gilbert V |

Table II. Surgical Procedures in Group III

| Patient | Age (y) | Procedure | Results |
|---|---|---|---|
| Eİ (male, R) | 10 | Humeral external rotation osteotomy, subscapularis release | Significant improvement in shoulder function |
| AT (female, R) | 16 | Pronator quadratus release, pronator teres rerouting, revision of radial head excision | Significant improvement in forearm prosupination |
| ZT (female, R) | 11 | Humeral external rotation osteotomy, subscapularis release, latissimus dorsi transfer | Satisfactory improvement in shoulder abduction and external rotation |
| AA (male, R) | 11 | Wrist arthrodesis | Satisfactory wrist stabilization |
| NS (male, R) | 16 | Humeral external rotation osteotomy, subscapularis release | Significant improvement in shoulder function |
| HG (male, L) | 15 | Humeral external rotation osteotomy, subscapularis release | Significant improvement in shoulder function |
| BA (male, R) | 11 | Wrist arthrodesis | Fair result, increased fingertip ulcerations |
| AÖ (male, R) | 13 | Wrist arthrodesis | Satisfactory wrist stabilization |
| AT (male, R) | 9 | FCR-ECRL, PL-EPL transfers pronator rerouting | Significant improvement in hand function |
| HRK (male, L) | 9 | ECU-AbPL, FCR-EDC transfer, ulnar dorsal capsulectomy, biceps rerouting | Significant improvement in hand function, improvement in forearm supination |
| MMA (male, R) | 9 | Latissimus dorsi transfer, trapezius transfer, pectoralis major PL-EPL transfer, AbPL tenodesis | Significant improvement in hand function and shoulder function |

## Discussion

Many infants with OBPP recover with minor or no residual functional deficits[24]. In our series 94 patients were first seen during their early childhood. Eleven of the patients who later had brachial plexus surgery, first underwent a home therapy program for a short period, and six patients were elected for surgical intervention at the first consultation. Seventy-seven (82%) of these 94 patients were treated only with a physical therapy program, and recovered completely.

The mean birth weight in Group I was 4,117 g, and in Group II 4,150 g. There was no statistical difference between these measurements, which were below the values stated in the literature. Although this might be related to constitutional factors, frequently stated risk factors may not be associated with OBPP[25].

In six cases (BY, OK, EB, SG, NK, AÜ) in Group II, preoperative ptosis partially (EB, SG) or totally (BY, OK, NK, AÜ) disappeared postoperatively. The alteration is usually manifested by the end of the third postoperative week, and continues for months. The mean age of these patients was 11 months and two of the cases were older than one year. Total or partial disappearance of ptosis after that age was probably related to the surgical procedure. The surgical procedure itself may disrupt a neural mechanism, which causes ptosis. In all these six cases, C8 and T1 roots were neurolysed to the level of the intervertebral foramina. This may decompress the preganglionic fibers to stellate ganglion and increase sympathetic input to the postganglionic neurones.

In three infants delivered by cesarean section paresis of the latissimus dorsi and triceps and paralysis of the wrist and finger extensors were present. Shoulder abduction, elbow flexion, and forearm supination were not affected in these infants, and the typical waiter's tip position was not present. This clinical picture was evaluated as intermediate lesion. As stated by Al. Qattan[26] this is a rare condition, although the incidence was slightly higher (~ 3%) in our series. Clinical findings suggesting relatively isolated C7 injury in three infants delivered by cesarean

section were probably due to the lateral traction maneuver applied to the arm of the infants[27]. These lesions were typically noticed by the pediatrician and resolved within six weeks.

There are more questions than answers in the field of obstetrical brachial plexus palsy. Indications and timing are the most debatable aspects[28]. It is clear that earlier surgical reconstruction leads to better clinical result, but there is a group of infants recovering even after 12 months, with poor deltoid and biceps function at the 4th month. Although criteria for timing of microsurgical intervention have been established, it may not be ethical to operate on all infants with no demonstrable deltoid or biceps function by the end of the 4th month. Six patients in Group I with no biceps contraction at the end of the 3rd month had improved significantly by 12 months, and no primary plexus surgery was needed. This finding clearly implies that there is a certain percentage of error in deciding early primary operation during the first months of life. The difficulty of predicting the outcome at the 4th month, and the possibilty of obtaining a better outcome with primary surgery may justify acceptance of a high margin of error. Parents and specifically mothers are very careful observers, and their impressions are very important in the formulation of the treatment. In addition, after the surgical repair, the infants spend most of their time with their mothers. Parent's motivation and cooperation is a key factor in the management of OBPP, not only during the first months of life, but also postoperatively, and during the later periods of life. For this reason we always await the mother's acceptance of the disability caused by OBPP. Early intervention carries the advantage of supplementing spontaneous improvement with the improvement gained solely by surgery. Late intervention, on the other hand, has the disadvantage of delayed nerve reconstruction. The optimal condition and timing for microneural reconstruction can probably be determined by very close cooperation of the parents, the surgeon, and the physiotherapist specified for the management of OBPP.

Another aspect of timing of treatment is brachial plexus surgery after the age of 24 months[29]. The mean age at the time of surgery in Group II was 17.3 months. If the four cases that were operated over the age of 35 months were excluded, the corrected mean age in the primary surgery group was 10.3 months. There were four cases in this series with neglected OBPP treated surgically over the age of 24 months. One child (NK) aged 41 months was referred to us at the age of 40 months because of flail arm. Severe fibrosis involving C5, C6, C7, C8 roots, upper trunk, and middle trunk was released. T2, T3, T4 intercostal nerves were routed to the axillary nerve and to the lateral cord. During the postoperative two years limited improvements in shoulder, elbow, and hand function were noted. Shoulder abduction was 30° and biceps was 3. Finger and wrist flexion and extension were present. The thumb obtained an opposition position, and intrinsic balance developed. Although sensation was not assessed properly before the operation, protective and deep sensations were elicited at the postoperative follow-up. Another neglected case with a flail upper extremity (EK) was operated at the age of 38 months. C5 root was partially avulsed, and there was only one fascicular structure transmitting electric impulse and provoking muscle contraction. C6 was fibrotic but transmitting impulses. All roots were neurolysed. T2, T3, T4 intercostal nerves were routed to axillary nerve, and C6 was grafted to the lateral cord. At the follow-up, shoulder was abducting to 30°, biceps was 3, and a good hand function (Gilbert IV) returned. Another case (HB) was referred to us at the age of 32 months. Her arm was flail and hand was completely insensitive to painful stimulation. During surgery severe fibrosis involving C5, C6, C7, and C8 roots was found. Most of the upper trunk was excised and C5 and C6 were grafted to the distal stump of the lateral cord. The clinical improvement was very satisfactory with a shoulder abduction of 90°, and satisfactory elbow (Gilbert 3/2/1) and hand (Gilbert IV) functions. In the fourth case (TK), C5 and C6 were severely fibrotic and avulsed. C5 root was grafted to axillary nerve, and C6 root was grafted to the lateral cord. At the follow-up, shoulder abduction was possible to 80°, biceps was 3, and satisfactory hand function was gained. In neglected cases with OBPP, shoulder and elbow functions may be reconstructed with several procedures, but satisfactory hand function, specifically hand sensation and fine intrinsic movements, are impossible to reconstruct with secondary reconstructive procedures. Even in patients above the age of three years with OBPP, there may be an indication for brachial plexus reconstruction,

as possible return of hand function may warrant the secondary surgical interventions for shoulder and elbow functions. Furthermore, brachial plexus reconstruction may increase the possibility of secondary tendon transfers for hand functions.

Computerized tomography CT, MRI, and EMG examinations are very widely used in the determination of neural damage in OBPP. We believe that careful serial clinical examinations performed at regular intervals including the sensibility, skin texture, and motor examinations of all muscle groups of the shoulder girdle and upper extremity are more important than any investigation in the decision-making process. EMG was found helpful in the determination of spontaneous healing potential during the conservative treatment and postoperative follow-up. CT and/or MRI are helpful in documentation for medicolegal purposes, and in the discussion of patient prognosis with parents.

Decision making during the first months of life is a very critical aspect of the treatment of OBPP. As a minimally invasive method, endoscopic visualization of the damaged brachial plexus can be very helpful in the planning and possibly in the execution of the treatment at very early phases. In patients with upper plexus involvement, endoscopy of the lower components may prevent unnecessary exposure and increased morbidity.

## Conclusion

A multidisciplinary team consisting of the pediatric neurologist, physical therapist, and specialized orthopedic surgeon, and close cooperation with parents are of crucial importance in the early diagnosis and optimal treatment of OBPP. As stated by Algimantas Narakas in 1978, "What we need is some other type of advance, porbably connected with the physiology of nervous tissue"[30]. This statement is still valid today, but improvements in surgical techniques and developments in biologic and pharmacological manipulation to support nerve regeneration and differentiation will increase our potential to deal with this problem.

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# Assessment of protein-energy malnutrition in children with chronic arthritis

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Protein-energy malnutrition (PEM) has been estimated to occur in 10 to 50% of children with juvenile chronic arthritis (JCA). Thirty-eight children with JCA were evaluated and their nutritional status determined, and they were compared with 23 healthy sex and age-matched children as controls. A standardized, 9-parameter comprehensive nutritional assessment profile was used. The simple anthropometric measurements, height and weight for age, were abnormal in 30% and 27% of the patients, respectively. A detailed evaluation revealed that 71% had abnormal somatic protein stores, and that they also had significantly low levels of visceral protein stores, when compared to their healthy peers. The results were consistent with the fact that inflammation put the JCA patients at significant risk for developing complicated malnutrition and it might result in PEM without any obvious signs of malnutrition. A nutritional screening test would be very useful in detecting early PEM in children with chronic arthritis.

*Key words: PEM, chronic arthritis.*

It is well known that many children with chronic diseases are poorly nourished; this is no less true for children with chronic arthritis. Protein-energy malnutrition (PEM) has been estimated to occur in 10 to 50% of children with juvenile chronic arthritis (JCA)[1]. Children with active JCA are often anorexic, and in one study, their dietary intake was only three-quarters of the recommended dietary allowance for age[2].

When a child is determined to be at risk of becoming nutritionally depleted, precipitating factors such as inadequate intake, reduced absorption, excessive losses, impaired utilization, or increased requirements must be established. Accurate assessment of a child's nutritional status is an important element of pediatric care. Successful nutritional assessment is predicated on an awareness of nutritional deficiencies secondary to other processes: disease states and drug therapies that precipitate specific nutrient depletion[3]. In this study, JCA patients were evaluated, their nutritional status was determined and they were compared with a healthy sex-and age-matched control group.

## Material and Methods

Thirty-eight children with JCA who were followed up in the Pediatric Rheumatology Unit were included in the study. They all satisfied the American College of Rheumatology (ACR)[4] and European League Against Rheumatism (EULAR)[5] criteria for JCA. Twenty-three healthy, age-and sex-matched subjects were selected as a control group. Twenty-one (55%) of the patients were receiving naproxen sodium, and 17 (45%) were receiving steroid + weekly oral methotrexate (10 mg/m$^2$/wk). All the patients receiving steroid therapy were on prednisone at the beginning, which was then switched to deflazacort during the low-dose regimen. The JCA patient was considered in "partial remission" when he received medication and had mild or no joint symptoms and the examination revealed minimal evidence of active disease, and "active" when there were persistent joint symptoms and physical evidence of active joint inflammation, despite receiving medication.

All children in the study were evaluated by the Pediatric Nutrition and Metabolism Unit. A Harpenden stadiometer and a Seca beam balance

scale were used to measure height and weight, respectively. A Holtain Ltd., Crymrch (UK) caliper was used to measure triceps skinfold thickness (tsf) (three times) at the midpoint between the acromion and the olecranon process, and the three measurements were averaged. Mid-arm circumference (mac) was measured at the same point and arm muscle area (ama) was calculated as: ama=[mac(cm)-0.314 x tsf (mm)]$^2$/12.56.

Anthropometrical parameters were expressed as percent of standard, i.e., the median value of the age-and sex-matched reference population. National Center for Health Statistics data was used for standard values[6]. Serum albumin and iron binding capacity were measured by conventional methods. Serum transferrin was calculated as transferrin = [0.8 x total iron binding capacity (TIBC)-43]. Serum prealbumin (PAB) and serum retinol binding protein (RBP) were assessed by radial immunodiffusion technique. Creatinine-height index (CHI) was calculated as CHI=(actual urinary creatinine/ ideal urinary creatinine) x 100. Table I shows the nutritional assessment parameters which are indicators of protein-energy malnutrition. Mann-Whitney U test was used for statistical analysis for comparison of the groups, and p values below 0.05 were regarded as significant.

Table I. Nutritional Assessment Parameters for Determining Protein-Energy Malnutrition

| Nutritional parameter | Abnormal value | | |
|---|---|---|---|
| Height for age | < 95% | | |
| Weight for height index | < 90% | | |
| Triceps skinfold thickness | < 90% | | |
| Arm muscle area | < 90% | | |
| Serum albumin | < 3.5 g/dl | | |
| Serum prealbumin | < 5$^{th}$ percentile | | |
| Serum retional binding protein | for adjusted norms | | |
| Serum transferrin | < 200 mg/dl | | |
| Creatinine-height index | severe < 40% | moderate 40%-60% | mild 60%-80% |

## Results

The patient and control groups were classified according to sex and age, and disease subgroups, duration, activity and the medications used were recorded (Table II). The mean age of the patients was 10.6 years (3.0-17.0 years), and of the control group 10.3 years (3.0-16.0 years). Forty-two percent were female and 58% were male in the JCA group, and 48% were female and 52% were male for healthy controls. The mean duration of JCA was 3.3 years (1-14 years). Disease onset was systemic in nine (24%), polyarticular in 20 (52%), and oligoarticular in nine (24%) patients; the course was systemic in two (5%), polyarticular in 20 (52%), and oligoarticular in 16 (43%). The number of patients receiving steroid therapy at the time of nutritional evaluation or during the preceding six months was 38 (36%), 35 (92%) were on low dose, and 3 (8%) were on high dose. At the time of the evaluation, 30 (79%) patients were noted to be in partial remission, and eight (21%) had active disease. Nutritional comparison of patients and controls is shown in Table III. It consists of three main parts: the first two columns compare the patients and controls. Patients' height for age, arm muscle area, serum prealbumin, retinol binding protein and transferrin levels were found to be significantly lower than those of the controls ($p < 0.05$). Patients with active disease and those in partial remission are compared in the third and fourth columns. Serum prealbumin, retinol binding protein and transferrin levels were found to be significantly lower in the active disease group ($p < 0.05$). There was no significant difference between the patients receiving naproxen versus methotrexate + deflazacort (MTX + DFC) by means of nutritional status, as defined in the fifth and sixth columns, respectively. Table IV compares the patient and control groups according to the abnormal nutritional parameters. Forty-two percent of the patients' height for age was under 95%; it was 7% for the control group ($p < 0.05$). Weight for height index was under 90% in 29% of patients, whereas all the controls were in the normal range ($p < 0.05$). Arm muscle area was under 90% in 71% of patients and in 31% of the control group ($p < 0.05$). None of the patients' serum transferrin levels was below 200 mg/dl, whereas levels were below 200 mg/dl in 39% of the controls ($p < 0.05$). Creatinine-height index was abnormal in 18% of patients and in none of the controls ($p < 0.05$). Height for age, weight for height index, arm muscle area, serum transferrin level and creatinine-height index were significantly lower in the patients with active disease than in those in partial remission. Height for age, serum albumin and transferrin levels and creatinine-height index were significantly lower in patients on MTX + DFC, when compared with those taking only naproxen.

Table II. Demographics and Patient Characteristics

| | | Patients (n = 38) | | Control group (n = 23) | | |
|---|---|---|---|---|---|---|
| Sex (F/M) | | 16/22 | | 11/12 | | |
| Age at time of study (yrs) | mean 10.6 | median 10.5 | range 3-17 | mean 10.3 | median 10.0 | range 3-16 |
| Age at disease onset | mean 6.6 | median 6.0 | range 0.5-15 | | | |
| Disease duration (yrs) | mean 3.3 | median 2.0 | range 1-14 | | | |
| Partial remission/active disease | | 30/8 (79% - 21%) | | | | |
| JCA subtype | Systemic | Polyarticular | Oligoarticular | | | |
| Onset | 9 (24%) | 20 (52%) | 9 (24%) | | | |
| Course | 2 (5%) | 20 (52%) | 16 (43%) | | | |
| Medications | | Naproxen 21 (55%) | MTX+DFC[1] 17 (45%) | | | |
| Steroid therapy Patients receiving at the time of study or during preceding 6 months n = 14 (36%) | | | | | | |
| Steroid dose (mg/kg/d)[2] | | low 35 (92%) | high 3 (8%) | | | |

1: Methotrexate (10 mg/m2/wk) + low-dose deflazacort.
2: Low dose = 0.5 mg/kg/d equivalent dose for prednisone.
High dose = 1-2 mg/kg/d prednisone.
JCA: juvenile chronic arthritis.

Table III. Nutritional Comparison of Patients and Controls, Patients With Active Disease and Those in Partial Remission, and Patients Receiving Naproxen Versus MTX + DFC

| Parameter | Patients n=38 | Controls n=23 | Active disease n=8 | Partial remission n=30 | naproxen n=21 | MTX + DFC* n=17 |
|---|---|---|---|---|---|---|
| Height for age (% std) | 99.8 ± 18.7[1] (69.2-183.8) | 10.4.4 ± 5.5[1] (95.3-113.1) | 90.3 ± 12.5 (69.2-108.9) | 102.4 ± 19.4 (88.9-183.8) | 104.5 ± 22.9 (85.5-183.8) | 94.0 ± 9.4 (69.2-108.9) |
| Weight for height index (% std) | 103.4 ± 17.5 (77.7-147.7) | 101.2 ± 12.8 (87.0-137.2) | 107.4 ± 20.9 (87.5-147.7) | 102.0 ± 16.9 (77.7-147.7) | 101.3 ± 13.7 (80.9-135.0) | 106.7 ± 20.9 (77.7-147.7) |
| Triceps skinfold (% std) | 108.7 ± 35.8 (12.0-150.0) | 120.1 ± 25.3 (76.5-150) | 102 ± 43.4 (45.0-150.0) | 102.4 ± 27.4 (43.5-150.0) | 103.7 ± 29.9 (58.5-150.0) | 114.2 ± 47.6 (12.0-150.0) |
| Arm muscle area (% std) | 81.6 ± 25.9[2] (40.5-150.0) | 96.7 ± 12.2[2] (69.0-130.0) | 77.3 ± 24.2 (46.5-126.0) | 81.2 ± 23.7 (40.5-150.0) | 83.1 ± 28.1 (40.5-150.0) | 83.3 ± 29.0 (45.0-150.0) |
| Serum albumin (g/dl) | 3.9 ± 0.5 (2.3-4.6) | 4.1 ± 0.3 (3.6-4.6) | 4.1 ± 0.2 (3.8-4.3) | 3.9 ± 0.6 (2.3-4.6) | 4.1 ± 0.5 (2.6-4.6) | 3.9 ± 0.6 (2.3-5.0) |
| Serum prealbumin (mg/L) | 172.8 ± 51.3[3] (69.0-299.6) | 245.4 ± 56.1[3] (162.9-337) | 178 ± 47.6[6] (69.0-270.0) | 210.3 ± 53.5[6] (156.2-310.6) | 188.2 ± 55.6 (89.1-299.6) | 179.0 ± 54.5 (69.0-268.5) |
| Serum retinol binding protein (mg/dl) | 34.5 ± 6.4[4] (19.4-46.0) | 44.4 ± 8.8[4] (29.6-55.8) | 35.4 ± 5.9[7] (19.4-39.0) | 42.0 ± 6.6[7] (27.2-46.0) | 35.6 ± 5.9 (20.1-46.0) | 35.1 ± 6.2 (19.4-42.2) |
| Serum transferrin (mg/dl) | 204.0 ± 25.4[5] (165.0-274.0) | 236.8 ± 44.0[3] (139.0-299.0) | 227.9 ± 45.2[8] (139.0-299.0) | 271.3 ± 15.08 (245.0-291.0) | 248.1 ± 41.1 (139.0-299.0) | 228.0 ± 45.9 (157.0-299.0) |
| Creatinine-height index (% std) | 124 ± 37.9 (22.5-150.0) | 137.6 ± 19.6 (84.0-150.0) | 131.8 ± 34.4 (245.0-291.0) | 122.1 ± 39.0 (22.5-150.0) | 128.6 ± 37.2 (22.5-150.0) | 118.6 ± 39.1 (51.0-150.0) |

*: Methotrexate (10 mg/m2/wk) + low-dose deflazacort.
1-8: $p < 0.05$ (Mann-Whitney U-Wilcoxon rank sum W test).

Table IV. Comparison of Patients and Controls, Patients With Active Disease and Those in Partial Remission, and Patients Receiving Naproxen Versus MTX + DFC Using the Nutritional Assessment Parameters Which Are Indicators of Protein-Energy Malnutrition

| Abnormal parameter | Patients n=38 | Controls n=23 | Active disease n=8 | Partial remission n=30 | naproxen n=21 | MTX + DFC* n=17 |
|---|---|---|---|---|---|---|
| Height for age (< 95%) | 16 (42%)[1] | 1 (7%)[1] | 6 (75%)[6] | 10 (33%)[6] | 6 (29%)[11] | 10 (59%)[11] |
| Weight for height index (< 90%) | 11 (29%)[2] | none[2] | 2 (25%)[7] | 9 (30%)[7] | 6 (29%) | 5 (29%) |
| Triceps skinfold (< 90%) | 11 (29%) | 2 (15%) | 3 (38%) | 8 (27%) | 6 (29%) | 5 (29%) |
| Arm muscle area (< 90%) | 27 (71%)[3] | 4 (31%)[3] | 7 (88%)[8] | 20 (67%)[8] | 15 (71%) | 12 (71%) |
| Serum albumin (< 3.5 g/dl) | 3 (8%) | none | 1 (13%) | 2 (7%) | none[12] | 3 (18%)[12] |
| Serum transferrin (< 200 mg/dl) | 9 (39%)[4] | none[4] | 10 (33%)[9] | none[9] | 2 (12%)[13] | 6 (29%)[13] |
| Creatinine-height index (abnormal) | 7 (18%)[5] | none[5] | 5 (63%)[10] | 2 (7%)[10] | 2 (10%)[14] | 5 (24%)[14] |

*: Methotrexate (10 mg/m²/wk) + low-dose deflazacort.
1-4: $p < 0.05$ (chi-square test).

## Discussion

A number of factors contribute to decreased food intake in children with JCA. Inflammatory mediators such as interleukin-1 and tumour necrosis factor are increased and they have been shown to cause anorexia[7,8,9]. The roles of interleukin-6 and the aforementioned clearly demonstrate a correlation between growth delay and JCA[10,11]. Recent studies indicating the role of adhesion molecules in JCA have focused on circulating levels of soluble E-selection (sE-selection), P-selection and intercellular adhesion molecule-1 (sICAM-1) in patients with JCA, and it was found that levels of sE-selection and sICAM-1 were significantly correlated with levels of soluble TNF receptor 2, especially in systemic arthritis[12]. Another important factor, fever, could contribute to the increased nutrient requirements in these patients. Children experiencing depression or severe pain because of their disease also become anorexic. In some families, socioeconomic factors might prevent families from purchasing adequate nourishment for their children. So, it is unlikely that growth retardation is due solely to steroid use[2]. In this study, we used a standardized, 9-parameter comprehensive nutritional assessment profile, and compared the patients with sex-and age-matched healthy controls. In a study done by Bernstein et al.[13], they found that 33% of children with JCA had heights below the 3rd percentile, and the ratio had increased to 53% after 7.5 years. In this study, the results were similar and 30% and 27% of the patients had heights and weights under the 3rd percentile, respectively. Henderson and Lovell[14] found that only 30% of patients with PEM had heights under the 5th percentile, but 90% of them had subnormal somatic protein stores, as measured by arm circumference, and arm muscle circumference and area. Thus, a detailed nutritional assessment was able to document more accurate data in these children, mostly by including the ones with mild PEM. We found a significant difference between the patients and sex-age matched control, in terms of arm muscle area. We also determined the levels of visceral protein stores (serum albumin, PAB and RBP) and also serum transferrin, as we knew they would be the early predictors of PEM. We agree that the significantly low levels of PAB and RBP in our patients, consistent with the results of Henderson and Lovell[14], support the interpretation that they result primarily from poor nutrition rather than from inflammation. Another important point is that when malnutrition is complicated by inflammation, weight loss tends to come from lean body mass such as skeletal muscle, rather than from fat[15-17]. Our results are also consistent with the fact that inflammation puts these patients at significant risk of developing complicated malnutrition and may result in PEM without any obvious signs of malnutrition. In a study from Kirel et al.[18], serum iron levels and transferrin saturation were low in all JCA patients, and there was a significant correlation between ferritin levels and C-reactive (CRP) and Erythrocyte sedimentation rate (ESR) indicating the disease activity. We found a significant difference between the visceral protein stores in patients and in the healthy control group, whereas there was no statistical difference in their subcutaneous fat stores, as also documented by Henderson and Lovell[14]. Henderson et al.[19] also proposed a nutritional

screening test with a sensitivity and specificity of 80% and 86%, respectively. We strongly support the use of this test in rheumatology clinics in order to document many JCA patients who may have undiagnosed mild PEM. Regarding the multidisciplinary evaluation of patients with JCA, there is a need for involvement of the pediatric Nutrition and Metabolism Unit to facilitate early recognition of potential nutritional problems in this population.

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# Fiberoptic flexible bronchoscopy via the laryngeal mask airway in children

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SUMMARY: Kiper N, Öcal T, Özçelik U, Anadol D, Göçmen A, Aypar Ü. Fiberoptic flexible bronchoscopy via the laryngeal mask airway in children. Turk J Pediatr 2001; 43: 197-199.

The laryngeal mask airway (LMA) is a new device for controlling the airway during many procedures. Aside from its use in different kinds of surgical procedures, fiberoptic flexible bronchoscopy can also be performed easily with this mask in children under sedation. This procedure was performed via LMA in 36 children (aged 2-16 years) who suffered from different kinds of respiratory diseases and were seen at Hacettepe University İhsan Doğramacı Children's Hospital, Pediatric Chest Disease Unit, during a seven-month period. The procedure was performed with success and no complications occurred. To the best of our knowledge, this is the first report from Turkey on flexible bronchoscopic evaluation via LMA in children with different kinds of respiratory diseases. We suggest that this technique can be used safely.

*Key words: laryngeal mask airway, fiberoptic flexible bronchoscopy.*

The laryngeal mask airway (LMA) is a relatively new device developed during the 1980s by Archie Brain in England[1]. Although it has been used in adults for upper airway management since 1983, this mask has become available for children only in the last 10 years[2-5].

The LMA is a simple small inflatable mask that forms a low pressure seal around the laryngeal inlet (Fig. 1). It consists of a silicone rubber tube connected at a 30° angle to a shallow bowl-shaped mask with an inflatable rubber cuff. This silicone tube opens through the center of the cuff and has two small bars traversing its aperture to prevent the epiglottis from occluding its lumen. After positioning, the rubber cuff is inflated through a pilot balloon to provide a seal over the laryngeal opening. The silicone tube has a standard 15 mm adaptor for connection to the anesthesia circuit.

The LMA is passed without visualization into the patient's hypopharynx unless there is resistance. When it is correctly placed its distal end lies directly over the glottis, thus providing a direct guide for passage of the bronchoscope and through the nose avoiding the possibility of trauma. This is a particular concern in small children and especially in those with congenital upper airway abnormalities and coagulation problems[6].

Fig. 1. Laryngeal mask airway.

Here we report 36 children in whom flexible bronchoscopy was performed easily and successfully via LMA under sedation. With this technique, full examination of the larynx, trachea and bronchial tree was completed without serious complication. To the best of our knowledge, this is the first report from Turkey on flexible bronchoscopic evaluation via LMA in children with different kinds of respiratory diseases.

## Material and Methods

Flexible fiberoptic bronchoscopy using an Olympus BF type P200 Evis bronchovideoscope was performed via LMA in 36 children at

Hacettepe University İhsan Doğramacı Children's Hospital, Pediatric Chest Disease Unit, during a seven-month period. All patients had an adequate period of fasting essential for this procedure. LMAs sized between 1 and 2 were used according to the age and weight of the patients. Prior to insertion of the LMA, propofol (1-1.5 mg/kg) was administered intravenously. Arterial oxygen saturation of the patients was monitored by 4500 Scout mini oxygen saturation monitor, and their electrocardiogram (ECG) and blood pressure by Sein Patient Monitor (SE-485) throughout the whole procedure. The LMA was inserted when sedation was adequate; it was inflated with 10 ml air and then connected to the T-piece system via a 15 mm Portex connector. Sedation was maintained with propofol and fentanyl (1-2 μg/kg). Spontaneous ventilation was maintained throughout the procedure permitting bronchoscopic evaluation of airway structures.

## Results

The size 1-2 LMA was used in 36 patients (20 girls, 16 boys) whose ages ranged from two to 16 years (mean age: 10.3 years) and whose weights ranged between 13 and 65 kg. Demographic data and duration of insertion of the mask are summarized in Table I. The LMA was correctly inserted on the first attempt in 30 cases. Among the remaining six patients, the LMA was inserted on the second attempt due to tonsillary hypertrophy in two patients and to unexplained factors in three patients, and on the third attempt in one patient again for unknown reasons. The LMA was removed with ease in all patients. No serious complications were observed after the procedure.

## Discussion

The LMA is a relatively new device and innovative means to control the airway during many procedures. Aside from its use for different kinds of surgical procedures, flexible bronchoscopy can also be performed easily with this mask in children under sedation[5,6]. The LMA provides a totally patent airway, so a full examination of the larynx, trachea and bronchial tree can be completed with this technique without potential trauma in the upper respiratory tract. Furthermore, no paralyzing agent is required during this procedure. Spontaneous ventilation, which is needed for evaluation of airway structures, is also maintained, which is particularly important for diagnosing laryngomalacia, tracheomalacia and tracheal obstruction in children[7]. Connection directly to a T-piece system provides additional

Table I. Demographic Details of Patients and Indications for Bronchoscopy

| Case number | Initials | Age (years) | Sex | Weight (kg) | LMA size | Indication for bronchoscopy |
|---|---|---|---|---|---|---|
| 1 | D.Ö. | 8 | F | 25 | 2.5 | Chronic obstructive pulmonary disease |
| 2 | H.K. | 11 | M | 35 | 2.5 | Bronchiectasis, atelectasis |
| 3 | E.B. | 7 | F | 21 | 2 | Kartagener syndrome, atelectasis |
| 4 | S.D. | 12 | F | 32 | 2.5 | Intrabronchial mass, tuberculosis (?) |
| 5 | N.K. | 16 | F | 55 | 3 | Castleman disease, lymphoma (?) |
| 6 | S.S. | 2 | M | 13 | 2 | Atelectasis |
| 7 | N.A. | 9 | F | 23 | 2.5 | Bronchiectasis, atelectasis |
| 8 | C.Y. | 11 | M | 26 | 2.5 | Primary ciliary dyskinesia, atelectasis |
| 9 | İ.A. | 15 | M | 56 | 3 | Atelectasis |
| 10 | B.A. | 12 | F | 42 | 3 | Hemoptysis |
| 11 | E.A. | 9 | M | 20 | 2 | Bronchiectasis |
| 12 | Ö.A. | 11 | F | 29 | 2.5 | Bronchiectasis, atelectasis |
| 13 | İ.C. | 15 | M | 48 | 3 | Non-Hodgkin's lymphoma, atelectasis |
| 14 | L.C.A. | 8 | M | 22 | 22.5 | Bronchiectasis |
| 15 | T.B. | 11 | M | 36 | 2.5 | Atelectasis |
| 16 | K.D. | 6 | F | 21 | 2 | Kartagener syndrome |
| 17 | M.D. | 12 | M | 32 | 2.5 | Kartagener syndrome, atelectasis |
| 18 | H.Ç. | 3 | M | 13 | 2 | Recurrent pneumonia |
| 19 | M.B.Ü. | 11 | M | 31 | 2.5 | Atelectasis |
| 20 | Y.K. | 8 | M | 27 | 2.5 | Bronchiectasis, atelectasis |
| 21 | D.M. | 10 | F | 30 | 2.5 | Atelectasis |
| 22 | Y.Ç. | 7 | F | 19 | 2 | Pulmonary alveolar microlithiasis |

Table I. Continued

| Case number | Initials | Age (years) | Sex | Weight (kg) | LMA size | Indication for bronchoscopy |
|---|---|---|---|---|---|---|
| 23 | N.M. | 6 | F | 65 | 3 | Bronchiectasis |
| 24 | Z.K. | 14 | F | 47 | 3 | Kartagener syndrome, bronchiectasis |
| 25 | L.Ü. | 9 | F | 23 | 2.5 | Bronchiectasis |
| 26 | S.Y. | 15 | F | 40 | 3 | Bronchiectasis |
| 27 | T.P. | 9 | F | 30 | 2.5 | Bronchiectasis |
| 28 | Z.K. | 16 | M | 44 | 3 | Bronchiectasis |
| 29 | K.K. | 16 | M | 56 | 3 | Bronchiectasis |
| 30 | Y.K. | 9 | F | 21 | 2 | Bronchiectasis, primary ciliary dyskinesia (?) |
| 31 | M.A.O. | 7 | M | 22 | 2 | Bronchial asthma, atelectasis |
| 32 | E.Y. | 13 | M | 35 | 2.5 | Cystic fibrosis (?), bronchiectasis, atelectasis |
| 33 | A.A. | 14 | F | 49 | 3 | Bronchiectasis |
| 34 | S.A. | 8 | F | 23 | 2.5 | Bronchiectasis |
| 35 | Y.Ç. | 11 | F | 31 | 2.5 | Bronchiectasis |
| 36 | G.D. | 12 | F | 33 | 2.5 | Bronchiectasis |

LMA: laryngeal mask airway.

advantages for aspiration or for delivering oxygen to the patient when necessary. Other advantages are its ease of insertion and the absence of contact with the vocal cords. It also avoids the possibility of trauma while passing the bronchoscope through the nose as it lies above the glottic opening and provides a direct guide. This is a particular concern in small children and also in patients with coagulation problems. Despite its many advantages, it should be kept in mind that the LMA does not protect the larynx and, therefore, should not be used in patients who are at high risk of regurgitation as it does not protect the airway from aspiration.

We used size 1 and 2 LMAs in our patients and no complications were seen. All but one patient tolerated size 2 very well.

Although Gürsoy[8] reported use of the LMA in children from Turkey who underwent surgical procedures, our report is the first report on using the LMA for flexible fiberoptic bronchoscopy in children in our country.

Our impression is that the LMA is considerably less stressful for the pediatric pulmonologist when first performing flexible fiberoptic bronchoscopy, especially in children under six years of age because it prevents the risk of nasal trauma and bleeding.

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# Preliminary pediatric transesophageal echocardiography experiences

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With transesophageal echocardiography (TEE), a new echocardiographic window is obtained which enables cardiologists to explore the heart from the esophagus and stomach. However, the procedure, when first undertaken, may present certain difficulties for the cardiologist in interpreting the anatomical findings and approaching a diagnosis. We thus convey our first experiences and results of TEE in 107 pediatric patients.

Transesophageal echocardiography (TEE) was performed in 107 pediatric patients at our institution between December 1998-February 2001, using the standard techniques and following the standard criteria suggested by the American heart Association. The mean age of 54 male (50.5%) and 53 female (49.5%) patients was 7.8 years. Intubation difficulty was experienced in four cases. In one case, while drawing the transducer back from the esophagus, it kinked at the hypopharynx. None of the cases had major hemorrhage or esophageal rupture, and only a few cases had minor pharyngeal injuries or hemorrhages.

We used TEE in detecting vegetations in patients with possible endocarditis, and evaluating the prosthetic valves and abnormal pulmonary venous return. We also used TEE to clarify preooperative anatomical details, postoperative complications and residual defects of complex congenital cardiac anomalies. Transcattheter closure of 47 secundum atrial septal defects (ASD)'s and a muscular ventricular septal defect (VSD) (both during patient selection and during the procedure) were accomplished under TEE guidance. As the pediatric cardiologists gain more experience in performing TEE, this technique will have a wider and more effective use in the pediatric population.

*Key words: transesophageal echocardiography, pediatric.*

Transesophageal echocardiography (TEE) has provided a new echocardiographic window, to view the heart from the esophagus and stomach. It is a semi-invasive procedure that compliments the transthoracic echocardiography (TTE). Whenever it is believed the procedure would provide additional information about the diagnosis, or when the TTE does not provide an adequate visualization, this procedure is performed by a team including pediatric cardiologists and physicians experienced in resuscitating and intubating children[1-5]. When first undertaken, the procedure may present some difficulties for the cardiologist in showing the anatomical structures and interpreting the diagnosis[1]. The American Society of Echocardiography has suggested some standard rules for cardiologists attempting the TEE[6], which we followed to perform the procedure in 107 pediatric patients. Herein to convey our preliminary results and experiences with this procedure.

## Material and Methods

One hundred and seven TEEs were performed between December 1998 and February 2001 in pediatric patients under general anesthesia, in the operating room or in the catheter laboratory. Toshiba Sonolayer SSH 160 A and ATL 3000 and

GE vingmed system five performance echocardiography machines, and 5 mHz biplane and multiplane transducers were used. The standard TEE techniques were applied[6].

In patients with atrial septal defect (ASD), the size of the septal defect; the anterior, posterior, superior and inferior rims; the total septal size; and the relation of the defect to the atrioventricular (AV) valves, superior vena cava (SVC), upper right pulmonary vein and to the coronary sinus were noted in caval, four chamber and aortic short-axis views. The procedure was repeated in patients whose ASDs were thought to be closed via the transcatheter route. During the second procedure the stretched ASD diameter was also measured by inflating a sizing balloon at the level of the defect.

## Results

The ages of the patients (54 male, 53 female) ranged from 2.5 to 18 years (mean: 7.8). TEE was performed in seven patients with infective endocarditis in whom TTE did not provide adequate information about vegetations; in three patients with prosthetic mitral valve to evaluate thrombi; in a patient with partial anomalous return of the pulmonary vein to clarify the anatomical defect; in a patient with transposition of the great arteries (TGA) who had a senning operation to determine the venous baffle obstruction; in a patient with thorax deformity and congenital mitral stenosis to confirm the mitral pathology; in a postoperative patient with double outlet right ventricle (DORV) to search for residual ventricular septal defect; in a patient with Kawasaki disease; in 91 patients with ASD and in a patient with muscular ventricular septal defect (VSD) (Table I).

We encountered resistance in four patients during intubation. In one patient, the tip of the transducer kinked at the hypopharynx as it was withdrawn from the esophagus. None of the patients had major complications such as haemorrhage, esophageal rupture or laceration.

In two of the seven patients with infective endocarditis, vegetations were observed on the VSD patch and in the pulmonary artery of a patient operated for tetralogy of Fallot, and on the tricuspid valve of a patient with VSD. None of the patients with prosthetic mitral valve had valve dysfunction, or thrombi. The partial anomalous return of the right upper pulmonary vein to the SVC was revealed by TEE. In a patient with congenital mitral stenosis and thorax deformity, the parachute mitral valve and single papillary muscle were confirmed with TEE. The venous baffle obstruction was demonstrated in a patient with TGA who had a senning operation. Suspected residual VSD was ruled out in a postoperative patient with

Table I. Results of the Transesophageal Echocardiography

| Transthoracic echo | Transesophageal echo | Number of patients |
|---|---|---|
| Operated TOF+IE | Vegetation on the VSD patch and in pulmonary artery | 1 |
| Inlet VSD+IE | No vegetation | 1 |
| VSD+IE | Vegetation on tricuspid valve | 1 |
| MR+IE | No vegetation | 1 |
| AV discordance+MR+IE | No vegetation | 2 |
| İnlet VSD+AV discordance+IE | No vegetation | 1 |
| MR with MVR | No thrombi | 3 |
| Congenital MS+thorax deformity | Shone anomaly | 1 |
| Partial anomalous return of pulmonary veins | Right upper pulmonary vein to SVC | 1 |
| Operated (senning) TGA | Obstruction of venous baffle | 1 |
| Operated DORV+VSD? | No VSD | 1 |
| Kawasaki disease | Normal coronary arteries | 1 |
| ASD | ASD | 37 |
| ASD | Closed by transcatheter technique | 47 |
| ASD | Not closed by transcatheter technique | 6 |
| ASD+dilated CMP | Not closed by transcatheter technique | 1 |
| Midmuscular VSD | Closed by transcatheter technique | 1 |
| Total | | 107 |

TOF : Tetrology of Fallot.
IE : Infective endocarditis.
VSD : Ventricular septal defect
MR : Mitral regurgitation
AV : Atrioventricular.
MVR : Mitral valve replacement.
MS : Mitral stenosis.
ASD : Atrial septal defect
CMP : Cardiomyopathy
SVC : Superior vena cava

DORV. The coronary arteries of the patient with Kawasaki disease were normal. Among the 54 patients scheduled for transcatheter closure of their ASD defects, 47 were successfully closed. The balloon-stretched ASD diameter in the remaining seven patients was too large (> 25 mm) for transcatheter closure. In all patients with device occlusion of the ASD, TEE was repeated immediately after the procedure. Twenty-one of these patients had trivial residual shunt. No SVC, upper right pulmonary vein, AV valve or coronary sinus obstruction was observed postprocedurally. TEE was also used during the VSD closure to measure the VSD diameter and select the appropriate device and after the procedure to check the residual shunt, which was only trivial.

## Discussion

Transesophageal echocardiography (TEE) is done under general anesthesia in children, especially those under 10 years of age[6]. Physicians experienced in handling infants and small babies should perform it, since it is a semi-invasive procedure[1,6]. The American Society of Echocardiography has suggested some standard rules for cardiologists intending to perform TEE[6]. These are:

- Having performed at least 30 endotracheal intubations, mostly to children under two years of age.
- Having interpreted complex heart diseases echocardiographically in at least 400 patients (50% being under 1 year of age), or for at least six months.
- Having done and interpreted 30-50 monoplane or biplane TEEs under supervision.

If the echocardiographer is not a pediatric cardiologist, and if an intraoperative TEE is needed, a pediatric cardiologist must be consulted during the procedure[1].

We started this study with a 22-year experience with TTE. Experienced anesthesiologists were ready to help with the intubation of small children.

No death has been reported in children due to TEE. Complications are rare, seen in only 1.6-4.9% of patients[1,6-8]. These are mostly insignificant pharyngeal hemorrhage, transient arrhythmias and hypotension (the latter is due to compression of the descending aorta, or the posterior pulmonary vein in total anomalous pulmonary venous return). Airway obstruction may be seen in children between 5-10 kg[6,9]. In a 15 kg patient, airway obstruction was reported with an adult TEE probe[6]. Therefore, the appropriate choice of probe is essential. The probe should always be carefully manipulated at anteflexion. When a clear image cannot be obtained or when the probe cannot be advanced forward, it should be kept in mind that it may have kinked[6].

We observed insignificant pharyngeal hemorrhage in a few of our patients; no case had massive hemorrhage. The anesthesiologists helped with the intubation of two cases in which there was resistance to the probe while advancing through the cricopharynx. In another case, inability to advance the probe was due to the kinking of the tip of the transducer at the level of the hypopharynx. When the procedure was repeated after the probe with appropriate position, it was successfully advanced to the esophagus. We did not observe arrhythmia, hypotension, or airway obstruction in any of the cases.

Although we did not encounter any difficulty in interpreting the images of basal short axis or four-chamber views, we did encounter some difficulty at first in interpreting the caval-interatrial septal image of the long-axis view. This was easily overcome, however, after working on a few cases.

The size of the applied probe is very important to obtain a better image[7,10,11]. A pediatric probe should be used for all children under 15 kg, whereas the adult probe is used for ones over 20 kg. The probe selection is done individually for the patients between 15-20 kg with regard to the uniqueness of the patient and the experience of the performing echocardiographer. When a small-diameter probe is used in children over 20 kg, the image quality may not be optimal due to the trapped air between the probe and the esophagus. We observed similar problems in four of our cases in whom we used pediatric probes.

Transesophageal echocardiography (TEE) is considered a more valuable and sensitive tool for demonstrating the vegetations in infective endocarditis when compared to TTE[1,6,12,13]. It was performed in seven patients with congenital heart disease and infective endocarditis in whom the TTE did not produce clear-cut images. Vegetations were observed with TEE in only two of these patients.

This procedure is also preferred for evaluating prosthetic valves and partial anomalous venous return. We performed TEE in three cases with prosthetic mitral valve and in one case with partial anomalous pulmonary venous return. TEE revealed no dysfunction of prosthetic valves and thrombus was not observed. The anomalous return of the upper right pulmonary vein to the SVC was confirmed with TEE.

The transesophageal echocardiography (TEE) may be used for guiding invasive procedures like ASD or VSD closure, as in our study[14]. We used TEE in selection of patients for transcatheter closure and during and after the procedure itself. In seven of our patients, who were accepted as suitable candidates for transcatheter closure, the procedure was not performed since the inflated balloon size of the ASD diameter was > 25 mm. Echocardiographic and angiographic measurements of the inflated balloon diameter were similar. The TEE immediately after and the TEE on the following day revealed no complications.

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# Overdiagnosis of pneumonia in children

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The aim of this study was to reevaluate patients diagnosed as pneumonia in our outpatient clinic in an effort to determine whether these patients really had pneumonia and needed antibiotic therapy. Over a 14-month period, 119 children who were diagnosed as pneumonia were prospectively evaluated. In order to find a relationship, specificity and sensitivity were defined. The diagnosis of pneumonia was ruled out in 48 of the 119 (40%) patient included. An incorrect diagnosis of pneumonia was made in 40% of cases and antibiotics were prescribed unnecessarily in 85%. Tachypnea, which had a specificity of 99% and sensitivity of 61%, was the most important criteria in diagnosing pneumonia. We believe that children who present with cough only do not always need antibiotic treatment. Tachypnea and auscultation findings are important criteria for diagnosing and treating pneumonia.

*Key words: overdiagnosis, pneumonia.*

Acute lower respiratory tract infections (RTIs) cause considerable morbidity and mortality in children[1]. In less developed countries, the mortality of these infections is 50 to 100 times greater, and every year more than 4,000,000 children under five years old die because of pneumonia[2,3].

The evaluation of an acutely ill child in whom pneumonia is a possibility is difficult. A major problem is the absence of a definitive "gold standard" for the diagnosis. Blood cultures are positive in only a small percentage of patients (10-20%), and in 30-40% of hospitalized patients[4]. Invasive techniques such as bronchoalveolar lavage, lung puncture and open lung biopsy are only applicable to a small group of patients. Therefore, determination of the precise etiology of pneumonia is very complicated in children. Furthermore, it is still not known which clinical or laboratory findings in lower RTIs can lead to the diagnosis of pneumonia and predict the need for antibiotics.

The aim of this study was to reevaluate patients diagnosed as pneumonia in our outpatient clinic in an effort to determine whether these patients really had pneumonia and needed antibiotic therapy.

## Material and Methods

Over a 14-month period, 126 children who were diagnosed as pneumonia and were prescribed antibiotics in the outpatient department of Hacettepe University İhsan Doğramacı Children's Hospital were prospectively evaluated at the Pediatric Chest Disease Department. Patients had no history of recurrent bronchopneumonia or immune deficiency. Seven patients who were excluded, failed to come to the hospital regularly for visits, so only 119 patients were included in the study.

Every patient was physically examined initially. Tachypnea was defined as respiratory rate ≥ 50/minute in infants between one and 11 months of age, ≥ 40/minute in infants between one and four years of age, and ≥ 30/minute in children aged five years and more[5]. Crackles, bronchial breath sounds or diminished breath sounds led to the diagnosis of pneumonia. Chest radiograph studies and complete blood cell counts were performed in every patient. Throat cultures were taken in all but 18 patients.

After being evaluated based on clinical findings, chest radiographs and complete blood cell counts, new treatment plans were made. No serologic or microbiological study was performed to determine the infectious agent.

Patients were examined in the Pediatric Chest Disease Unit every day for the first three days, and then in intervals depending on the patients' condition, at least in every 10 days, until the symptoms subsided.

After the evaluation and treatment of the patients were completed, a radiologist independently reviewed the radiographs without knowledge of any patient's clinical history, therapy plan or prognosis.

In order to find a relationship between antibiotic therapy and pulmonary symptoms, chest radiographs, complete blood cell counts, and specificity and sensitivity were defined in the standard manner (Table I)[6,7].

Table I. Definitions Used to Evaluate Diagnostic Tests

$$\text{Sensitivity} = \frac{\text{True positives}}{\text{True positives} + \text{False negatives}}$$

$$\text{Specificity} = \frac{\text{True negatives}}{\text{True negatives} + \text{False positives}}$$

## Results

Among 119 children analyzed, 74 were male (62.2%) and 45 were female (37.8%). Most patients (41.3%) were between two and five years old. Two patients (1.7%) were less than two months, 31 (26%) were between two and 12 months, and 37 (31%) were more than five years old.

The most common presenting symptoms were cough (94%), nasal discharge (79%), fever (70%) and wheezing (50%). Those symptoms were present both in patients with and without infiltration in their radiographs. Chest pain was absent among patients with normal radiographs but present in 7% of patients with infiltration. Of patients with infiltration, 19.3% had respiratory distress, which was described as difficulty in breathing, whereas only 2% of patients with no infiltration had this complaint. A comparison of presenting symptoms with chest radiographs is seen in Table II. Five patients with chest pain and seven patients with respiratory distress were treated with antibiotics.

Time between initiation of symptoms and admission was 8.5 days in patients with normal chest radiograms, 6 days in patients with infiltration who were not treated with antibiotics, and 3.7 days in patients who were given antibiotic therapy.

Table II. Presenting Symptoms

| Symptom | Number of patients with normal radiograph (%) | Number of patients with infiltration in radiograph (%) |
|---|---|---|
| Fever | 30 (62) | 53 (74.6) |
| Cough | 47 (98) | 65 (91.5) |
| Wheezing | 24 (50) | 35 (49.2) |
| Nasal discharge | 41 (84) | 53 (74.6) |
| Sore throat | 7 (14.5) | 5 (7) |
| Chest pain | – | 5 (7) |
| Respiratory distress | 1 (2) | 13 (19.3) |
| Vomiting | 3 (6.2) | 6 (8.4) |
| Sputum expectoration | 3 (6.2) | 6 (8.4) |
| Convulsion | 1 (2) | 1 (1.4) |
| Same history in family | 19 (40) | 24 (33.8) |

The physical examination findings of patients in relation with chest radiographs and treatment are shown in Table III. History of fever was absent in 36 patients (30%). Tachypnea was not detected in five patients with a history of respiratory distress. None of the patients with tachypnea had normal radiographs; 11 of them were treated with antibiotics and one had no antibiotics.

Table III. Physical Examination Findings

| Findings | A n: 48 | B n: 53 | C n: 18 |
|---|---|---|---|
| Fever: 36.5-36.9 °C | 29 | 27 | 5 |
| Fever: 37-37.4 °C | 11 | 13 | 1 |
| Fever: 37.5-38.5 °C | 5 | 8 | 8 |
| Fever: 38.6 °C and more | 3 | 5 | 4 |
| Tachypnea | – | 1 | 11 |
| Dyspnea | – | – | 6 |
| Abnormal auscultation findings* | – | 6 | 15 |

A : Patients with normal radiograph.

B : Patients with infiltration on radiograph treated without antibiotics.

C : Patients with infiltration on radiograph treated with antibiotics.

*: Crackles, bronchial breath sounds, localized diminished breath sound.

With auscultation, lung sounds were normal in 52 patients. One patient with normal breath sounds had tachypnea with infiltration at the right upper segment and was treated with antibiotics. Chest radiograph findings and antibiotic treatment according to auscultation findings are shown in Table IV.

When chest radiographs were taken into consideration, it was determined that 48 (40%) patients with normal chest radiographs were not

treated with antibiotics; auscultation findings were normal in 28 of them. Fifty-two patients (44%) with peribronchial infiltration, linear atelectasis and interstitial infiltration were also not treated with antibiotics except for a patient who had fever, tachypnea and respiratory distress whose radiographs revealed consolidation on the 8th day of follow-up. The remaining 19 patients (16%) had consolidation and pleural reaction in radiographs and 17 of them were treated with antibiotics.

Table IV. Chest Radiograph Findings and Antibiotics Treatment According to Auscultation Findings

| Findings | n | A | B | C | Antibiotic treatment |
|---|---|---|---|---|---|
| Normal | 52 | 28 | 23 | 1 | 1 |
| Course crackles | 42 | 20 | 19 | 3 | 2 |
| Fine crackles | 12 | – | 3 | 9 | 9 |
| Bronchial sounds | 4 | – | – | 4 | 4 |
| Diminished sounds | 5 | – | 3 | 2 | 2 |
| Prolonged expirium | 4 | – | 4 | – | – |
| Total | 119 | 48 | 52 | 19 | |
| Antibiotic treatment | | – | 1 | 17 | 18 |

A : Patients with normal radiograph.

B : Patients with peribronchial thickening, infiltration, linear atelectasis, and interstitial infiltration in radiographs.

C : Patients with consolidation, segmentary infiltration and pleural reaction in radiographs.

Leukocyte count was below 10,000/mm$^3$ in 66 (56%), between 10,000/mm$^3$ and 14,999/mm$^3$ in 32 (27%), between 15,000/mm$^3$ and 19,999/mm$^3$ in 10 (8%) and more than 20,000/mm$^3$ in 11 patients. Among 66 patients who had less than 10,000/mm$^3$ leukocytes, only five were treated with antibiotics, whereas nine out of 21 patients with more than 15,000/mm$^3$ leukocytes were prescribed antibiotics. There were 12 patients with more than 80% polymorphonuclear leukocytes, and eight of them had antibiotic therapy. Only one patient with more than 60% lymphocytes was treated with antibiotics.

Throat cultures revealed beta hemolytic streptococcus in two patients and they were treated with penicillins, and staphylococcus coagulase negative was present in two other patients. The remaining cultures yielded normal pharyngeal flora.

Table V summarizes the antibiotics prescribed in the outpatient clinics and the patients' compliance with the drug treatment. After being reevaluated in our department, 18 of 119 patients decided to continue their recommended therapies for seven days.

Table V. Antibiotics Prescribed in Outpatient Clinic

| Prescribed antibiotic in outpatient clinic | Number of patients | A | B | C | D |
|---|---|---|---|---|---|
| Procaine penicillin | 103 | 40 | 52 | 8 | 3 |
| Cotrimoxazole | 7 | 5 | 1 | 1 | – |
| Amoxicillin | 4 | 2 | 2 | – | – |
| Sulbactam-ampicillin | 5 | 5 | – | – | – |
| Patients whose antibiotics were continued | 18 | 5 | 10 | 1 | 2 |

A : Patients who did not use the prescribed antibiotic.
B : Patients who used the prescribed antibiotic for 1 day.
C : Patients who used the prescribed antibiotic for 2 days.
D : Patients who used the prescribed antibiotic for 3 days.

As a result, the diagnosis of pneumonia was ruled out in 48 (40%) of 119 patients who had normal chest X-rays, no tachypnea, no dyspnea and normal auscultation findings or only coarse crackles, as can be seen in Tables III and IV. Although only 18 patients (15%) were treated with antibiotics, every patient included in the study recovered. There was an overdiagnosis of pneumonia in 40% of patients and unnecessary use of antibiotics in 85%.

Sensitivity and specificity for defining correlations between antibiotic therapy and symptoms, radiographs, leukocytes and peripheral blood cell count are shown in Table VI.

Table VI. Sensitivity and Specificity

| Findings | Sensitivity | Specificity |
|---|---|---|
| Tachypnea | .61 | .99 |
| Auscultation findings | .83 | .94 |
| Chest radiographs* | .94 | .98 |
| Leukocytes < 15,000/mm$^3$ | .50 | .88 |
| Leukocytes < 20,000/mm$^3$ | .22 | .93 |
| Polymorphonuclear leukocytes | .44 | .96 |

* Segmentary infiltration, consolidation, pleural reaction.

## Discussion

Respiratory tract infections are one of the most common diseases worldwide. According to one study from the United States, children aged less than two years old had acute RTIs six times a year[8].

It is known that upper and lower RTI symptoms may mimic each other. Moreover, there is always a risk for addition of a bacterial infection to a viral infection. As a result, there have always been difficulties in treating this disease. In our country, there is a tendency to prescribe antibiotics to patients with upper RTIs. However, it should be kept in mind that viral pathogens are the most commonly encountered microorganisms responsible for lower RTIs in children less than

four years old, except in the neonatal period[8,9]. In a study from our department, it was shown that viruses, especially respiratory syncytial virus (RSV), were the most common causes of lower RTIs in children[9].

There are numerous reports about diagnosing pneumonia with symptoms as well as with clinical and radiological findings[6,8,9,11,12]. The diagnostic symptoms of pneumonia are cough, sputum expectoration, tachypnea, dyspnea, cyanosis, retractions, chest pain, and clinical findings like crackles and sometimes bronchial sounds. In our study, cough, fever, nasal discharge and wheezing were the most common symptoms both in patients with and without pneumonia diagnosed clinically and radiologically. These were not enough for discrimination of upper and lower RTIs, but the presence of chest pain and respiratory distress only in patients with pneumonia was noticable.

There has always been disagreement in the published literature about the relationship between fever and the etiologic agent. Some authors believe that the reliability of high fever in diagnosing bacterial infection is low[13-15]. It has been shown that even fever of more than 40 °C is not a factor for identifying viral and bacterial pneumonia[12]. In our study, 38% of patients with fever between 37.5-38.5 °C, and 33% of patients with fever of more than 38.6 °C were treated with antibiotics. Three patients with fever of more than 38.6 °C were not diagnosed to have pneumonia and were not given antibiotic therapy. As fever is a symptom of both upper and lower RTIs, we believe that patients who have only fever should not be treated with antibiotics unless there are other symptoms and findings indicating pneumonia; presence of fever alone should not indicate lower RTI. High fever is not a safe criteria for identifying viral or bacterial infection; only four patients with a fever of 38.6 °C needed antibiotic therapy. Our results showed that clinical remission was achieved only with supportive therapy in 101 patients, although most of them had fever by history or physical examination.

Tachypnea and respiratory distress are considered to be safe criteria for pneumonia by the World Health Organization[1,16]. In different studies, the sensitivity and specificity of tachypnea were found to be very high[1,17]. In our study, tachypnea was a very important criterion for diagnosing pneumonia, with a sensitivity of 61% and specifitiy of 99%. Our findings suggest that the respiratory rate can be used to decide which patients with cough should be treated with antibiotics.

Crackles are the main auscultation findings of pneumonia; however, bronchial and tubular sounds are also possible. In our study, the sensitivity and specificity of auscultation findings for antibiotic therapy was very high, in accordance with the published studies[6]. There were auscultation findings including crackles, bronchial breath sounds and localized diminished breath sounds in 15 patients out of 18 who were prescribed antibiotics.

Although radiological findings are not always helpful in differentiating viral from bacterial pneumonia, consolidation located in one lobe, pleural effusion and abscess are indicators of bacterial pneumonia, whereas perihilary infiltations in more than one lobe generally indicate viral infection[18]. In our study, 51 patients with perihilary and peribronchial infiltration, overexpansion, atelectasis and interstitial infiltration were not given antibiotics, and clinical and radiological remission were achieved in all of them. Radiological findings like segmentary infiltration, consolidation and pleural reaction were found to be the most sensitive and specific criteria for starting antibiotic therapy, and 17 patients with those findings were prescribed antibiotics.

There are published reports about the relationship between clinical and radiological findings which point out normal chest radiographs in infants without respiratory distress, and suggest that there is even no need for chest radiographs in such patients[19,20]. Our results support these findings, as only one of 52 patients with normal auscultation findings and only two patients without respiratory distress were given antibiotics.

In our study, 7.5% of patients with less than 10,000/mm$^3$ leukocytes were given antibiotics, whereas 54.5% of patients with more than 20,000/mm$^3$ leukocytes had antibiotics. Our findings are in accordance with another study, which showed that patients with pneumonia who had a leukocyte count of more than 15,000/mm$^3$ recovered earlier with antibiotics when compared to others with a leukocyte count less than 10,000/mm$^3$.[21].

In our study, we accepted that antibiotics taken by patients when they were first diagnosed in the outpatient clinic did not improve their clinical findings, because procaine penicillin and oral antibiotics were not expected to have reached therapeutic blood levels in just a few days. In any case, 52 patients were recruited for the study before taking their prescribed drugs, and 47 of them improved without antibiotics.

In conclusion, we found that overdiagnosis of pneumonia and unnecessary antibiotic use are very common. We believe that children who present with cough alone do not always need antibiotic treatment. High fever is also not a good indicator of pneumonia. However, tachypnea and auscultation findings are important criteria for diagnosing and treating pneumonia. Therefore, we suggest that only patients who present with cough and fever, and who have tachypnea and positive auscultation findings together with segmentary infiltration and consolidation in their chest radiographs should be treated with antibiotics.

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# Screening for tuberculosis in a primary school in Ankara

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**Tuberculosis is still an important health problem in developing countries. A screening program was conducted upon learning that one of the teachers of a primary school in Ankara was diagnosed to have active pulmonary tuberculosis. A total of 341 students in the same building with the index case were screened for tuberculosis. There were 109 students with positive tuberculin test reaction. A higher ratio of tuberculin test positivity among the students of the teacher with active tuberculosis versus students vaccinated with BCG one year previously according to the routine vaccination program was determined. Isoniazid prophylaxis was given to the students with positive tuberculin test. The study shows the importance of an urgent work-up of index cases and their environment to prevent the spread of tuberculosis.**

*Key word: tuberculosis screening, children, close contacts, school, tuberculosis prophylaxis.*

Tuberculosis is still an important health problem, especially in developing countries. In Turkey, the incidence of tuberculosis was reported as 30.3/100,000 in 1998[1]. In some developed countries, incidence of it has started to rise, making tuberculosis a problem once again. In the United States, the incidence of tuberculosis was 9.3/100,000 in 1985, but started to rise the in 1986. This increase in tuberculosis incidence can be attributed to several factors, including the human immune deficiency virus epidemic, the immigration of large numbers of persons from countries in which tuberculosis is highly prevalent, the rise of multidrug-resistant mycobacterial organisms and the decline of tuberculosis control programs[2].

Rapid diagnosis and medical intervention is essential to prevent the spread of tuberculosis. Although the diagnostic value of tuberculin skin test in cases of malnutrition, tuberculous meningitis, miliary tuberculosis and immunosuppression is controversial, it is an easy, widely available and inexpensive method for detecting Mycobacterium tuberculosis infection, which is very important for the screening programs[3].

According to the recently updated recommendations of the Centers for Disease Control and Prevention (USA), tuberculin testing should be performed in persons belonging to risk groups, one of which includes close contacts (i.e. those sharing the same household or other enclosed environments) of persons known or suspected to have tuberculosis[2,4].

This study was conducted based on the information that one of the teachers of a primary school in Ankara was diagnosed to have active pulmonary tuberculosis. The aim of this study was to screen all the students in the school for tuberculosis who were suspected to be exposed to the index case.

## Material and Methods

The index case with active pulmonary tuberculosis was the teacher of one of the first phase classes in a primary school. She was diagnosed to have active pulmonary tuberculosis by positive findings in chest X-ray and microbiologic investigations for tuberculosis. Microbiologic tests included identification of acid resistant bacillus (ARB) in sputum by acid fast stain, growth in sputum culture with the BACTEC TB system and positive polymerase chain reaction (PCR) assay for Mycobacterium tuberculosis. She had treatment for tuberculosis for nine months. After two months of treatment, ARB in sputum and culture for tuberculosis were negative. There were 32 students in the teacher's class. This

teacher was working in one of the buildings of the school with 10 classrooms, five of them to first phase and the other five to second phase. In these classrooms, there were 361 children in total. All children suspected to be exposed to the index case during breaks, in the facilities or during lunch-time in the common restaurant were included in the study. There was no air conditioning system in the school.

The children, parents and the teachers obtained oral and written information about the screening, and parents provided written informed consent for their child to participate. Parents were asked to complete a questionnaire about symptoms of their child including cough, night sweats and fever.

The children in the second phase classes were vaccinated with BCG one year previously according to the routine vaccination program in Turkey. But the children in the first phase classes had not yet been vaccinated at the time of study.

Seven children were not allowed to participate by their parents, eight were absent when the test was administered and five were absent when skin test reaction was measured. These 20 children were excluded from the study and a total of 341 were tested, including 174 children from first phase classes and 167 children from second phase classes.

All children were examined by four pediatricians, and the number of BCG scars on the left shoulders of the children were determined. A 5 tuberculin unit dose (0.1 ml) of PPD (Tuberculin Purified Protein Derivative, Biolek, Ukraine Kharkiv) was administered by two experienced persons on the middle 1/3 of the volar surface of the left arm. The same pediatricians measured the indurations after 72 hours using the ball-point pen method[5].

A transverse diameter induration of 10 mm or more in children with no BCG scars and of 15 mm or more in children with one or more BCG scars was reported to be positive[6]. The children with a positive tuberculin test reaction were invited to the hospital, and detailed physical re-examinations and chest X-rays were performed.

## Results

A total of 341 children (aged 1-9 years) were screened in the study. There were 203 boys and 138 girls.

Thirty-one of 174 children (17.8%) in first phase classes and 78 of 167 children (46.7%) in second phase classes, in a total 109 children, were found to have a positive tuberculin test (Table I).

Table I. Tuberculin Test Results According to First and Second Phase Classes

| | Tuberculin test result | | | | | |
|---|---|---|---|---|---|---|
| | Positive | | Negative | | Total | |
| Phase | No | % | No | % | No | % |
| 1 | 31 | 17.8 | 143 | 82.2 | 174 | 100 |
| 2 | 78 | 46.7 | 89 | 53.3 | 167 | 100 |
| Total | 109 | 31.9 | 232 | 68.1 | 341 | 100 |

Out of 32 children in the class of the teacher with active tuberculosis, 11 (34.4%) had a positive tuberculin test reaction. The ratio of tuberculin test positivity was higher in this class in comparison to the other first phase classes and the difference was statistically significant ($p < 0.05$) (Table II).

Table II. Tuberculin Test Results in First Phase Classes

| | Tuberculin test result | | | | | |
|---|---|---|---|---|---|---|
| | Positive | | Negative | | Total | |
| First phase classes | No | % | No | % | No | % |
| 1 | 2 | 5.7 | 33 | 94.3 | 35 | 100 |
| 2 | 7 | 17.5 | 33 | 82.5 | 40 | 100 |
| 3 | 8 | 24.2 | 25 | 75.8 | 33 | 100 |
| 4 | 3 | 8.8 | 31 | 91.2 | 34 | 100 |
| 5 (Teacher's Class) | 11 | 34.4 | 21 | 65.6 | 32 | 100 |
| Total | 31 | 17.8 | 143 | 82.2 | 174 | 100 |

The first phase and second phase students were compared in terms of tuberculin test positivity, excluding the students in the class of the teacher with active tuberculosis. The ratio of tuberculin test positivity was higher among the second phase students and the difference was statistically significant ($p < 0.05$) (Table I).

The eight of children with no BCG scar all had negative tuberculin test results. There were 249 children with one BCG scars and 80 children with two scars. The number of children in these groups with a positive skin test was 78 (31.3%) and 31 (38.7%), respectively. All four children with three scars also had negative skin test (Table III).

The physical examination and chest X-ray of children with positive test results revealed no evidence of active tuberculosis.

Parents of all children with a positive tuberculin reaction were invited to meetings organized to

inform them about skin test results and the necessity of isoniazid chemoprophylaxis (5 mg/kg/day) for the tuberculosis, to increase the compliance. Two pediatricians were present in these meetings and they answered any questions. The parents of 70 children accepted the treatment and received their prescription.

Table III. Tuberculin Test Results According to the Number of BCG Scars

| Number of BCG Scars | Tuberculin test result: Positive No | Positive % | Negative No | Negative % | Total No | Total % |
|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 8 | 100 | 8 | 100 |
| 1 | 78 | 31.3 | 171 | 68.7 | 249 | 100 |
| 2 | 31 | 38.7 | 49 | 61.3 | 80 | 100 |
| 3 | 0 | 0 | 4 | 100 | 4 | 100 |
| Total | 109 | 31.9 | 232 | 68.1 | 341 | 100 |

The children were followed for six months. During follow-up only one child had a 3-fold increase of transaminases at the end of the 5th month. The child was asymptomatic and transaminase levels returned to normal after discontinuation of the drug for two weeks.

## Discussion

Screening for tuberculosis is very important to prevent the spread of the disease in countries where it is prevalent.

The American Thoracic Society and Centers for Disease Control and Prevention recently issued recommendations for tuberculin testing[4,7]. In this study, the children screened for tuberculosis were in one of the risk groups according to these recommendations, which included close contacts of a known tuberculosis case in an enclosed environment. The teacher in our study with active tuberculosis was working in one of the buildings of the school containing 10 classrooms. The students in this building used the same garden, toilets, restaurant and other facility areas. All children were suspected to be exposed to active tuberculosis and were screened for the disease.

The comparison of the teacher's class with other first phase classes which had the same circumstances in terms of recent BCG vaccination revealed a higher ratio of tuberculin test positivity in the teacher's class. This result signifies a higher risk of exposure among the students sharing the same classroom with the index case. This information may be helpful for subsequent screening programs in definition of "close contacts" in such places like schools where the index case can have a large number of contacts with different degrees of exposure. In our study, because the teacher possibly had contact with other students in particular situations and because students in her class had contact with other students, it was decided to screen all the students in the building and give prophylaxis to tuberculin positive cases.

Both specificity and sensitivity of the tuberculin test are variable. On avarage, 10-25% of patients with active tuberculosis do not react to tuberculin. False negativity may be as high as 50% in patients critically ill with disseminated tuberculosis. Effective use of tuberculin testing requires an understanding of characteristics that are inherent in the test itself and of the extrinsic to the test that influence the interpretation of test results. The latter characteristics have to do with the likelihood of tuberculosis in the person or population being tested. The utility of the tuberculin skin test depends on the prevalence of cross reactions with nontuberculous bacteria. In populations with cross-reactions, the tuberculin skin test may be assumed to have a specificity of almost 99%[8].

In spite of its variable specificity and sensitivity, the tuberculin skin test is the only method for detecting Mycobacterium tuberculosis infection[8] and it is easily available and inexpensive, very important features making it widely used in screening programs.

Bacillus Calmette Guerin vaccination also influences tuberculin skin test interpretation. Especially in countries where more than one BCG vaccine is recommended, revaccination can considerably alter the tuberculin skin test response and the diagnosis of tuberculosis[9,10].

Our screening program revealed a skin test positivity of 46.7% among the children in the second phase classes, whereas it was 17.8% in the first phase classes. The second phase students received their last BCG vaccine one year previously according to the routine vaccination program in Turkey. This was also taken into consideration in the interpretation of results.

For persons who have recently had close contact with a case of active tuberculosis, skin test reactions are likely to represent infection with M. Tuberculosis. Thus, although the higher

percentage of skin test positivity in second phase students versus first phase students can be attributable to the recent BCG vaccination, it was not possible to rule out the possibility of test positivity due to exposure to the active case. As a result, all children with a positive tuberculin skin test were given isoniazid chemoprophylaxis.

Any index case of tuberculosis causes a significant problem in such places where the number of contacts is a large and vulnerable. Screening such a large number of contacts consumes time and money. Periodic screening of people dealing with susceptible groups, especially children, is more practical.

The result of this study was reported to the local health authority, local goverment of the city and to the Ministry of Health to attract their attention to tuberculosis control programs, especially in schools, dormitories, day-care centers and military services.

This study is important in the sense that it constitutes an example and reminder as to how fastidiously we must work on index cases and their environment to prevent the spread of tuberculosis.

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# Serum lipid peroxidation levels in small-for-gestational-age babies

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The levels of lipid peroxidation in sera of asymmetric small-for-gestational-age (SGA) babies at the second hour of life were investigated. Lipid peroxidation levels, measured as malondialdehyde (MDA), were 3.3 ± 1.1 and 3.9 ± 1.2 mmol/L in SGA and appropriate-for-gestational age (AGA) groups, respectively. The difference was not significant ($p>0.05$). This result may indicate that free radical scavengers are sufficient in SGA babies.

*Key words: lipid peroxidation, Malondialdehyde, SGA, IUGR.*

Fetal growth is affected by fetal growth potential during the first half of the pregnancy and by maternal environment and uteroplacental functions during the second half[1]. Various criteria are used in defining small-for-gestational-age (SGA) babies. SGA may be defined as birth weight below the 10th percentile for gestational age or more than two standard deviations below the mean for gestational age[2]. The ponderal index can be used to identify infants whose soft tissue mass is below normal for the stage of skeletal development. Thus, a ponderal index below the 10th percentile may be used to identify SGA infants[3,4]. The ponderal index is not affected by gestational age, race or sex, and is thus preferred to define SGA. In 20% of babies with SGA, fetal growth is affected at the very beginning of gestation (symmetric SGA). In babies with asymmetric SGA, especially during the third trimester of gestation, maternal complications such as preeclampsia, chronic hypertension, diabetes mellitus, chronic cardiac and renal diseases and factors related to the placenta and uterus disturb the uteroplacental blood flow. In 50% of babies with asymmetric SGA, the hypoxia risk is increased due to the impaired uteroplacental blood flow[5].

Free oxygen radicals that increase during the reperfusion phase after hypoxia in perinatal asphyxia are thought to be responsible for the organ damage[6]. Free radicals cause cell membrane injury by lipid peroxidation, and the aldehyde products cause intracellular and extracellular harm. Malondialdehyde (MDA), an aldehyde that appears during lipid peroxidation, is an indirect indicator of lipid peroxidation[7].

In this study, MDA levels, an indicator of lipid peroxidation, are searched in the sera of the babies with asymmetric SGA who were thought to have intrauterine chronic hypoxia and fetal malnutrition.

## Material and Methods

*Patients*: Term babies of 38 weeks' or more than 38 weeks gestation according to the Dubowitz score[8], with no history of drug usage, illness, syndrome, chromosomal abnormality or intrauterine infection were selected for the study. All of the babies had arterial oxygen saturation of more than 95% and normal blood glucose concentration. In the determination of the babies with SGA the ponderal index (PI) = (body weight/length$^3$) x 100 was used; babies having PI under 10% were considered as asymmetric SGA[3,4].

The study was approved by the Medical Ethics Committee of Pamukkale University Hospital.

*Collection and preparation of samples*: The sera of the venous blood samples which were taken at the second hour after birth were separated and were stored at -70 °C for biochemical studies.

*Determination of TBARS*: In this study we used the thiobarbituric acid method for determination of lipid peroxidation. Although the thiobarbituric acid assay is not specific for MDA, measurement

of TBARS is an easy and reliable method which is used as an indicator of lipid peroxidation and free radical activity in biological samples. Lipid peroxidation in sera were determined using the method of Uchiyama and Mihara[9]. Tetramethoxypropane was used as the standard and the level of TBARS was calculated as micromoles of MDA per liter.

*Statistics*: Values are expressed mean ± SD. The Student's t test was used for statistical analysis. A $p < 0.05$ value was considered to represent a significant difference between the compared values.

## Results

Malondialdehyde (MDA) levels as mean ± SD of 32 term SGA babies in the study group and in 19 term appropriate-for-gestational age (AGA) babies in the control group were 3.3 ± 1.1 and 3.9 ± 1.2 mmol/L, respectively. No maternal illness or special diet during pregnancy was found in the obstetrical charts or reported by the mothers. There was no statistically significant difference between the mean values of the two groups ($p > 0.05$). As Table I shows, there were no statistically significant differences between gestational age, sex, Apgar score, length or head circumference.

Table I. Perinatal data of SGA and control groups (median ± SD)

| | SGA | Control |
|---|---|---|
| n | 32 | 19 |
| Male | 17 | 10 |
| Female | 15 | 9 |
| Gestational age (weeks) | 39.7 ± 0.9 | 39.7 ± 0.9 |
| Birth weight (g) | 2350 ± 212 | 3326 ± 291 |
| Length (cm) | 48.2 ± 1.4 | 49.8 ± 1.3 |
| Head circumference (cm) | 34.1 ± 0.9 | 34.9 ± 0.8 |
| Apgar score (5 min) | | |
| Median | 9 | 10 |
| Range | (7-10) | (7-10) |

There were no statistically significant differences between the groups.

SGA: small-for-gestational-age.

## Discussion

In 20% of babies with SGA, fetal growth is likely to be affected from the early stages of gestation (rapid cell proliferation stage); a proportional retardation is seen in weight, length and head circumference, and the PI is found normal[5]. In the etiology of this group, termed symmetric, chromosomal abnormalities, dysmorphic syndromes, congenital metabolic diseases, drug usage and intrauterine infections can be present[1].

Since a fetus gains 85% of its body weight during the second half of pregnancy, any impairment of uteroplacental blood flow during this period will definitely disturb food and oxygen transfer to the baby[5]. Also, in a fetus undergoing chronic hypoxia, protein/amino acid metabolism fails and the fetal weight decreases[10]. Although the length and head circumference are protected, because of the inadequate weight gain, these babies are termed asymmetric SGA, and their ponderal indexes are found lower. In 50% of asymmetric SGA babies, the intrauterine chronic hypoxia risk has increased because of their impaired uteroplacental blood flow[5].

Free oxygen radicals are known to be involved in cellular damage. They contribute to various organ injury at the stages of initiation and/or progression. Organ dysfunction induced by free radicals may be a major component of hypoxic ischemic disease of the heart, intestines, liver, kidney and brain.

Free oxygen radicals appear at mitochondrias when oxygen is not completely saturated with cytochrome oxidase enzyme during hypoxia and ischemia. Other sources are prostaglandin synthesis from arachidonic acid and xanthine and uric acid formation from hypoxanthine reactions during active phagocytosis[11]. It has been reported that free oxygen radicals are produced during the reperfusion phase following hypoxemia, and that hyperoxia increases free oxygen radical production[6]. Animal studies show that activities of antioxidant enzymes in the fetal lung and other tissues are lower than at term[12-14]. A recent study by Phylactos et al.[15] show that this is also the case for humans, at least in erythrocytes. By using a sensitive technique they demonstrated that preterm infants with gestational age between 29 and 34 weeks had only 50% activity of Cu/Zn superoxide dismutase in cord erythrocytes compared with term babies. The activity of this enzyme in erythrocytes increased toward the expected day of delivery, however, it was still lower than in term AGA babies. In newborn rabbits, short-term malnutrition caused a decrease in the enzymes (superoxide dismutase) that metabolize the free radicals in the intestine[16]. Similarly, we believe that in SGA babies with fetal malnutrition, the enzymes

inactivating free oxygen radicals might be decreased. There has been no study performed in SGA babies on this subject.

Ishimoto et al.[17] in 1997, investigated the involvement of oxygen-derived free radicals in the pathogenesis of intrauterine growth retardation (IUGR) in rats induced by ischemia of the uterine horn. The placental levels of lipid peroxidates were significantly increased and IUGR was induced. Pretreatment with superoxide dismutase and catalase inhibited the increase in placental lipid peroxidates and prevented IUGR. Results indicate that oxygen-derived free radicals may be important in the development of postischemic uteroplacental hypoperfusion and of ischemia-reperfusion induced IUGR in the rat.

We believe that in SGA babies with fetal malnutrition, the enzymes inactivating free oxygen radicals might be decreased, and that lipid peroxidates might be important for the pathogenesis of IUGR. We could find no study performed in SGA babies on this subject in the relevant literature. However, in this study we did not find a statistically significant difference in MDA levels of SGA and AGA babies at the second hour of life. Lipid peroxidates may have been decreased by free radical scavengers after birth. The role of free oxygen radicals in SGA babies has not been studied in detail. Further studies are required to determine whether oxygen-derived free radicals are involved in the pathophysiology of human IUGR.

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# Complications of the two major operations of Hirschsprung's disease: a single center experience

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This study was designed to determine and compare the results of the Duhamel and Swenson procedures. The hospital records of patients who had undergone the Swenson or Duhamel operation over a 17-year period were reviewed and the patients were contacted for a final evaluation. The early and late complications of these operations were defined and compared. It was determined that the Swenson operation had been performed in 138 patients and the Duhamel in 59. Among the various complications, such as wound infection, dehiscence, anastomotic leak, adhesive intestinal obstruction, pelvic abscess, intraabdominal abscess, mucosal prolapsus, anastomotic stricture and fistulas, only the anastomotic stricture showed significantly higher percentages in patients who had undergone the Swenson procedure. When urinary incontinence, enterocolitis, soiling and constipation were considered, there was no significant difference between these two groups. There was one death in the Swenson group and none in the Duhamel group. The authors suggest the Duhamel operation as a simpler and safer method for the treatment of Hirschsprung's disease.

*Key words: Hirschsprung's disease, Duhamel pull through, Swenson pull through, complications.*

Hirschsprung's disease was first presented by Harold Hirschsprung in 1886[1,2]. Although many operations had been suggested for the treatment of the disease, the first successful surgical approach was described by Swenson and Bill[3] in 1948. Since then several operations have been developed but there is still controversy as to the best procedure. Operations and modifications of these have been introduced with better results[4-8]. Complications and complication rates of these operations have been reported in different series[9-18]. The purpose of this study was to compare the results of the Duhamel and Swenson operations of Hirschsprung's disease through a single center experience.

## Material and Methods

One hundred and thirty-eight Swenson and 59 Duhamel operations performed in the Department of Pediatric Surgery Hacettepe University Children's Hospital over a 17-year period were retrospectively reviewed to compare the early and late complications and the final results of the two major operations of Hirschsprung's disease.

The diagnosis of Hirschsprung's disease was based on barium enema and confirmed by full-thickness rectal biopsy through the absence of ganglion cells. The patients had initially undergone a colostomy procedure. The timing of the definitive operation was based on 1) general condition of the patient, 2) distal colonographic findings, and 3) age of the patient. The Swenson operation[3,19,20] was performed in 138 patients and the Duhamel operation[5,6] in 59 patients. The Duhamel operation was initially performed using crushing clamps. Subsequently, 36 patients underwent Duhamel operation with staplers.

Patients were evaluated for the presence of 1) wound infection, 2) dehiscence 3) anastomotic leak, 4) adhesive intestinal obstruction, 5) sepsis, 6) pelvic abscess, 7) intraabdominal abscess,

8) mucosal prolapsus, 9) anastomotic stricture, 10) fistula formation, 11) incisional hernia, 12) urinary incontinence, 13) enterocolitis, 14) soiling, 15) constipation and 16) mortality. Since some patients were recorded as lost to follow-up, a questionnaire was mailed to these patients including enquiries on 1) urinary incontinence, 2) enterocolitis, 3) soiling, 4) constipation and 5) other complaints. They were requested to come for a final evaluation and, if not possible, to answer the questionnaire.

Data was analyzed using chi-square test and Fisher's exact test with Yates' continuity correction, and p values less than 0.05 were considered significant.

## Results

Eighteen female and 120 male patients had undergone Swenson operation and 12 female and 47 male patients had undergone Duhamel operation. In the Swenson group the age distribution of patients at operation was as follows: 8.8% below 15 mo, 55.5% between 16 mo-3 years, 31.4% between 4-11 years, and 4.4% above 12 years, The age distribution in the Duhamel group was 20.3% below 15 mo, 66.1% between 16 mo-3 years, 11.9% between 4-11 years, and 1.7% above 12 years.

In our series wound infection was detected in 23 patients (16.7%) who had undergone Swenson operation and in four patients (6.8%) who had undergone Duhamel operation (Table I). Dehiscence was detected in 12 patients in the Swenson group (8.7%) and in one patient in the Duhamel group (1.7%). Sepsis was encountered in seven patients (5.1%) in the Swenson group and one patient (1.7%) in the Duhamel group. While anastomotic leak was encountered in seven patients (5.1%) in the Swenson group, no leak was detected after the Duhamel operation. Adhesive intestinal obstruction was observed in 13 paitents after the Swenson operation (9.4%) and in two patients (3.3%) after the Duhamel operation. Ten patients in the Swenson group and two patients in the Duhamel group required adhesioloysis. Pelvic abscess developed in nine patients (6.5%) in the Swenson group and in one patient (1.7%) in the Duhamel group. Intraabdominal abscess was detected in four patients (2.9%) in the Swenson group and in one patient (1.7%) in the Duhamel group. Mucosal prolapsus was detected in one patient (0.7%) in the Swenson group but in none of the Duhamel group. Anastomotic stricture was one of the most common complications in the Swenson group, appearing in 29 patients (21.2%). This complication was detected in only two patients (3.4%) in the Duhamel group ($p < 0.05$). In three patients (2.2%) in the Swenson group, fistulas were detected, namely rectovaginal, ileorectal and ileorectal + perineal. No fistula was detected in the Duhamel group. Incisional hernia was detected in one patient (0.7%) in the Swenson group and in one patient (1.7%) in the Duhamel group.

Table I. Early and Late Complications of the Swenson and Duhamel Procedures

| Complication | Swenson | Duhamel |
|---|---|---|
| Wound infection | 16.7% (138/23) | 6.8% (59/4) |
| Dehiscence | 8.7% (138/12) | 1.7% (59/1) |
| Anastomotic leak | 5.1% (138/7) | – (59/0) |
| Adhesive intestinal obstruction | 9.4% (138/13) | 3.3% (59/2) |
| Pelvic abscess | 6.5% (138/9) | 1.7% (59/1) |
| Intraabdominal abscess | 2.9% (138/4) | 1.7% (59/1) |
| Mucosal prolapsus | 0.7% (138/1) | – (59/0) |
| Anastomotic stricture | 21.2% (138/29) | 3.4% (59/2) |
| Fistula | 2.2% (138/3) | – (59/0) |
| Incisional hernia | 0.7% (138/1) | 1.7% (59/1) |
| Urinary incontinence | 1.4% (74/1) | 11.4% (35/4) |
| Enterocolitis | 26.1% (88/23) | 20.8% (48/10) |
| Soiling | 35.2% (71/25) | 18.9% (37.7) |
| Constipation | 1.2% (84/1) | 2.6% (39/1) |
| Death | 0.7% (138/1) | – (59/0) |

• The numbers in parenthesis denote (total number/evaluated).

Late complications were evaluated through follow-ups taken from charts, and patients lost to follow-up were called back for an evaluation. Twenty-eight patients in the Swenson group and 20 patients in the Duhamel group either responded to a questionnaire or came for a control visit. This data was combined with the data obtained from hospital charts to evaluate the late complications. Urinary incontinence (enuresis nocturna) was the complaint of one patient in the Swenson group (1.4%) and of four (11.4%) in the Duhamel group. One patient in the Swenson group and one patient in the Duhamel group had periodic micturition problems. Enterocolitis was detected in 23 patients (26.1%) in the Swenson group and in 10 patients (20.8%) in the Duhamel group. Soiling was the complaint of 25 patients (35.2%) in the Swenson group and of seven patients (18.9%) in the Duhamel group initially. But soiling was permanent in only 12 patients in the

Swenson group and in one patient in the Duhamel group. Even in this group toilet training and loperamide treatment were beneficial. Constipation was detected in one patient (1.2%) in the Swenson group and in one (2.6%) in the Duhamel group. There was only one death in our series, after the Swenson operation, which was due to pelvic abscess and sepsis.

## Discussion

In a multicentric study of the Duhamel operation, in 2.2% of cases anastomotic leak was reported following the procedure[8]. No anastomotic leak occurred after the Duhamel operation in our series. In the survey of the Surgical Section of the American Academy of Pediatrics (SSAAP), occurrence of anastomotic disruption was investigated and was 11.2% after the Swenson operation and 2.4% after the Duhamel operation[12]. In a multinational retrospective study of the Swenson operation, anastomotic leak was detected in 5.6% of Swenson procedures, which is in concordance with our results. Anastomotic stricture was reported to be higher in the Swenson operation (13%) than in the Duhamel operation (2%)[13]. In a multicentric study of the Duhamel operation, anastomotic stricture was detected in 0.7% of cases[8]. In our series anastomotic stricture occurred more frequently after the Swenson operation. The results of other series support this.

Micturition disturbances were reported in 4% and 12% of cases in the Duhamel and Swenson operations, respectively[13]. The incidence of urinary incontinence appeared to be high in the Duhamel group, but the ages of three patients in this group were below four, and the problem resolved during follow-ups in this group. Swenson reported soiling occurrence as 3.2% in his series[17]. We oserved that soiling may be present in higher percentages soon after the operation but that it subsides with time and conservative treatment even in school-aged children. Satisfactory results may be obtained with loperamide treatment and toilet training in some patients.

In the SSAAP survery, enterocolitis appeared in 5.9% and 15.6% of the patients after the Swenson and Duhamel procedures, respectively[12]. Enterocolitis was detected in 33.7% and 13.9% of the patients who had undergone Swenson and Duhamel operations, respectively, in another series from Japan[11]. In the present study enterocolitis appeared to be a major problem in the treatment of Hirschsprung's disease as well. Moore et al.[13] reported constipation as a major complication of the Duhamel operation. They reported constipation in 26% of cases after the Duhamel operation and in 17% after the Swenson operation. Another series revealed a constipation rate of 8.1% after the Duhamel operation[8]. We detected lower percentages than reported in these series.

Grosfeld et al.[10] reported no operative mortality after the Duhamel operation. Sherman et al.[16] reported a 1.3% mortality between 1979-1989 with the Swenson operation. In the survey of the members of the SSAAP, overall mortality rates of 2.5% and 1.8% were detected after the Swenson and Duhamel operations, respectively[12]. In a multicentric study, 1.6% mortality was detected after the Duhamel operation[8]. There was no mortality in our series after the Duhamel procedure.

Based on our comparison of the two procedures, we suggest the Duhamel procedure is a simpler and safer method for the treatment of Hirschsprung's disease.

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# Socioeconomically advantaged infants attending a university well-child clinic in Ankara: are they breast-feeding optimally?

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This longitudinal observational study aimed to determine the rates of initiation, duration and correlates of breast-feeding by mothers living in a socioeconomically advantaged urban environment in Turkey. Healthy, term infants born at Ankara University Faculty of Medicine Hospital who would be brought to the well-child clinic regularly for at least 12 months were enrolled. Data on feeding practices were obtained at the 1st, 2nd, 3rd, 4th, 5th, 6th, 9th and 12th month well child care visits. Breast-feeding outcome was categorized based on recommendations by the World Health Organization (WHO). The majority of the 295 participating mothers were older than 20 years, high school graduates, and lived in apartment housing, and 54.6% were employed. The rates of breast-feeding were 97.9%, 90.1%, 76.9% and 36.9% at 1, 4, 6 and 12 months, respectively, and rates of exclusive breast-feeding were 89.8%, 59.3% and 2.0% at 1, 4 and 6 months, respectively. At 6 months 69.8% of infants were receiving cow's milk and by 12 months only 23.4% of the infants had been breast-fed according to WHO recommendations. Neither gender; birth weight of infant; age, education, parity, previous breast-feeding experience of mother; nor the status of living as extended versus nuclear family were related to breast-feeding outcome. Mothers who were working (RR: 3.89, 95% CI: 1.42-10.65) and those who had less than 4 months postpartum leave from work (RR: 4.20, 95% CI: 2.16-8.17) were more likely to not breast-feed optimally. The results of this study indicate that even where breast-feeding is normative behavior, it may not be optimally practiced, leading to potentially detrimental nutrition for infants. Promotion of breast-feeding even in advantaged urban populations is needed.

*Key words: breast-feeding duration, maternal employment, cow's milk.*

Breast-feeding was initially key for the survival of the human species, and it has been normative behavior for all populations until the advent of formula[1]. The benefits of breast-feeding for infants living in developing[2-3] as well as industrialized countries[4] are well documented. The World Health Organization (WHO) has recommended breast-feeding promotion throughout the world, suggesting breast-feeding be exclusive for the first four to six months of life and continued up to at least 12 months of age, with the introduction of appropriate infant foods during the second half of the first year[5]. Breast-feeding promotion programs have been successful in increasing the rate of breast-feeding initiation and duration in some developing countries[6,7]. Unfortunately, however, changes in the characteristics of populations, urbanization in particular, have almost universally negatively affected breast-feeding duration[8-11].

Although studies have been conducted on the rates of initiation and duration of breast-feeding in impoverished populations throughout the developing world[12-15], the duration of breast-feeding, reasons for its termination, and overall feeding practices of urbanized and more advantaged populations in developing countries have been investigated less intensively[16]. This information is crucial for interventions aimed at sustaining and increasing breast-feeding rates as populations in developing countries reach more advantaged living standards. It is

important also to find out what infants are fed when breast-feeding is supplemented and/or terminated, particularly due to the widespread practice of introducing cow's milk early into infants' diets, the association of cow's milk with iron deficiency, and the detrimental effects of iron deficiency anemia[17-19].

Turkey is a developing country with high rates of urbanization[20]. Breast-feeding has been the normative mode of infant feeding in Turkey, and it is endorsed at all socioeconomic and cultural levels. Although rates of the initiation of breast-feeding are very high, the rates of exclusive breast-feeding during the first six months and continuation up to 12 months have been reported to be much lower, especially for urbanized populations[21-24]. Although it is known that higher maternal education and residence in urban environments are risk factors for shorter breast-feeding duration in Turkey[22], information on predictors of breast-feeding duration for advantaged infants living in the cities is limited.

The purpose of this study, therefore, was to ascertain the rates of the initiation and duration of breast-feeding, and the determinants of the duration of breast-feeding by mothers living in an advantaged urban environment in Turkey. This study also aimed to determine the rates and timing of feeding cow's milk to infants during the first year of life. For an advantaged population consisting of middle class families we investigated whether:

1. The duration of breast-feeding would be dependent on factors previously reported in the literature such as maternal education, age, parity or previous breast-feeding experience.
2. Formula feeding took the place of breastfeeding.
3. Isolation from the support and traditional influences provided by the extended family influenced breast-feeding duration.
4. Maternal employment outside the home as a result of urbanization and modernization affected the duration of breast-feeding.
5. Iron-fortified formula was used in place of cow's milk to supplement or replace breastfeeding.

## Material and Methods

### *Eligibility Criteria*

Infants born at the hospital of Ankara University Faculty of Medicine serving an urban middle class population, who would be brought to the well-child clinic of the pediatric department regularly for at least 12 months and who met the following criteria were enrolled in the study: 1) no history of prenatal complications including maternal infection, use of medication or exposure to X-ray; 2) no major congenital malformations; 3) no illness or other complication during the neonatal period; 4) single birth; 5) birth weight between 2500-4500 g; and 6) gestational age between 37-41 weeks. Infants with a chronic illness, or acute illness requiring hospitalization during the first 12 months, were excluded from the study.

All infants enrolled in the study received the standard breast-feeding promotion activities conducted at Ankara University Hospital, which has adopted the Baby Friendly Hospital initiative. Rooming-in was provided and mothers were encouraged to start nursing soon after delivery. Counselling on feeding practices was provided throughout the hospital stay and supplements to breast-feeding were discouraged by the pediatric staff. During well-child follow-up, mothers were also counselled on feeding methods, and exclusive breast-feeding was routinely promoted up to four to six months, with continuation of breast-feeding promoted thereafter. Working mothers were counselled on expressing and storing breast milk.

### *Data Collection*

Data on feeding practices were obtained prospectively by a structured interview at each of the 1, 2, 3, 4, 5, 6, 9 and 12 month well-child care visits. In order to avoid the Hawthorne effect[25], the possibility of changing feeding practices due to being enrolled in a study on infant feeding, mothers were not notified that they were participating in a study on infant feeding until the infant was 12 months of age. When infants were 12 months old, mothers were told that we were conducting a study on infant feeding methods, and that data on feeding provided by them to the clinic was requested to be included in the study, and their oral consent to participate was obtained. Predictors of breast-feeding duration were addressed either by an interview in person or a telephone interview conducted after the 12-month visit. This information included: 1) parental age, level of education, parity, previous breast-feeding experience, income and housing status; 2) status of living as extended versus nuclear family; and

3) maternal part-time or full-time employment outside the home, and duration of postpartum maternal leave from work.

This study was approved by the ethical committee of Ankara University Faculty of Medicine.

*Analysis of Data*

Feeding method at each time point was categorized into seven groups: 1) exclusive breast-feeding; 2) breast-feeding and supplementing with only formula; 3) Breastfeeding and supplementing with cow's milk with or without solids; 4) breast-feeding and supplementing with formula and cow's milk with or without solids; 5) exclusive formula feeding; 6) formula feeding and supplementing with cow's milk with or without solids; and 7) Feeding cow's milk with or without solids. Although other studies have defined exclusive breast-feeding as not giving anything (including water) other than breast-milk[26], in our study population, giving infants water was an extremely common practice and was not categorized separately in any of the groups.

Breast-feeding outcome was categorized based on recommendations by the WHO[5]. Infants breast-fed for less than four months (exclusive or partial breast-feeding) were categorized as "non-optimal outcome"; those breast-fed exclusively for at least four and at most six months, with partial breast-feeding continuing to at least 12 months, were categorized as "optimal outcome." Analysis of chi-square was performed on dichotomized possible predictors and their relationship to the non-optimal outcome of breast-feeding, and risk ratios were computed[27]. Maternal and paternal age, birth weight and monthly income were also analyzed as continuous variables by Student's t test. For all analyses, SPSS[28] was used.

## Results

*Sociodemographic Characteristics of the Sample*

During the time of data collection, 295 infants were found to be eligible for the study. All infants were followed up to 12 months of age regarding feeding practices but data on predictors of the outcome of breast-feeding were complete for only 227 infants (76.9%). There were no differences in rates of initiation or duration of breast-feeding between those infants with complete data and those without. Therefore, the results of duration of breast-feeding and feeding practices will be reported on the whole group, but results of predictors of breast-feeding outcome will be reported only for those 227 infants with complete data.

As seen in Table I, gender was distributed equally among the infants studied. The majority of the mothers were between 20-35 years of age, and the majority of both mothers and fathers had graduated at least from high school. Most infants were the only children. Most families lived in apartment houses and half of the families were owners of their homes. Approximately 8% lived in homes that are considered "shanty" but with running water and electricity. Most families did not live with other relatives but as a nuclear family. During the first year postpartum, 45.4% of the mothers did not work outside the home, 10.1% and 44.5% worked part-time and full-time, respectively.

Table I. Sociodemographic Characteristics of Sample

| | N (227) | % |
|---|---|---|
| Infant male gender | 114 | 50.2 |
| High school/university graduate mothers | 175 | 77.1 |
| High school/university graduate fathers | 197 | 86.8 |
| Maternal age between 20-35 years | 203 | 89.4 |
| Infant single child | 145 | 63.9 |
| Nuclear family constellation | 215 | 94.7 |
| Housing | | |
| Apartment flat | 204 | 89.9 |
| Villa | 5 | 2.2 |
| Shanty house | 18 | 7.9 |
| Maternal occupation | | |
| Not working | 103 | 45.4 |
| Working part-time | 23 | 10.1 |
| Working full-time | 101 | 44.5 |

All but four mothers initiated breast-feeding during the first 24 hours postpartum. During the first month postpartum, 284 (96.3%) infants were being breast-fed exclusively, 6 (2.0%) were given breast-milk and formula, 4 (1.4%) received only formula, and 1 was breast-fed and given cow's milk. As seen in Figure 1, exclusive breast-feeding rates declined to 59.3%, 25.4% and 2.0% at ages 4, 5 and 6 months, respectively. Rates of breast-feeding supplemented with cow's milk with or without solids increased during this time period from 16.6% to 48.8% and 69.8% at 4, 5 and 6 months of age, respectively. At 4 months of age, the most common practices of infant feeding were exclusive breast-feeding (59.3%) and breast-feeding supplemented with cow's milk with or without solids (16.6%). At 6 months of age, the

most common practices of infant feeding were breast-feeding supplemented with cows milk with or without solids (69.8%), followed by feeding cow's milk and solids (16.8%). Exclusive formula feeding peaked at 4 months, during the peak decline of exclusive breast-feeding, but the number of infants receiving formula exclusively did not exceed 19 (6.4%). Formula being used as the only supplement to breast-feeding was more common, and reached a maximum of 43 infants (14.6%) at 3 months. Rates of formula feeding and supplementing with cow's milk with or without solids were lower and did not exceed the 6.5% maximum at 6 months. Rates of feeding only cow's milk with or without solids were very low during the first 3 months but increased from 2% to 16.8% between 4 and 6 months. Cow's milk was given as pasteurized non-fortified whole milk in all cases.

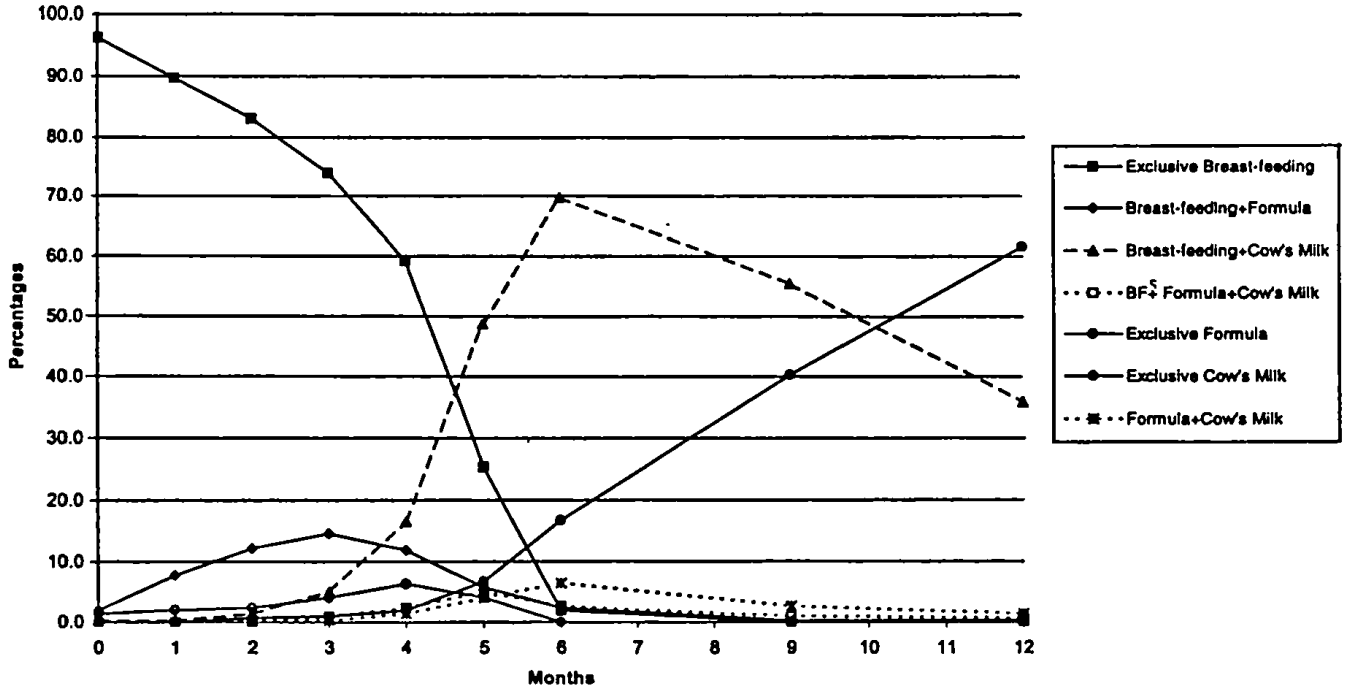


Fig. 1. Rates of different feeding practices by months.

At 12 months of age, most infants were fed cow's milk and solids (61.7%); only 35.9% were still being breast-fed. All infants that still breast-fed at 1 year of age were supplemented with cow's milk and solids. Only seven infants were given formula as well as other foods until 12 months; all of these infants were also given cow's milk in addition to formula.

*Factors Predicting the Outcome of Breast-feeding*

Sixty-nine infants (23.4%) were breast-fed according to the WHO recommendations and classified in the "optimal outcome" group whereas 21 infants (7.1%) were breast-fed for less than 4 months and classified as the "non-optimal outcome" group. As seen in Table II, neither gender or birth weight of infant, parity, previous breast-feeding experience, age, years of education of mother, variables reflecting economic status including monthly income and housing status, nor the status of living as extended versus nuclear family was not associated with breast-feeding outcome. The only variables that were significantly related to non-optimal breast-feeding outcome were maternal employment and duration of maternal absence from work postpartum. Mothers who were working had a risk ratio of 3.89 (95% CI: 1.42-10.65) of being in the non-optimal group versus mothers who were not working. Mothers who had less than four months postpartum leave of absence from work had a risk ratio of 4.20 (95% CI: 2.16-8.17) of being in the non-optimal outcome group compared to mothers that had more leave.

Rates of not breast-feeding at each evaluation time point for mothers who worked full-time and mothers who did not work are seen in Table III. Since only 23 mothers worked part-time, differences of breastfeeding rates at each time point between this small group and the groups of mothers working full-time or not working at all did not reach a level of

significance. This group was therefore excluded from further analyses. Between 4 and 6 months, mothers who worked full-time had significantly increased risks of not breastfeeding than mothers who did not work. This risk was highest at 4 months (RR: 3.82, 95% CI: 1.31-11.13) and decreased thereafter. During the first 3 months and after six months, the difference in breast-feeding outcome between those mothers who worked and those who did not work did not reach a level of significance.

Table II. Risk Factors and the Duration of Breast Feeding

| | BF for 12 months (n=69) | | BF for less than 4 months (n=21) | |
|---|---|---|---|---|
| Risk factor | n | % | n | % |
| Gender | | | | |
| Male | 32 | 46.4 | 9 | 42.9 |
| Female | 35 | 50.7 | 12 | 57.1 |
| Maternal education | | | | |
| ≥ high school | 49 | 71.0 | 18 | 85.7 |
| ≤ secondary school | 20 | 29.0 | 3 | 14.3 |
| Paternal education | | | | |
| high school | 56 | 81.2 | 18 | 85.7 |
| ≤ secondary school | 13 | 18.8 | 3 | 14.3 |
| Maternal occupation* | | | | |
| Housewife | 39 | 56.5 | 4 | 19.0 |
| Working | 30 | 43.5 | 17 | 81.0 |
| Maternal leave** | | | | |
| < 4 months | 6 | 8.7 | 10 | 47.6 |
| ≥ 4 months | 63 | 91.3 | 11 | 52.4 |
| Family composition | | | | |
| Nuclear | 64 | 92.8 | 19 | 90.5 |
| Extended | 5 | 7.2 | 2 | 9.5 |
| House ownership | | | | |
| Owner | 36 | 52.2 | 10 | 47.6 |
| Renting | 33 | 47.8 | 11 | 52.4 |
| Housing | | | | |
| Apartment | 60 | 87.0 | 20 | 95.2 |
| Shanty home | 9 | 13.0 | 1 | 4.8 |
| Dimensional Factors | | | | |
| | Mean | SD | Mean | SD |
| Maternal age | 28.53 | 4.93 | 28.14 | 3.51 |
| Paternal age | 32.85 | 5.90 | 30.95 | 2.69 |
| Birth weight | 3335 | 427 | 3345 | 395 |
| Income (Million TL) | 52 | 25 | 58 | 23 |

BF: Breast-feeding.
TL: Turkish liras.
*: p¢0.05.
**: p¢0.001.

Table III. Decline in Breast-feeding Rates of Working (N=101) and Not Working (N=103) Mothers

| Months | Not BF working n (%) | Not BF not working n (%) | RR of not BF | 95% CI |
|---|---|---|---|---|
| 1 | 2 (1.98) | 2 (1.94) | 1.02 | 0.15-7.10 |
| 2 | 2 (1.98) | 3 (2.91) | 0.68 | 0.11-3.98 |
| 3 | 6 (5.94) | 3 (2.91) | 2.04 | 0.51-8.66 |
| 4 | 15 (14.85) | 4 (3.88) | 3.82 | 1.31-11.13 |
| 5 | 21 (20.79) | 8 (7.77) | 2.67 | 1.24-5.76 |
| 6 | 28 (27.72) | 16 (15.53) | 1.78 | 1.03-3.09 |
| 9 | 47 (46.53) | 34 (33.01) | 1.41 | 0.99-1.99 |
| 12 | 67 (66.33) | 54 (52.43) | 1.27 | 1.00-1.59 |

BF: Breast-feeding.
RR: Relative risk.
CI: Confidence intervals.

## Discussion

This study aimed to understand the duration and determinants of breast-feeding for Turkish mothers of healthy infants living in an advantaged urban environment. The sociodemographic characteristics of our sample reflect an advantaged, educated, urban, middle class population that differs greatly from traditional populations living in rural environments, or from indigent populations living in metropolitan areas in Turkey. We believe that studies on a population such as this one may provide crucial information in shaping nutritional interventions as populations in a developing country such as ours move from the more traditional to more modern standards. Almost all infants in this study were breast-fed exclusively during the first month postpartum, and 59.3% were breast-fed exclusively for 4 months. These rates are higher than the previously reported 63% and 21% rates of exclusive breast-feeding for 1-and 4-month-old Turkish infants, respectively[24, 29]. Only 11.6% of 4-6 month old infants in the nationally representative Turkish Demographic and Health Survey conducted in 1998 were being exclusively breast-fed[21]. These discrepancies may have been due to differences in sociodemographic characteristics between our sample and the other samples which included less advantaged families. The breast-feeding promotion practices at Ankara University Faculty of Medicine Hospital may also have affected the high rates. In our hospital, which has adopted the UNICEF Baby Friendly initiative, rooming-in is provided, and the infant-mother dyad is supported after delivery to commence nursing. The policy of breast-feeding exclusively up to 4 to 6 months is emphasized

at the postpartum discharge, and by pediatricians during each of the well child care visits. Mothers are instructed on nursing techniques and methods of expressing and storing their milk if they should start working.

Exclusive breast-feeding rates declined during the first 4 months postpartum and reached 2% at 6 months of age. The steady decline to 4 months could not be explained by medical advice, but the sharp decline between 4 to 6 months could have been augmented by pediatricians' recommendations for even well growing infants to be started on solids after 4 months. Interestingly, even in this more economically advantaged and educated population of middle class families in Turkey, exclusive formula feeding did not exceed 6.4%. We believe that the high rate of exclusive breast-feeding is protected in Turkey by the extremely high prices of formula relative to family income and by the exclusion of formula in insurance coverage. However, at 3 months of age, 1 out of 7 infants were being supplemented with formula; this must draw attention to a potential increase in the rate of formula feeding in this population. The low rates of giving formula coupled with the high rate of feeding cow's milk exclusively (16.6% at 6 months) implies that even in a population that is more advantaged financially and in the educational level of parents, the use of cow's milk as a main infant food cannot be avoided. The association of cow's milk with iron deficiency and the detrimental effects of iron deficiency anemia have been widely documented[17-19]. Iron deficiency anemia in Turkish infants is reported to reach 75% for an urban population[30], and the high rates throughout the world[31] call for global, urgent and effective interventions. The peak for the introduction of cow's milk in our study was 4 months of age. Pediatricians in our clinic, as well as many others in Turkey, in complying with the WHO recommendations, advise supplementing breast-feeding for 4-month-old infants. We believe that the WHO should consider strongly recommending not ceasing exclusive breast-feeding until infants are 6 months of age.

Only 27.5% of infants in this study were fed according to the recommendations of the WHO, and 1 out of 10 were breast-fed for shorter than 4 months. The results of the National Demographic and Health Survey 1998 do not provide us with a comparison for these rates, since the percentage of infants breast fed exclusively for 4 or 6 months and then continued with breast-feeding until 12 months is not given for that sample[21]. However, in the 1998 survey, 52.4% were still breastfeeding at 12 months compared to 36.9% in our sample. This discrepancy may have been due to the larger number of more educated mothers in our sample (77.1% versus 18.1% in the National Demographic and Health Survey), leading to the higher probability that more mothers in our sample may have been working outside their homes. Promotional efforts on breast-feeding need to be guided by information on determinants of the discontinuation of breast-feeding. In our study, non-optimal breast-feeding was not related to parameters such as maternal age, parity, education level, previous breastfeeding experience, higher income and therefore higher ability to purchase formula, or to traditional factors such as extended family living together. Although these factors have been previously reported in the western literature to influence rates and duration of breast-feeding[32], we believe that these factors may not be in operation where breast-feeding is considered normative behavior and is endorsed by the population at large. Instead the termination of breast-feeding in populations such as ours may be more strongly associated with factors that directly affect the togetherness of the mother and infant.

Our results concur with others[33,34] that have found that optimal breast-feeding practices are affected by whether or not the mother is working and by the duration of her postpartum leave from work. Although the International Labor Organization has set standards for paid maternity leave of 12 weeks since 1919, only 32 countries have ratified the conventions so far[35,36]. In Turkey, absence from work is allowed for 40 days following normal vaginal delivery and 60 days after a caesarean section. New regulations permit a mother to negotiate a 6-month unpaid leave from some jobs. Dilemmas of breast-feeding for working mothers have been previously emphasized in the literature[37]. It is important when developing policies aiming to promote breast-feeding for working mothers in developing countries to consider the psychological, sociocultural, political and economic facets of this issue as well as the medical. It has been previously emphasized in the literature that many working mothers may experience guilt and depression from not being able to provide adequate nutrition and supportive care for their infants[38-40]. This is likely

to be augmented for mothers living in urbanized environments in developing countries where they may be cut-off from extended family and where child-care facilities may be of poor quality. On the other hand, one of the main factors associated with postnatal depression is unemployment after a maternity leave[40]. Furthermore, the working status of the mother brings invaluable benefits to the health and development of children in developing countries[22]. Despite multifaceted benefits of maternal employment, in developing countries such as Turkey, society may be still struggling with transitions from the more traditional and conservative family where women are viewed primarily as homemakers and caretakers of their children to the point where they are wage-earners with equal rights and similar responsibilities as men. Premature emphasis and support of the mothering responsibilities of the working woman, such as an increased duration of paid absence from work postpartum, may result in a greater preference of men over women in the work force and hinder women's access to labor. We would like to underscore the need for breast-feeding promotion programs for working mothers in the developing world to move concordantly with policies for increasing and sustaining women's right of access to work.

Another implication of our results involves clinical practice of pediatricians and other primary health care providers. During our study we observed that questioning whether or not and when a mother would be returning to work was not a routine part of the well-child care visit and thus, although breastfeeding promotion was intended, the main reason behind non-optimal infant feeding was overlooked. We recommend determining the working plans of each mother and providing anticipatory guidance for this transition as a part of routine well-child care.

Our study is limited in that it reflects the practices of a specific population of mothers at one center. Both local and cross-cultural studies are needed in order to test whether our results can be generalized. It also would have been desirable to examine the cultural beliefs regarding breast-feeding that have been found to affect rates and duration[41]. Practices such as giving pacifiers to nursing infants were not examined in this study. Another limitation of our study was our inability to identify the determinants of optimal breast-feeding outcome for mothers who worked. We were unable to interview working mothers further regarding what helped them sustain breastfeeding despite full-time work. The effects of the nature of maternal occupation on breast-feeding duration, specifically, whether mothers who were working in certain professions such as those related to health care delivery were more likely to breast-feed longer, were not investigated. We also do not know whether working mothers were able to express and use stored milk as routinely recommended. We propose that factors related to the longer continuation of breast-feeding may be a focus for future studies.

The results of our study indicate that even for a socioeconomically advantaged population where breast-feeding is normative behavior, it is not optimally practiced, leading to the early introduction of cow's milk. We believe that local government, health service and international efforts are needed in the 21st century to promote breast-feeding more effectively even for advantaged infants, and even in countries where breast-feeding is highly practiced.

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# The impact of pre-and perinatal factors on attention-deficit and disruptive behavior disorders

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SUMMARY: Şenol S, Şener Ş, Ergenekon E, Gücüyener K. The impact of pre- and perinatal factors on attention-deficit and disruptive behavior disorders. Turk J Pediatr 2001; 43: 231-236.

Diagnosis of attention-deficit and disruptive behavior disorders defines a group of disorders which have common properties. This group consists of attention-deficit hyperactivity disorder, conduct disorder and oppositional defiant disorder. In order to differentiate these disorders, which share similar properties, it is important to verify the existing differences. In this respect, differences between and distribution of perinatal factors in these three disorders were investigated. The study was conducted in the Child Psychiatry and Pediatric Neurology Departments over a 20-month period. Two hundred and seventy children out of 1,556 attendant with various complaints were diagnosed to have one of the following disorders: 121 had attention-deficit hyperactivity disorder, 50 had oppositional defiant disorder and 99 had conduct disorder. The prenatal and perinatal data of the patients were evaluated retrospectively by a neonatologist. With regard to the investigated parameters, none showed any significant difference between the three groups when compared. The three disorders, which share many similarities in terms of the symptoms, also show similarities in terms of perinatal factors. Since we did not find any study similar in design, our results, although statistically not significant, are discussed in light of the little data available.

*Key words: attention-deficit and disruptive behavior disorders, perinatal risk factor.*

"Attention-deficit and disruptive behavior disorders (ADDBD)" diagnosis is used to define a group of disorders which start during childhood and adolescence and share common clinical features. It is thought that three different but closely related behavioral patterns lie beneath the basis of these disorders. These are attention-deficit/learning-deficit, hyperactivity/impulsivity and problem behavior[1]. The World Health Organization's[2] International Classification of Mental and Behavioral Disorders: Diagnostic Criteria (ICD-10) for Research includes hyperkinetic and conduct disorders under "behavioral and emotional disorders occurring in childhood and adolescence". The same disorders are under the general heading of ADDBD in the American Psychiatric Association's[3], The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). This group includes attention-deficit/hyperactivity disorder (ADHD), conduct disorder (CD) and oppositional defiant disorder (ODD). These three disorders are also defined as externalizing disorders[4].

Attention-deficit/hyperactivity disorder, a heterogeneous disorder, is a major clinical and public health problem throughout the world. DSM-IV[3] recognizes three subtypes of ADHD: predominantly inattentive predominantly hyperactive impulse, and combined. The diagnosis is established on the basis of history of symptoms representing the cardinal constructs of ADHD: inattention, impulsiveness and hyperactivity. Low birth weight was identified by the National Collaborative Perinatal Project (NCPP)[5] as a clear risk factor for ADHD. Klebans et al.[6] made comparisons among the four birth weight groups: extremely low birth weight (ELBW), very low birth weight (VLBW), low birth weight (LBW) and normal birth weight (NBW). The ELBW children had lower attention and lower overall social competence than all other birth weight groups as measured by classroom teachers[6]. All LBW children had lower attention and higher day dreaming and hyperactivity scores than NBW children.

Research on premature infants provides some clues to the neuroanatomy of ADHD. Dynamic imaging studies of children have shown that ADHD is associated with lowered glucose metabolism primarily in the periventricular areas and the prefrontal cortex[7]. In the susceptible prematures, germinal matrix-intraventricular hemorrhage-related lesions in the caudate nucleus may disrupt the migration of cells from the germinal matrix to subcortical structures such as the thalamus and then to the prefrontal cortex[8,9].

Another longitudinal group of studies showed that germinal matrix hemorrhage has been associated with more subtle cognitive difficulties in attention, spatial memory and ability to inhibit behaviors (frontal cortex functions)[10,11].

Although this disorder has been recognized in children prior to age three, it may be difficult to distinguish preschool children with ADHD from those with conduct or oppositional defiant disorders. Most children can be diagnosed by age six to seven by entering primary school, when their externalizing symptoms are most evident. Due to the diagnostic difficulties, there is a wide array of prevalence rates reported, ranging between 2-5%[3,12-15].

Lately an improved understanding of the neurobiology along with genetics of ADHD, and of diseased areas in the brain has been achieved, stressing the importance of the striatum and corticostriato-thalamocortical loops as a substrate for the disorder[16]. Among the lesional factors, pre-and perinatal events are the leading ones[17]. Recent studies have also implicated prenatal and perinatal events[18,19], prematurity, the medical status of the mother before and during pregnancy[20,21], and complicated pregnancy/labor as risk factors for ADHD[22]. Öktem and Sonuvar[23] presented the demographic variables of children diagnosed as ADHD including birth, early development, family characteristics, and mental and neurological signs during a ten-year period.

In this respect the purpose of the present study was to investigate whether pre-and perinatal events have any special effect as a risk factor on disruptive behavioral disorders (conduct disorder or oppositional defiant disorder) when compared to ADHD.

## Material and Methods

The study included 270 children who had ADDBD, out of 1,556 who were referred to Gazi University Faculty of Medicine Departments of Child Psychiatry and Pediatric Neurology due to various illnesses over a period of 20 months. All referred children were independently evaluated by two child psychiatrists according to DSM-IV criteria[3], during an interview. All children diagnosed to have ADDBD by both child psychiatrists were included in the study and subtyped further according to DSM-IV criteria (Table I). During the interview every DSM-IV criterion for the relevant disorder was scored by the evaluating psychiatrist, giving a maximum total score of 9 for predominantly inattentive type ADHD, 9 for predominantly hyperactive impulsive type ADHD, 8 for ODD and 15 for CD. These scores were used in the comparisons.

Table I. Diagnosis of the Patients According to DSM-IV Criteria

| DSM-IV diagnosis | n | % |
|---|---|---|
| Attention-deficit and disruptive behavior disorders | 270 | 17.4 |
| Attention-deficit/hyperactivity disorder | 121 | 7.8 |
| Oppositional defiant disorder | 50 | 3.2 |
| Conduct disorder | 99 | 6.4 |
| Other DSM-IV dignoses | 1166 | 74.9 |
| No diagnosis (developmental complaint) | 120 | 7.7 |
| Total | 1556 | 100.0 |

All the children were required to have an IQ above 70, to be medically healthy and nonpsychotic, and to have no abnormality according to their neurological examination made by a pediatric neurologist. The medical records of the mothers and children were evaluated by a neonatologist, the pre-perinatal period, early postnatal events and post medical history. Any psychiatric disorders alone or associated with ADDBD were also screened.

All the children were evaluated by classroom teachers who observed the children with regard to the 28 questions comprising the Conners' Teacher Rating Scale[24-27]. The adaptation of the rating scale to Turkish children was made by Şener et al.[28] Conners' Parent Rating Scale consisted of 48 questions, and Turkish adaptation was made by Dereboy et al.[29].

Statistical analysis was performed by SPSS for Window (Statistical Package for Social Sciences for Windows. Release 6.0 SPSS Inc. (1989-1993). Student's test was used to compare differences between the groups, with $p < 0.05$ accepted as significant and all others as non-significant.

## Results

During the 20-month period, of the 1,556 children referred, 270 patients were evaluated. The mean age of the 270 patients (202 male, 74.8%; 68 female, 25.2%) included in the study was 10.6 ± 3.3 (range 6-16 years) and the diagnoses are shown in Table I.

Some of the subjects in the ADDBD group were found to also have other co-morbid disorders of the same group. While 83 subjects in the ADHD group did not have any other co-morbid disorder of the same diagnosis group, 38 were diagnosed to have CD of ODD, in addition to ADHD (Table II). The clinicians were asked to establish the primary diagnosis for every case for statistical analysis. Further comparisons were performed according to those diagnoses.

Table II. Comorbid Diagnosis of Patients in the ADDBD Group and Association with Hypoxia

| DSM-IV diagnosis | n | % | Hypoxia + |
|---|---|---|---|
| ADHD-IA | 13 | 4.9 | 1 |
| ADHD-HA | 16 | 5.9 | – |
| ADHD-C | 54 | 20.0 | 5 |
| ODD | 23 | 8.5 | 3 |
| CD | 93 | 34.5 | 2 |
| ADHD-IA+ODD | 3 | 1.1 | 1 |
| ADHD-HA+ODD | 9 | 3.3 | – |
| ADHD-IA+CD | 6 | 2.2 | – |
| ADHD-HA+CD | 12 | 4.4 | – |
| ADHD-C+ODD | 17 | 6.3 | 1 |
| ADHD-C+CD | 24 | 8.9 | 2 |
| Total | 270 | 100.0 | 15 |

ADHD-IA: Attention-deficit hyperactivity disorder, predominantly inattentive type. ADHD-HA: Attention-deficit hyperactivity disorder, predominantly hyperactive impulsive type. ADHD-C: Attention-deficit hyperactivity disorder, combined type. ODD: Oppositional defiant disorder. CD: Conduct disorder. ADDBD: Attention-deficit and disruptive behavior disorders.

Statistical comparison between hypoxic and non-hypoxic subjects according to secondary diagnoses was not done, as the sample sizes were quite small in most groups. However eight out of 10 subjects in the hypoxic group had a secondary diagnosis, while only 50 of the 111 subjects in the non-hypoxic group had secondary diagnoses; the difference was statistically significant ($\chi^2 = 7.63$, $p < 0.01$) (Table III).

All 270 patients diagnosed to have ADDBD were grouped according to the following criteria: unexpected or a planned pregnancy, gestational age, type of pregnancy, birth complications (icnluding hypoxia) and birth weight (Table IV).

About one fourth of the patients were born after an unplanned pregnancy; nearly all of the ADDBD patients had a history of planned pregnancy.

Except for planned and unexpected pregnancies, where a significant difference between the groups existed ($p < 0.01$), there were not any statistically significant differences between the compared groups with regard to the defined criteria ($p > 0.05$).

The Conners' Teacher and Parent Rating Scales were also compared with reference to birth complications and type of delivery. These data and statistical results are shown in Table V.

With regard to the diagnostic groups of ADDBD, comparison of the scores showed no statistical significance. There was no statistically significant relation among the diagnosis groups (with or without hypoxia) with respect to ADDBD, ADHD, and Conners' Teacher and Parent Rating scores ($p > 0.05$) (Table VI).

Table III. Comorbid Secondary Diagnoses of the 121 Subjects With or Without Coexistence of Hypoxia

| | ADHD-IA | | ADHD-HA | | ADHD-C | | Total* | |
|---|---|---|---|---|---|---|---|---|
| Comorbid diagnoses | Hypoxia – | Hypoxia + | Hypoxia – | Hypoxia + | Hypoxia – | Hypoxia + | Hypoxia – | Hypoxia + |
| Depression | 2 | – | – | – | 6 | – | 8 | – |
| Anxiety disorders | – | – | 1 | – | | – | 1 | – |
| Tic disorders | – | – | 3 | – | 4 | 1 | 7 | 1 |
| Enuresis | 2 | 1 | 4 | 1 | 14 | 2 | 20 | 4 |
| Encopresis | – | – | 2 | | 3 | 1 | 5 | 1 |
| Stuttering | 1 | – | – | – | 1 | – | 2 | |
| Learning disabilities | 1 | 1 | – | – | 3 | 1 | 4 | 2 |
| Other (dyslexia, eating disorders, alopecia areata) | – | – | – | – | 3 | – | 3 | – |
| Total secondary diagnoses | 6 | 2 | 10 | 1 | 34 | 5 | 50 | 8 |
| No secondary diagnoses | 8 | – | 15 | – | 38 | 2 | 61 | 2 |
| Total* | 14 | 2 | 25 | 1 | 72 | 7 | 111 | 10 |

ADHD-IA: Attention-deficit hyperactivity disorder, predominantly inattentive type. ADHD-HA: Attention-deficit hyperactivity disorder, predominantly hyperactive impulsive type. ADHD-C: Attention-deficit hyperactivity disorder, combined type.
*$\chi^2 = 7.63$, df = 1, $p < 0.01$.

Table IV. Comparison Among the Groups Based on Defined Criteria

| | DSM-IV diagnosis | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | ADHD-IA | | ADHD-HA | | ADHD-C | | ODD | | CD | | Total | |
| Pregnancy* | n | % | n | % | n | % | n | % | n | % | n | % |
| Planned | 16 | 100.0 | 24 | 92.3 | 62 | 78.5 | 40 | 80.0 | 67 | 67.7 | 209 | 77.4 |
| Unplanned | – | – | 2 | 7.7 | 17 | 21.5 | 10 | 20.0 | 32 | 32.3 | 61 | 22.6 |
| Duration of pregnancyə | | | | | | | | | | | | |
| Preterm | – | 1 | 3.8 | 11 | 13.9 | 7 | 14.0 | 6 | 6.1 | 25 | 9.3 | |
| Term | 15 | 93.8 | 24 | 92.4 | 65 | 82.3 | 40 | 80.0 | 89 | 89.9 | 233 | 86.3 |
| Postterm | 1 | 6.2 | 1 | 3.8 | 3 | 3.8 | 3 | 6.0 | 4 | 4.0 | 12 | 4.4 |
| Type of laborə | | | | | | | | | | | | |
| Spontaneous | 13 | 81.3 | 22 | 84.6 | 59 | 74.7 | 42 | 84.0 | 81 | 81.8 | 217 | 80.4 |
| C/S | 3 | 18.7 | 4 | 15.4 | 18 | 22.8 | 7 | 14.0 | 12 | 12.1 | 44 | 16.3 |
| Intervention | – | – | – | – | 2 | 2.5 | 1 | 2.0 | 6 | 6.1 | 9 | 3.3 |
| Hypoxiaə | | | | | | | | | | | | |
| no | 14 | 87.5 | 25 | 96.2 | 72 | 91.1 | 47 | 94.0 | 97 | 98.0 | 255 | 94.4 |
| yes | 2 | 12.5 | 1 | 3.8 | 7 | 8.9 | 3 | 6.0 | 2 | 2.0 | 15 | 5.6 |
| Birth weightə (g) | ADHD-IA A.mean±Sd | | ADHD-HA A.mean±Sd | | ADHD-C A.mean±Sd | | ODD A.mean±Sd | | CD A.mean±Sd | | F | significant |
| | 3228.13 ± 407.0 | | 3353.08 ± 503.7 | | 3423.04 ± 583.7 | | 3295.00 ± 583.0 | | 3413.74 ± 519.0 | | 0.850 | > 0.05 |

A.mean ± Sd: arithmetic mean ± standard deviation.
ADHD-IA : Attention-deficit hyperactivity disorder, predominantly inattentive type.
ADHD-HA : Attention-deficit hyperactivity disorder, predominantly hyperactive impulsive type.
ADHD-C : Attention-deficit hyperactivity disorder, combined type.
ODD : Oppositional defiant disorder.
CD : Conduct disorder.
C/S : Cesarean section.
* $\chi^2 = 13.57$, df = 4, $p < 0.01$.
ə not statistically significant.

Table V. Conners' Teacher and Parent Rating Scales and Comparison Based on Birth Complication

| Hypoxia | n | Hyperactivy criterion score* | Attention-Deficit criterion score* | ADHD Total criterion score* | ADDBD criterion score | Conners' teacher rating scales score | Conners' parent rating scales score |
|---|---|---|---|---|---|---|---|
| no | 255 | 4.76 ± 3.4 | 4.69 ± 2.9 | 9.46 ± 5.9 | 16.56 ± 5.2 | 36.8 ± 11.3 | 58.76 ± 15.0 |
| yes | 15 | 5.87 ± 2.9 | 6.47 ± 2.4 | 12.33 ± 4.9 | 18.33 ± 4.3 | 43.13 ± 12.5 | 64.53 ± 12.4 |
| Type of labor | | | | | | | |
| Spontaneous | 217 | 4.76 ± 3.5 | 4.71 ± 2.9 | 9.47 ± 5.9 | 16.61 ± 5.2 | 36.08 ± 11.4 | 59.17 ± 15.2 |
| C/S | 44 | 5.30 ± 3.0 | 5.23 ± 2.9 | 10.52 ± 5.6 | 16.52 ± 5.2 | 39.77 ± 11.3 | 59.77 ± 13.1 |
| Intervention | 9 | 4.22 ± 3.3 | 4.56 ± 1.4 | 8.78 ± 4.4 | 18.33 ± 4.3 | 38.33 ± 12.1 | 53.78 ± 18.0 |
| Pregnancy | | | | | | | |
| Planned | 209 | 4.94 ± 3.4 | 4.96 ± 2.8 | 9.90 ± 5.7 | 16.77 ± 5.3 | 37.19 ± 11.3 | 59.40 ± 15.0 |
| Unplanned | 61 | 4.43 ± 3.5 | 4.21 ± 3.0 | 8.64 ± 6.3 | 16.26 ± 4.9 | 35.28 ± 11.7 | 58.02 ± 14.7 |
| Duration of pregnancy | | | | | | | |
| Preterm | 25 | 5.44 ± 3.6 | 5.28 ± 3.1 | 10.72 ± 6.4 | 16.44 ± 5.5 | 37.92 ± 12.6 | 62.04 ± 18.1 |
| Term | 233 | 4.74 ± 3.4 | 4.74 ± 2.9 | 9.48 ± 5.8 | 16.59 ± 5.1 | 36.55 ± 11.3 | 58.71 ± 14.3 |
| Postterm | 12 | 5.17 ± 3.4 | 4.75 ± 2.8 | 9.92 ± 5.8 | 18.42 ± 5.9 | 38.33 ± 13.3 | 60.25 ± 19.6 |

C/S : Cesarean section.
ADHD: Attention-deficit hyperactivity disorder.
* According to the sum of DSM-IV attention-deficit/hyperactivity disorder diagnosis criterion items.

Table VI. Conners' Teacher-Parent Rating Scales and ADDBD-ADHD Score of Patients With or Without Hypoxia

| Diagnosis | | n | ADDBD score* | ADHD score** | Conners' teacher rating scales score | Conners' parent rating scales score |
|---|---|---|---|---|---|---|
| ADHD | hypoxia – | 111 | 18.43 ± 4.38 | 14.64 ± 2.58 | 39.22 ± 11.60 | 59.17 ± 16.23 |
| | hypoxia + | 10 | 19.17 ± 3.54 | 14.17 ± 2.66 | 44.17 ± 11.38 | 64.08 ± 11.67 |
| ODD | hypoxia – | 47 | 15.80 ± 6.22 | 7.07 ± 4.90 | 34.38 ± 12.33 | 55.07 ± 17.52 |
| | hypoxia + | 3 | 18.67 ± 4.73 | 9.33 ± 3.79 | 38.67 ± 16.65 | 68.33 ± 6.51 |
| CD | hypoxia – | 97 | 14.72 ± 4.99 | 4.63 ± 3.88 | 34.08 ± 9.90 | 59.96 ± 12.10 |

ADDBD: Attention-deficit and disruptive behavior disorders.

* According to the sum of DSM-IV attention-deficit/hyperactivity disorder (ADHD)+ conduct disorder (CD) and oppositional defiant disorder (ODD) diagnosis criteria items.

** According to the sum of DSM-IV attention-deficit/hyperactivity disorder diagnosis criteria items.

## Discussion

When researching the risk factors related to ADHD and other disruptive behavioral disorders, may of the previous reports indicate mostly the relation between prematurity and birth weight. McCormick et al.[30] examined three preterm groups: very low birth weight (VLBW) (< 1500 g), low birth weight (LBW) (1500-2500 g) and normal birth weight (NBW) (over 2500 g), ranging in age from five to 17 years at follow-up. They concluded that VLBW and hyperactivity contribute independently to academic problems. Parents and teachers rate British children born weighing less than 1,250 g as more overactive, more easily frightened and clumsier than their classmate controls[31]. When the groups in our study were compared regarding parent and teacher rating scores, although parents' ratings were higher than those of the teachers, there was no significant difference. There was also no significant difference when grouped according to the presence of birth complications and type of delivery. In terms of prematurity, the most common predictable behavioral problem appears to be ADHD. In general, studies have indicated that somewhere between 5-35% of premature children have characteristics consistent with ADHD[27]. In our sample population, we could not identify any difference between groups in terms of the defined criteria or the rating scales of teachers and parents; the data was not statistically significant.

To determine the prevalence of disruptive behavior disorders in LBW infants (BW ≤ 200 gr), Pharoah et al.[32] studied 233 matched case-control pairs attending normal primary school and 36 unmatched children attending a special school. On the parental questionnaire screen 36% of the cases and 22% of the controls had a behavior disorder, and on the teacher questionnaire this ratio was 27% and 12%, respectively. Hyperactivity was more common among males than their control (21% versus 5%). O'Callaghan[33] also showed that although the prevalence of ADHD was not increased in ELBW children, they experienced marked problems in reading, spelling, mathematics, and writing when compared to control children. They were nearly three times more likely to be delayed by more than a year in all aspects. Milberger et al.[34] evaluated the role of pregnancy, delivery and infancy complications in the etiology of ADHD and showed positive associations. Moreover, those complications were associated with the correlates of ADHD, such as impaired cognitive functioning and poor school performance.

Since we did not use a control group in our study, the main purpose was to investigate any differences between subgroups of ADHD and other disruptive behavior disorders with regards to pre-and perinatal factors. Analysis of the existing data showed no significant difference between the groups in terms of the defined criteria except for history of unwanted pregnancy among patients in the conduct disorder group (32.3%). This result can be interpreted in two ways: either children with CD are born to mothers with an unwanted pregnancy, or those children are so troublesome that parents may think that the pregnancy was unwanted. Although our study is a retrospective evaluation in an ongoing large study, we can postulate that these pre-and perinatal events, prematurity, low birth weight, and hypoxia-related complications, may also be risk factors for ODD and CD, as well as for ADHD. ODD and CD patients could also be at risk for a range of developmental disabilities seen in patients with ADHD.

We recognize that a firm conclusion cannot be reached on this subject in view of the small number of patients in our study, without also thoroughly examining family dynamics, socioeconomic factors, and home environment,

and without following/evaluating the children to adulthood. Our aim was just to relate findings from a new non-investigated point of these disorders; i.e. risk factors occurring very early in life. This new perspective will hopefully provide the pediatrician, child psychiatrist, neonatologist, and psychologist with a better understanding of the disorders and aid their efforts in intervention.

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# Gaucher disease type I: analysis of two cases with thalassemic facies and pulmonary arteriovenous fistulas

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SUMMARY: Gürakan F, Koçak N, Yüce A, Özen H. Gaucher disease type I: analysis of two cases with thalassemic facies and pulmonary arteriovenous fistulas. Turk J Pediatr 2001; 43: 237-242.

Here we report two unusual patients with Gaucher disease type I. Both girls admitted with hepatosplenomegaly, growth retardation, and anemia at four and 2.5 years of age, and Gaucher cells were seen on bone marrow aspirates. Thalassemic face was first noted at 8 and 11 years of age, respectively, with frontal bossing and maxillary hypertrophia. Although they had unconjugated hyperbilirubinemia, high reticulocytes, polychromasia, and normoblasts on peripheral smear, other laboratory tests for hemolytic disease were negative. Radiological examination revealed typical bone involvement of Gaucher disease, as well as costal enlargement and obliteration of paranasal sinuses, the latter two reported in hemolytic diseases. Cyanosis, digital clubbing and recurrent lung infections led to contrast echocardiography that revealed diffuse pulmonary arteriovenous shunting in both. Diagnosis was confirmed by low leukocyte beta glucosidase levels and mutations N370S7/L444P (Case 1) and N370S/? (Case 2). These features, all reported for the first time, may show a new clinical course in Gaucher disease.

*Key words: Gaucher disease, thalassemia, pulmonary arteriovenous fistulas.*

Gaucher disease (GD) is an inherited metabolic disorder caused by the defective activity of acid beta glucosidase and accumulation of glucosylceramide-laden macrophages of the retuculoendothelial system[1]. Three clinical subtypes have been recognized. Type I, the defining feature of which is the absence of neurologic involvement, is the most common. There is great heterogeneity within type I GD. The bone marrow and spleen are two of the more extensively involved organs. Anemia, coagulation abnormalities, visceral enlargement and structural skeletal changes occur at some point during the course of the illness in most patients[2]. In this report we describe two children with GD type I, pulmonary arteriovenous fistulas and some clinical and laboratory findings resembling thalassemia major, a distinct type not found among the 95 patients diagnosed in the same clinic.

## Case Reports

### *Case 1*

This four-year-old girl, product of a nonconsanguineous marriage, was first noted to have abdominal enlargement at age one. On admittance to our hospital 1985, growth retardation, hepatosplenomegaly (5 and 7 cm below the costal margins), moderate anemia (9.6 g/dl) and Gaucher cells on bone marrow aspirate were found. Her second visit was five years later, at which time she was subicteric and had thalassemic face with overgrowth of maxilla, prominence of the upper incisors, frontal bossing, flattening of the nasal bridge and separation of the orbits. Her liver was firmly palpable below the right costal margin and a huge spleen filled the whole abdomen. She had severe anemia (5.2 g/dl), thrombocytopenia (45000/mm$^3$), leukopenia (2400/mm$^3$) and reticulocytosis (2%). Splenectomy was performed, and histological examination of the liver and spleen also revealed Gaucher cells. Her hematological findings normalized postoperatively for one year. In 1991 she admitted with severe left femoral head pain, which at first could not be differentiated from septic arthritis. Her next visit to our hospital was in 1996, at 13 years of age. She complained of recurrent leg pain, recurrent conjunctivitis, and fatigue. She had a

thalassemic face (Fig. 1a), scleral subicterus, very thin extremities, growth retardation without any development of secondary sexual characteristics,

Fig. 1a. Facial appearance of Case 1.

and firm hepatomegaly 8 cm below the right costal margin. Her Hb level was 10.6 g/dl, mean corpuscular volume 91.6 fl, red blood cell count 3.5 x $10^6$/$mm^3$, red cell distribution width 20.8, reticulocyte count 1.6%, and platelet count 126,000/$mm^3$. Peripheral smear revealed anisocytosis, poikilocytosis, polychromasia, normoblasts and target cells. Hemoglobin electrophoresis, plasma Hb and haptoglobin, and glucose 6 phosphate dehydrogenase levels were found normal. Direct and indirect Coombs' tests, acid Ham test, and cold agglutinins were negative. Bone marrow aspiration revealed a great number of Gaucher cells and normal erythropoietic activity. Radiological evaluation, reported earlier[3], revealed Erlenmeyer flask appearance on the long bones, bilateral femoral head necrosis, bilateral sacroiliac joint involvement and coarse trabeculation, typical skeletal changes of GD type I[4]. Maxillary and frontal sinuses had no pneumatization on the sinus X-rays (Fig. 2a) and tomography, which may be seen in thalassemia[5], but has not been reported in GD. Chest X-rays demonstrated widening of the ribs and coarse trabeculation of vertebrae. Pseudocyts were present on maxilla, mandibula, and sphenoid, metacarpal and phalangeal bones, together with coarse trabeculation. Biochemical tests were normal except for high triglyceride (326 mg/dl) and unconjugated bilirubin (1.8 mg/dl) levels. Abdominal ultrasonography showed a huge and hyperechoic liver; cirrhosis was not present histologically. Mild cyanosis led to evaluation of blood gases that showed hypoxia. Constrast echocardiography revealed multiple diffuse pulmonary arteriovenous shunting. Leukocyte beta glucosidase activity was found deficient (0.17 mmol/gh, normal range 1-5). She was found to carry N370S and L444P point mutations, as a compound heterozygote.

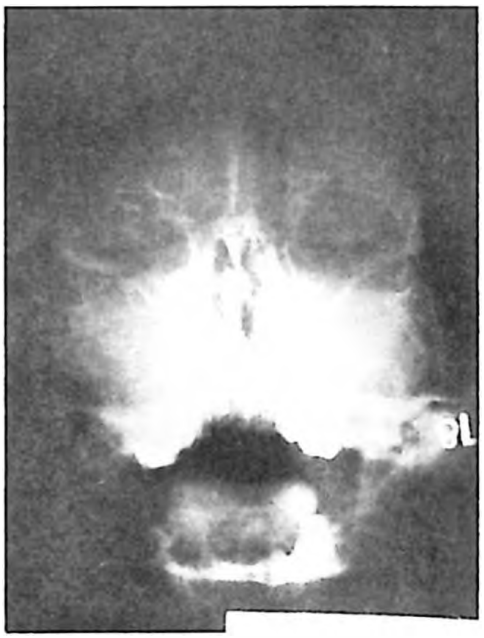

Fig. 2a. Waters radiograph of Case 1 showing no pneumatization in paranasal sinuses and coarse trabeculation of maxilla and mandibula.

*Case 2*

The girl was first seen in our hospital at the age of 2.5 years, in 1984. She was one of the siblings of a GD patient who died at seven years of age. She was from the same town in the northwest of Turkey as Case 1, but the families were not related. Her complaints were abdominal enlargement, fatigue and paleness. Her parents were nonconsanguineous and her eight siblings were healthy. She had growth retardation, and firm hepatosplenomegaly of 5 and 12 cm respectively, below the costal margins. Hematological examination showed anemia (6.4 g/dl) and thrombocytopenia (100,000/$mm^3$). Hypochromia, anisocytosis, poikilocytosis, and target cells were seen on the peripheral smear. Bone marrow aspiration revealed Gaucher cells. Biochemical tests were normal except for a high unconjugated bilirubin level (1.3 mg/dl). Long bone radiographs were also normal. Splenectomy was performed, revealing Gaucher cells in the liver and spleen histologically. Although the hematological

values normalized after the splenectomy, the Hb level declined to 7.1 g/dl, and the reticulocyte count increased to 2% one year later. She complained of oral and nasal bleeding episodes, recurrent abdominal pain and fever, and had pyuria. A rectal inflammatory polyp causing hematochezia was removed in 1988. Low serum iron saturation, anisocytosis, poikilocytosis, hypochromia, target cells, and normoblasts on the peripheral smear were detected at that visit, while the Hb level was 9 g/dl and the reticulocyte count 2.2%. In spite of iron supplementation and removal of the polyp, her Hb level declined to 7.2 g/dl. Her first skeletal complaints started at nine years of age, with right pelvic pain. Her sclerae were icteric, extremities cachectic, and abdomen huge. A systolic murmur of third degree was heard on the left sternal margin. Her hemoglobin level was 4.5 g/dl and the aforementioned changes were defined on the peripheral smear again. Femoral X-rays revealed Erlenmeyer flask sign. In 1992, chronic cough, recurrent lung infections, and petechia started. Physical examination revealed an 11-year-old girl with a weight of 23 kg and height of 120 cm. Scleral icterus and digital clubbing were other physical findings. Hemoglobin level was 7.9 g/dl; Hb electrophoresis, plasma Hb and haptoglobin values and peripheral smear for fetal Hb normal; and Coombs' test negative. Low serum albumin, high serum alanine amino transferase and unconjugated bilirubin levels (3.7 g/dl, 63 U/L and 0.8 mg/dl, respectively) were detected. Thalassemic facial appearance was first defined in 1993 (Fig. 1b) when she was 14 years old. Growth retardation (28 kg weight, 136 cm height) without any secondary sexual development, digital clubbing, cyanosis, and facial appearance were very striking. Bleeding episodes, lung problems and pyuria were continuing. Liver was nodularly palpated 20, 15 and 10 cm below the right, mid and left costal margins, respectively. She had moderate anemia (8.9 g/dl), mild reticulocytosis (1.6%), and the same peripheral smear findings defined before with the addition of polychromasia. Except for mild elevations alanine aminotransferase (70 U/L), triglyceride (223 mg/dl), and unconjugated bilirubin (2.1 g/dl), biochemical tests were normal, as well as haptoglobin, G6PD, Coombs', and cold agglutinin studies. Erythrocyte half-life studies demonstrated a normal life span of red blood cells. Prothrombin and partial thromboplastin times were longer than in controls. Radiological evaluation revealed typical changes for GD on femur, tibia and pelvic X-rays. Bilateral maxillary and frontal sinuses also seemed to be obliterated on the Waters radiography (Fig. 2b). Abdominal ultra-sonography revealed a huge, hyperechogenic, nodulated liver. Scintigraphic examination did not show any accesory spleen. Contrast echocardiography revealed multiple diffuse pulmonary arteriovenous shunting. Her leukocyte beta glucosidase activity was found low (0,29 μmol/gh, normal range 1-5) and plasma chitotriosidase activity high (> 180 μmol/gh, normal range 4-76), typical for GD. She was found to carry N370S mutation, as a heterozygote, but no other mutation could be demonstrated after screening for the six most common.

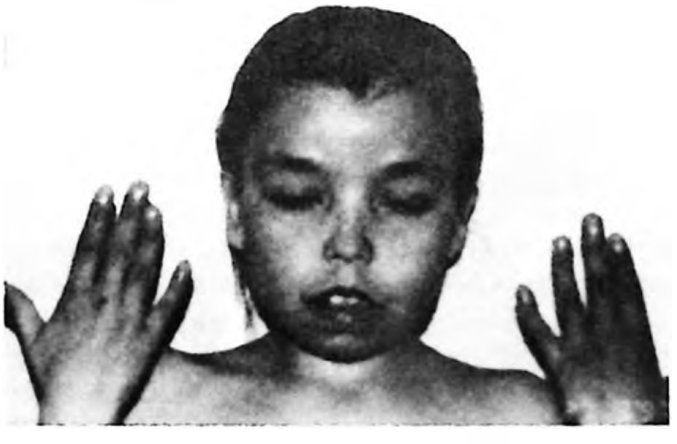

Fig. 1b. Facial appearance of Case 2.

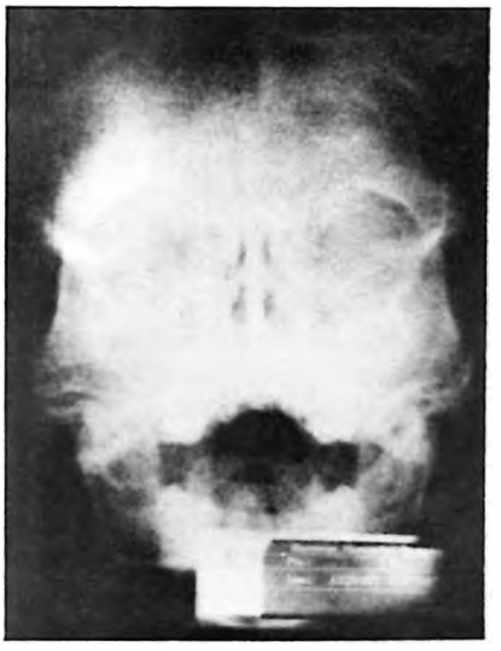

Fig. 2b. Waters radiograph of Case 2 showing no pneumatization in paranasal sinuses and coarse trabeculation of maxilla and mandibula.

## Discussion

These two well documented GD type I patients are interesting on two points: the phenotypic and radiological findings resembling thalassemia major and the multiple pulmonary arteriovenous fistulas. Radiological bone changes in chronic adult type GD include failure of remodeling that produces the Erlenmeyer flask deformity, osteopenia, osteosclerosis, joint degeneration, ischemic necrosis, bone destruction, and pathologic fractures[4]. Bone lesions due to Gaucher cell infiltration of the bone marrow are present in 50 to 75% of the patients, and are usually associated with atrophy of marrow cells and fibrosis. Destruction of bone results from multiplication of Gaucher cells packed in the intramedullary spaces, expansion of cortical spaces, pressure atrophy and ischemic necrosis. The femur is the most commonly affected bone. Spine, hips, shoulders, tubular bones, and the pelvis are the other frequent sites of involvement. Mandibular and maxillary involvement is rarely reported in GD[6,7]. Among 16 cases aged between 12-67 years, most discovered incidentally on routine dental radiographs only one patient had pacification of maxillary sinuses by a thick yellow material consisting of Gaucher cells and signs compatible with chronic sinusitis such as fever and headache[8]. This patient did not have any atypical facial appearance or jaw bone changes. Our patients differ from the above-mentioned case as they showed sinus opacification together with maxillary and mandibular destruction, at a relatively young age, and typical facial appearance resembling thalassemia major. Sphenoid bone involvement present in our first case, and severe maxillary and mandibular coarse trabeculation (in both cases) resulting in a foam-like appearance have also not been reported in GD before. The basic process of bone involvement in GD is similar to that in other diseases where proliferation or infiltration of bone marrow takes place. Coarsening of the bony textural pattern may occur in a wide variety of diseases including the congenital anemias. In thalassemias, extreme hypertrophy of the bone marrow in medullary and sometimes extramedullary sites, in order to compensate for chronic hemolysis, is well known. Involvement of the facial skeleton because of the proliferation of bone marrow resulting in severe disfigurement has been described in some reports[5]. The typical facial appearance of thalassemia major in inadequately transfused patients develops as a result of these changes. Maxillary overgrowth, displacement of teeth, prominence of malar bone, retraction of upper lip, malocclusion, and depression of the nose are well known features. Paranasal sinus obliteration and coarse trabeculation of the jaws are also reported[9]. Our two patients showed all these typical findings, but not diploic space widening on lateral skull X-ray, which is an outstanding feature of thalassemia. At the same time, they did not have thalassemia or any other hemolytic condition. The mechanism is probably the same: widening of the bone marrow because of heavy infiltration of Gaucher cells and to compensate for chronic anemia. Severity of skeletal changes due to Gaucher disease does not necessarily correlate with the size of the liver or spleen or bone marrow findings[2]. Splenectomy does not influence the natural course of bone disease, though the opposite was believed for long time. People who undergo splenectomy have the same incidence of significant bone involvement at autopsy, as do those who did not have their spleen removed[4]. However, anemia may contribute to the osseous changes by stimulating the activity of the bone marrow, thus creating more space for the invasion of foamy cells.

Gaucher disease is commonly accompanied by anemia. Its pathogenesis is complex and not well understood. It is usually ascribed to the replacement of bone marrow with Gaucher cells, occasionally due to hemorrhages because of thrombocytopenia and rarely an acquired hemolytic anemia. Another mechanism is that the total circulating red cell mass is in normal limits, but the plasma volume, and thus the total blood volume, is greatly expanded, so that dilutional anemia occurs[10]. Splenectomy corrects the high plasma volume and, therefore, the dilutional anemia. However, some patients become transfusion dependent in spite of the splenectomy. Red cell life span studies have demonstrated normal to reduced levels in GD[11,12]. A huge spleen traps the circulating erythrocytes, including transfused normal red cells, which in hemolysis[13]. Recurrence of anemia after splenectomy is a result of progressive bone marrow infiltration with Gaucher cells, and can lead to myelophthisis, myelofibrosis, and bone marrow failure. The mechanism was probably the same in our patients, as their anemia recurred after some years together with facial changes.

Pulmonary involvement and symptoms are rare in type I GD, and include alveolar infiltration of Gaucher cells and obliteration of gas exchange tissue[14]. Intrapulmonary shunting in cirrhosis was first described in 1956[15], and refers to the entry of systemic venous blood into the arterial circulation without exposure to alveolar oxygen. It has been reported in cryptogenic, postnecrotic, primary biliary cirrhosis; chronic active hepatitis; alpha 1 antitrypsin deficiency; Wilson's disease; and congenital hepatic fibrosis[16], but not in GD. Mechanisms of intrapulmonary shunting are thought to be: 1- an imbalance between vasoconstrictive and vasodilatory substances that are abnormally metabolized by an impaired liver, and 2- unusual regulation of certain pulmonary vessels which results in vasodilatation during hypoxia and thus impaired hypoxic vasoconstriction. Intrapulmonary shunting does not seem to be associated with liver function tests, ascites, splenomegaly, portal or pulmonary hypertension, specific types of liver disease, or digital clubbing[17]. Diagnosis is considered in patients with chronic liver disease and hypoxemia and confirmed by technetium scanning or contrast two-dimensional echocardiography with intravenous injection of isotonic saline or indocyanine dye. The diagnosis was made by echocardiography in our patients. It would be possible to explain intrapulmonary shunting in these children with GD if cirrhosis was demonstrated, but they did not have cirrhosis. Although liver enlargement and dysfunction are common in GD, cirrhosis is seen in relatively few cases and hepatic failure is rare[18]. Osteoporosis and osteomalacia can result in rib fractures and abnormalities of the thoracic cage which may cause reductions in lung volume. Severe rib involvement in both of our cases may have contributed to hypoxia, but is not adequate to explain the development of pulmonary arteriovenous fistulas.

Another interesting point about these cases is that, despite coming from the same region of the country, without any consanguinity between the two families, and having a very unique and similar course, these girls are not similar genetically. The first patient carries N370S and L444P mutations as a compound heterozygote, while the second has N370S mutation as a heterozygote but no other detected mutation after screening for six common ones. Just as considerable heterogeneity in phenotype is sometimes apparent among siblings who have inherited identical disease producing alleles[19], the opposite is also possible: different genotypes can result in similar phenotyhes.

These two cases with thalassemic face, obliteration of paranasal sinuses, and intrapulmonary shunting, all unusual findings in GD, may be examples of a new clinical subtype.

## Acknowledgement

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# Abetalipoproteinemia: a case report

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SUMMARY: Selimoğlu MA, Eşrefoğlu M, Gündoğdu C, Kılıç A. Abetalipoproteinemia: a case report. Turk J Pediatr 2001; 43: 243-245.

Abetalipoproteinemia is a rare autosomal recessive disorder characterized by steatorrhea, poor weight gain, acanthocytosis and retinitis pigmentosa. Here we peresent a six-month-old patient with abetaliporoteinemia.

He had a history of chronic diarrhea from the first month of life. He was cachectic and his motor development was delayed. Microscopic examination of the stool revealed fat. Mild anemia with reticulocytosis, acanthocytosis, low triglyceride, low cholesterol, low-density lipoprotein, high-density lipoprotein, and apolipoprotein A and B were detected. Ophthalmological examination was normal. Peroral jejunal capsule biopsy revealed normal villi and significant lipid deposition in the cytoplasm of affected cells. The patient was given large doses of vitamins E and A.

*Key words: abetalipoproteinemia, acanthocytosis, steatorrhea.*

Abetalipoproteinemia (ABL) is a rare autosomal recessive disorder in which patients are unable to produce the apolipoprotein B moiety of the beta-lipoprotein. This results in an inability to transport lipid material out of the intestinal epithelial cells, and a foamy lipid material accumulates within the cell cytoplasm[1]. It was first described in two siblings of consanguineous parents who developed progressive ataxia in association with fat malabsorption, atypical retinitis pigmentosa and abnormally formed red cells which were later termed acanthocytes[2]. This rare disorder is characterized by steatorrhea, poor weight gain, acanthocytosis and retinitis pigmentosa[1,3]. The first Turkish case was reported by Özsoylu et al.[4] in 1985. We present here an infant with ABL to emphasize the diagnostic role of peripheral smear, serum triglyceride, and cholesterol levels in patients with failure to thrive and steatorrhea.

## Case Report

A six-month-old male infant was admitted to our hospital with a history of chronic diarrhea characterized by green and foul smelling stool since the first month of his life. He was the second child of healthy nonconsanguineous parents. Family history was unremarkable. After two months of breastfeeding, a commercially available formula was introduced because of failure to gain weight. His body weight was 3330 g, length was 58 cm (both below 3rd percentile), ratio of midarm circumference to head circumference was 0.20 (severe malnutrition), and relative weight was 65%. His motor development was delayed and ophthalmological examination was normal. He had no organomegaly.

Laboratory tests revealed: hemoglobin 8.8 g/dl and mean corpuscular volume 75 fl. A slight reticulocytosis was detected (4%). In peripheral blood smear acanthocytosis was observed (Fig. 1). His blood biochemistry revealed low triglyceride (8 mg/dl) cholesterol (48 mg/dl), low-density lipoprotein (LDL) (20 mg/dl, normal: 65-150 mg/dl), high-density lipoprotein (HDL) (34 mg/dl, normal: 35-60 mg/dl), apolipoprotein A (apo A) (84 mg/dl, normal: 94-199 mg/dl) and B (apo B) (< 35 mg/dl, normal: 49-109 mg/dl). Prothrombin time was 16 seconds. Serum aspartate aminotransferase and alanine aminotransferase levels were 95 U/L and 82 U/L, respectively. Serum albumin was within normal limits. Sweat test was negative. Stool was positive for fat. Peroral jejunal capsule

biopsy samples were prepared as frozen sections, and stained with hematoxylin-eosin (HE) and Sudan black. On light microscopy, the villi were of normal height; the cells lining the crypts and those in the lamina propria were normal. Epithelial cells covering the villi were columnar, with basal nuclei surrounded by vacuolated, foamy cytoplasm (Figs. 2-4). Frozen sections stained with Sudan black showed significant lipid deposition in the cytoplasm of affected cells. Thus, cytoplasm of columnar cells covering the tips of the villi reacted strongly with the Sudan black (Fig. 5). In order to make the diagnosis of homozygous hypobetalipoproteinemia, LDL and apo B levels of the mother were studied and were within normal limits.

The patient was given large doses of vitamins E and A (200 mg/kg/day and 20,000 IU/day, respectively) and a diet containing 180 kcal/kg/day energy.


Fig. 3. Villus is intact. Epithelial cells have many vacuoles in their cytoplasm (arrow). Nuclei which are located basally are seldom observed. Lamina propria containing blood vessels (b) is observed beneath the epithelium (HE X 20).

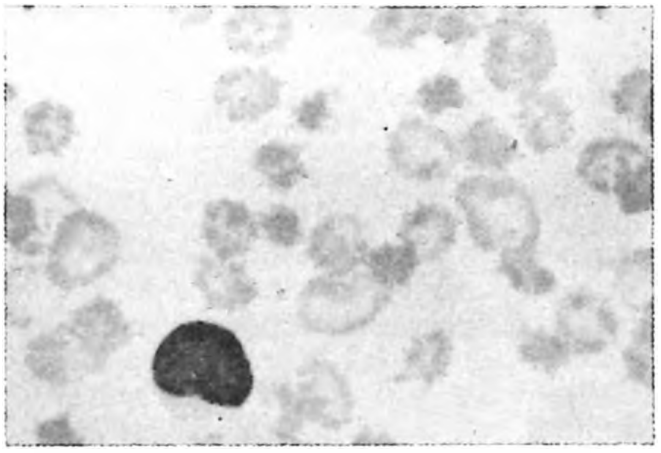

Fig. 1. Peripheral blood smear contains numerous acanthocytes (Wright-Giemsa, oil immersion X 100).

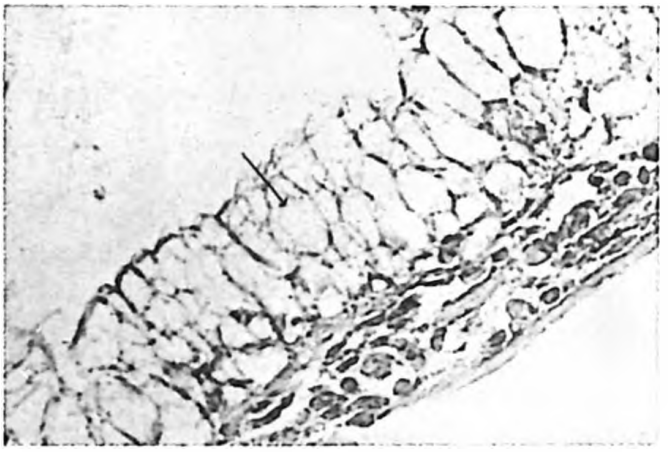

Fig. 4. Cytoplasms of the epithelial cells have foamy appearance. Nuclei are not observed in most of cells (HE X 40).

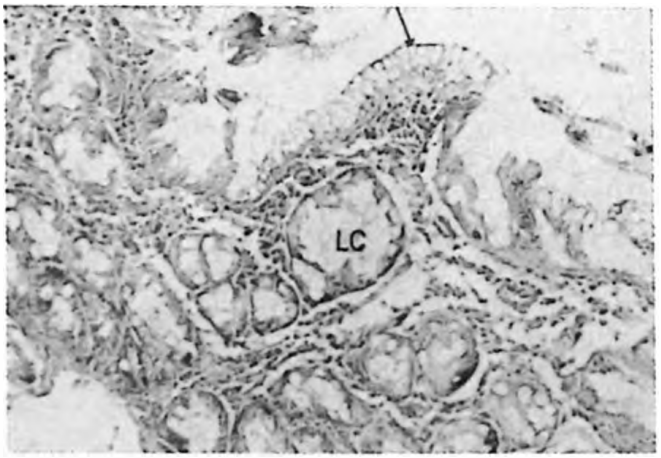


Fig. 2. Simple columnar epithelium composed of cells containing many clear vacuoles (arrow) in their cytoplasm. Lieberkühn's crypts (LC) in the lamina propria are seen (HE X 10).

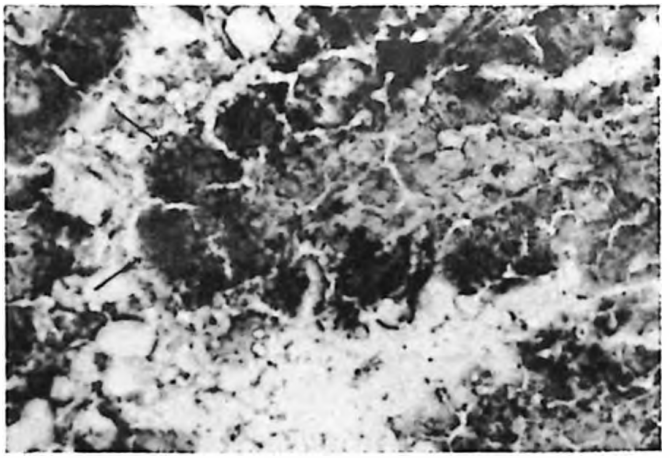

Fig. 5. Cytoplasm of the cells covering the villi react strongly with Sudan black (arrow). These cells have lipid deposition in their cytoplasm. Lipid droplets stained blue-black are observed (Sudan black X 20).

## Discussion

Clinical findings of ABL are usually a result of the low absorption and transport of lipids, especially the fat soluble vitamins, A, D, E, and K[1,5]. Malabsorption of fat is common in ABL and often begins in infancy with steatorrhea and poor weight gain. Children with ABL have often been misdiagnosed as having celiac disease[3,5]. In addition to ABL, cystic fibrosis, combined immune deficiency, Wolman's disease and chylomicron retention disease should be kept in mind in infants with steatorrhea beginning in the first months of life[1].

The most prominent and debilitating symptoms are neurological and usually begin in the second decade. The first sign of disease is usually the loss of deep-tendon reflexes, followed by decreased distal lower extremity vibratory and proprioceptive senses and cerebellar signs[3,5]. Although our case was only six months old, his motor development was delayed. Patients with ABL develop atypical retinitis pigmentosa, but it is not seen until the adolescent period[1,3,6]. The ophthalmological examination of our case was normal. Oral vitamin E was given because of its preventive role[7].

Acanthocytosis is widely recognized as a typical feature of ABL in over 50% of red cells[8]. The total content of phospholipids in acanthocyte membranes is normal but their distribution is distinctly abnormal[8]. We observed acanthocytosis in our patient. The most dramatic finding may be the lipid and lipoprotein profile with a total cholesterol level from 20 to 50 mg/dl, low triglyceride levels, and negligible levels of VLDL, LDL, and apo B[3,9]. In the patient with ABL, most of the cholesterol and triglyceides are present in HDL; however, even the HDL levels are lower than normal[1,3].

Recently, it was reported that the lack of synthesis of apo B-48 is not due to the absence of the gene on chromosome 2[1,10]. The microsomal triglyceride transfer protein (MTP) is a heterodimer composed of the multifunctional enzyme, protein disulfide-isomerase, and a unique large, 97-kDa, subunit. It is found as soluble protein within the lumen of the endoplasmic reticulum of the liver and intestine and is required for the assembly of VLDL and chylomicrons[11]. Chromosome 4 includes the MTP gene (4q22-24). Mutations in the 97-kDA subunit of the MTP which result in an absence of MTP functions have been shown to cause ABL[12,13]. Jejunal biopsy is diagnostic in ABL. The appearance of the jejunal biopsy herein described was essentially similar to those in previous reports[1,14]. Treatment consists of high doses of vitamins A and E.

We present this rare genetic disease to emphasize the dignostic role of peripheral smear, serum triglyceride, and cholesterol levels in patients with failure to thrive and steatorrhea.

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# A case of Netherton's syndrome with cerebral infarction

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SUMMARY: Çalıkoğlu E, Anadolu R, Şanlı H, Erdem C. A case of Netherton's syndrome with cerebral infarction. Turk J Pediatr 2001; 43: 247-249.

Netherton's syndrome, a rare congenital disease of childhood, is characterized by variable cutaneous erythematous eruptions with different manifestations. A five-year-old boy, who presented with ichthyosis linearis circumflexa, atopic manifestations and pili torti, had spastic hemiparesia due to cerebral infarction. Netherton's syndrome can easily be misdiagnosed as Leiner's disease, generalized psoriasis or nonbullous congenital ichthyosiform erythroderma, especially in the neonatal period, because of its nonspecific clinical and histological features. Pediatricians should consider this syndrome in the differential diagnosis of the generalized erythematous skin disorders of childhood associated with various abnormalities.

*Key words: erythematous eruption, atopic manifestation, hair shaft keratinization defect, autosomal recessive inheritance, spastic hemiparesia.*

Netherton's syndrome is a rare congenital disease characterized by hair shaft keratinization defects, atopic manifestations and variable erythematous skin eruptions. Here we present a case of Netherton's syndrome with spastic hemiparesia due to cerebral infarction.

## Case Report

A five-year-old boy, born to consanguineous parents who were cousins, was admitted to our hospital with erythematous skin lesions in July 1999.

Because of generalized exfoliative erythroderma in the neonatal period, he was hospitalized and treated with antibiotics against suspected sepsis.

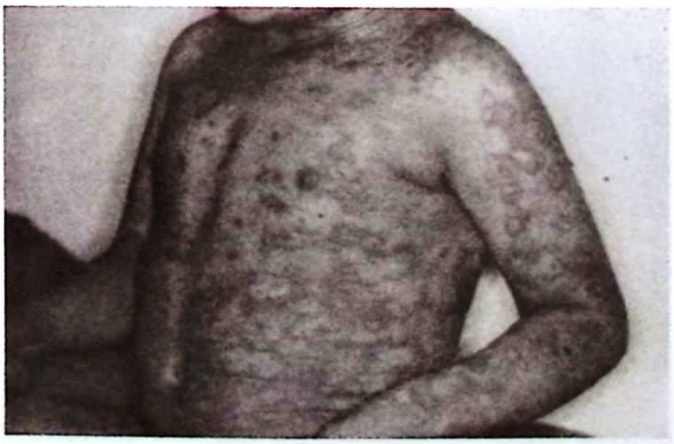
Physical examination revealed bilateral allergic conjunctivitis and spastic hemiparesia on the right side of the body with augmented deep tendon reflexes. There was no abnormality in the other organ systems.

Dermatological examination showed generalized erythematosquamous eruptions (Fig. 1a) and some annular erythematous plaques with a double-edged scaly rim on the extremities (Fig. 1b). Thick, adherent and yellow scales covered especially the scalp hair and forehead. There was some sparse and fragile hair on the vertex. Polarization microscopy of scalp hair showed small fractures and pili torti (Fig. 2).

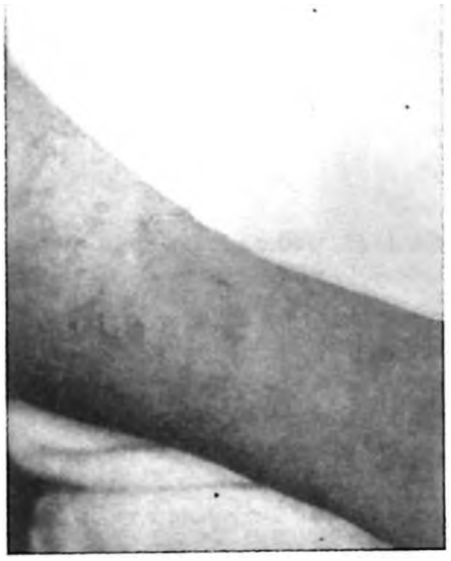
Complete blood counts, urinalysis, erythrocyte sedimentation rate, liver function tests, renal function tests, electrolytes, total proteins, and amino acid profile were normal. Total IgE level was 2,000 IU/L (normal range: 0-100 IU/L).

Magnetic resonance (MR) imaging of the brain showed encephalomalasia with multiple cysts secondary to cerebral infarction as a result of occlusion of the arteria cerebri media (Fig. 3).

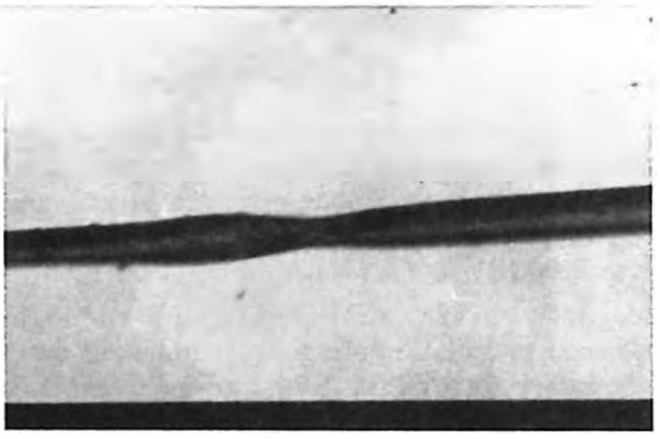
The dermatopathologic examination revealed marked papillomatosis. The stratum corneum was thick and the granular layer decreased. This biopsy specimen was reported as psoriasiform dermatitis.



Fg. 1a. Generalized erythematous skin eruptions of the patient.



Fg. 1b. Characteristic annular erythematous plaques with a double-edged scaly rim on the extremities of the patient.



Fg. 2. Pili torti is seen on the polarization microscopy.

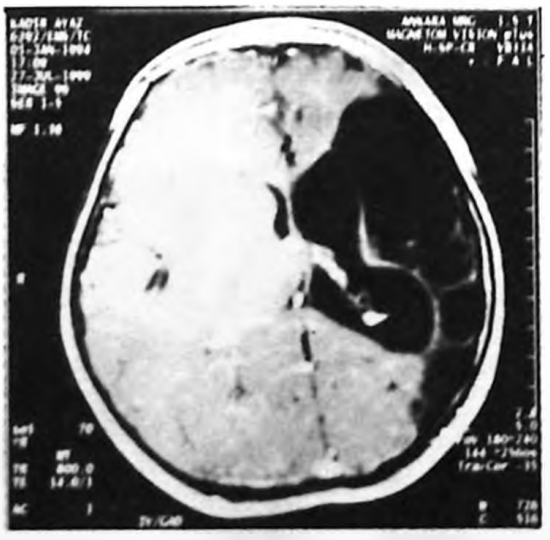


Fig. 3. T1 weighted magnetic resonance imaging of the brain showed encephalomalasia with multiple cysts secondary to cerebral infarction.

## Discussion

Netherton's syndrome is a rare and severe autosomal recessive disease characterized by hair shaft keratinization defects, atopic manifestations and variable erythematous eruptions ranging from congenital ichthyosiform erythroderma to ichthyosis linearis circumflexa (ILC)[1-3].

Netherton's syndrome causes severe neonatal disease which can be easily misdiagnosed as Leiner's disease, generalized psoriasis or nonbullous congenital ichthyosiform erythroderma because of the nonspecific histological features[2,4]. The patients develop generally migrating erythematous patches with a double-edged scaly rim, one of the characteristic signs of ILC, after two years of age[3]. Infrequently, hypernatremia, aminoaciduria, mental deficiency, neurological defects, delayed growth, recurrent infections and hyper- or hypoglobulinemia may be detected in the neonatal period[1].

The patient had a history of neonatal sepsis. Spastic hemiparesia was detected in his neurological examination. MR imaging of the brain revealed cerebral infarction due to occlusion of the arteria cerebri media with unknown etiology.

The histopathologic features of ILC are frequently indistinguishable from psoriasis or seborrheic dermatitis[5]. Yoshiike et al.[6] detected many clinical, morphological and biochemical similarities between ILC and psoriasis. It is believed that Netherton's syndrome is a hyperproliferative situation with a reduced epidermal transit time. The biopsy specimen of the patient was reported as psoriasiform dermatitis.

Trichorrhexis nodosa, pili torti, monilethrix, angle-bent hair and trichorrhexis invaginata may develop in patients as hair shaft defects of the syndrome[1]. The polarization microscopy showed pili torti.

Atopic manifestations can be seen in the syndrome[7]. Allergic conjunctivitis was observed in the patient's physical examination, and total IgE rate was elevated. Topical tretinoin, local corticosteroid, emollients and cyclosporine have been used in the treatment of Netherton's syndrome. However, no single treatment showed sufficient beneficial results[1,8]. A relative reduction in the severity of the lesions was achieved with cyclophosphamide therapy[9]. Low-dose retinoid therapy and PUVA seem to also be effective[10-12].

The patient's parents refused all treatment modalities aside from topical emollients.

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# Complex partial seizure mimicking psychotic reaction in an adolescent

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SUMMARY: Serdaroğlu A, Gücüyener K, Bilir E, Soysal Ş. Complex partial seizure mimicking psychotic reaction in an adolescent. Turk J Pediatr 2001; 43: 251-253.

**A previously healthy 15-year-old boy initially diagnosed to have acute psychotic reaction had a history of a single generalized seizure and prolonged amnestic states of varying intensity and duration. An ictal electroencephalogram (EEG) showed bitemporal ictal discharges starting from the left side. Carbamazepine was started. A magnetic resonance imaging (MRI) obtained on the 10th day of the antiepileptic therapy showed increased signal intensity on the T2 weighted images. The patient's memory function markedly improved during 10 months' follow-up with antiepileptic treatment, although he described brief attacks of dizziness. A repeat MRI examination showed normal findings. The amnestic states were thought to be due to frequent complex partial seizures, and transient MRI changes to hippocampal edema. This case illustrates the importance of epileptic disorders in the differential diagnosis of psychiatric conditions.**

*Key words: complex partial seizure, psychotic reaction, MRI changes.*

The hippocampus, a deep structure of the mesiotemporal lobe, is critically important for the regulation of short-term memory[1]. Electrical stimulation or transient ischemia of the mesiotemporal lobe causes transient global amnesia (TGA)[2,3]. The pathophysiology of TGA is still unclear; factors other than ischemia influencing the deep temporal structures may be responsible[4]. We present a 15-year-old boy with complex partial seizures and prolonged amnesia who was misdiagnosed with a psychotic reaction.

## Case Report

A 15-year-old right-handed boy was admitted to the emergency room with a history of a single generalized seizure and loss of consciousness. He had generalized tonic-clonic movements lasting for two or three minutes followed by 30 minutes of somnolence. No aura was described. The history included memory disturbances for the past two months: the patient could not remember most of the events that had occurred during this period. Once he had entered another classroom instead of his own. He had been seen by a child psychiatrist and diagnosed with an acute psychotic reaction triggered by his grandmother's death. His past family and medical histories were significant for an uncomplicated febrile convulsion at age two. He had been a healthy child otherwise. Two previous electroencephalograms (EEG) and cranial computerized tomography (CT) were normal.

In the emergency room he was an alert pleasant boy with stable vital signs. Physical examination was normal. On mental status examination, he was oriented to person, place, year and month, but not to date. Serial events and calculations were intact. Judgement and interpretation were normal. He had some disturbance in immediate- and short-term memory, and he could not remember any details of subjects told in the class. However, he was not seriously concerned with his memory impairment. The rest of the neurological examination was normal. Laboratory studies including complete blood count (CBC), electrolytes, cerebrospinal fluid antibodies, herpes simplex type I-II, rubella, rubeola, adenoviruses, Epstein-Barr virus (EBV) and oligoclonal band were all negative. A routine scalp 16 channel EEG and cranial CT scan with contrast injection were normal. During long term EEG monitoring there were bitemporal ictal discharges starting from the left side and quickly spreading to other parts of both hemispheres. The initial abnormality consisted in 4-5 Hz, 30-

70 microvolt rhythmic sharp waves beginning in the left temporal region and becoming bilateral in one second, with maximal amplitude at electrodes T3 and T5. The discharges lasted 30 seconds and were followed by diffuse 2-3 Hz irregular slowing with no lateralization. He was unable to carry on a conversation during ictal discharges. Medical treatment with carbamazepine (CBZ) (400 mg/day) was initiated. Magnetic resonance imaging (MRI) was obtained at the 10th day of the CBZ treatment. $T_2$ weighted CTR/TE/NER showed increased signal intensity at the hippocampi bilaterally (Fig. 1). Three months later, his memory function was improved. On nine months' follow-up he had no recurrent amnestic episodes, but had infrequent, brief attacks of dizziness with transient impairment of consciousness. EEG after 10 months was completely normal and the follow up MR examination demonstrated no signal change of the hippocampus (Fig. 2).

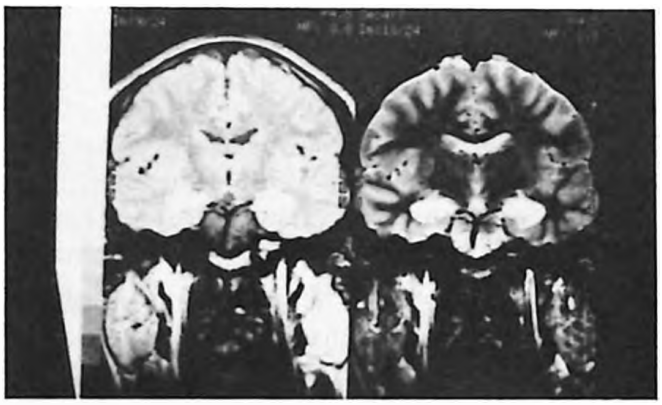

Fig. 1. T2 weighted images of the initial MRI demonstrated high signal intensity of the bilateral hippocampal region with no apparent structural change.

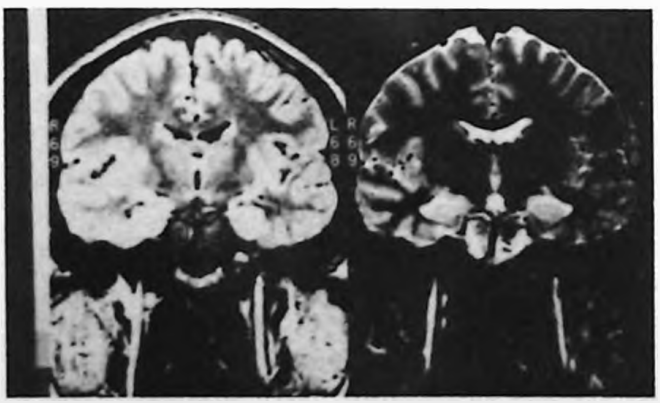

Fig. 2. Ten-month follow-up MRI demonstrated marked improvement with no obvious signal range of the hippocampus.

## Discussion

This patient's amnestic states can be explained by both ictal and postictal changes. The hippocampus has been known for a long time to be critical for the formation and recall of short-term memory[1]. A previous study has suggested interictal epileptiform discharges due to transient global amnesia in epileptic patients[4].

The hippocampal lesion in our patient's MRI was a focal signal intensity change; no mesiotemporal sclerosis or hippocampal atrophy was observed. The differential diagnosis of focal signal intensity changes in patients with complex partial seizures includes vascular, neoplastic and inflammatory disorders. This differentiation can be especially difficult in patients with status epilepticus. The reversibility of the findings on consecutive MRIs in accordance with clinical improvement of memory supports hippocampal edema[6-8]. Reversible focal CT or MRI abnormalities have been reported in epilepsy due to cerebral edema resulting from increased energy requirement during repetitive ictal discharges, increased regional cerebral blood flow, or regional breakage of the blood brain barrier[5,6]. Sammantino et al.[5] described three patients with striking focal cerebral edema whose neurological deficits resolved as the edema regressed gradually, although the resolution of images on serial CT scans usually lagged behind clinical improvement.

This patient probably had frequent temporal lobe complex partial seizures in the previous two months. He presented with gradually increasing memory disturbance and unusual behavior as the most prominent complaints. More subtle symptoms such as brief episodes of unconciousness or dizziness were probably missed by his parents, pediatrician and child psychiatrist. He therefore had received the diagnosis and treatment of acute psychotic reaction. This case exemplifies the importance of careful investigation for epileptic disorders in patients presenting with psychiatric symptoms.

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# Megakaryocyte emperipolesis in a child with chronic neutropenia: an unusual coexistence

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SUMMARY: Aslan D, Yetgin S. Megakaryocyte emperipolesis in a child with chronic neutropenia: an unusual coexistence. Turk J Pediatr 2001; 43: 255-256.

The term emperipolesis defines the temporary presence of one cell within another's cytoplasm. In clinical use, megakaryocyte emperipolesis is the penetration of hematopoietic cells into the cytoplasm of megakaryocytes. The pathophysiological significance of megakaryocyte emperipolesis is uncertain. It has been described in association with neoplastic disorders, and in a few instances in idiopathic thrombocytopenic purpura, iron deficiency anemia, bleeding, and during the administration of recombinant human granulocyte colony-stimulating factor. However, megakaryocyte emperipolesis in a patient with chronic neutropenia has not been reported. In the current report, emperipolesis of hematopoietic cells within megakaryocytes in a boy with chronic neutropenia is described and the possible mechanisms are discussed.

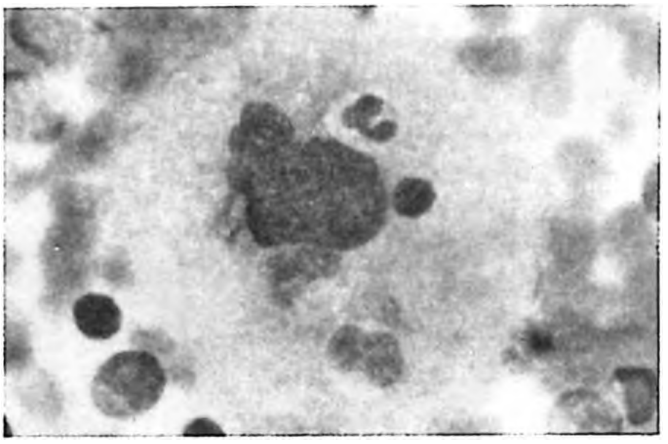
*Key words: megakaryocyte emperipolesis, chronic neutropenia.*

Marrow cells may enter megakaryocytes by a phenomenon that is referred to as emperipolesis[1]. Although the morphological appearance of this process is quite striking, the pathophysiological significance of mekaryocyte emperipolesis is uncertain. It has been described in association with neoplastic disorders[2,3], and in a few instances in idiopathic thrombocytopenic purpura (ITP), iron deficiency anemia[4], bleeding[1], and during the administration of recombinant human granulocyte colony-stimulating factor (rhG-CSF)[5], in order of decreasing frequency. However, megakaryocyte emperipolesis in a patient with chronic neutropenia (CN) has not been reported. In this article, emperipolesis of hematopoietic cells within megakaryocytes in a boy with CN is described.

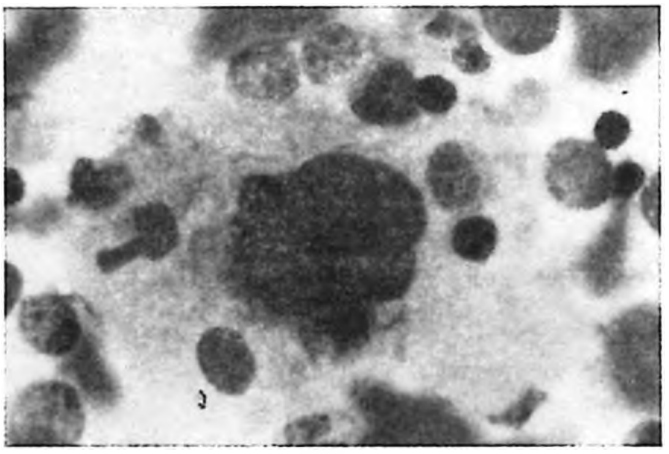
## Case Report

A four-year-old boy was admitted with the complaint of bilateral earache. Physical examination revealed bilateral redness and swelling of the tympanic membranes consistent with otitis media. His hemoglobin level was 10.9 g/dl, white blood cell (WBC) count $3.0 \times 10^9$/L with 10% neutrophils, 68% lymphocytes, 16% monocytes, and 6% eosinophils, and platelet $316 \times 10^9$/L. His past history revealed recurrent infections (2 episodes of otitis media, 2 of sinusitis, and 1 of acute gastroenteritis) between the age of one and four years. Neutropenia was found to be constant during a follow-up period of two months (WBC mean $2.7 \pm 0.2$, range $2.4\text{-}3.1 \times 10^9$/L; absolute neutrophil count mean $322 \pm 121$, range 156-540). Immunoglobulin levels were within normal range and viral markers such as cytomegalovirus, herpes simplex virus, hepatitis B virus, and hepatitis C virus were negative. In his past history there was neither a chronic use of any drug nor an exposure to chemicals. There was no evidence of any systemic illness. The complete blood counts and the total neutrophil counts of the peripheral blood of the parents were within normal limits.

In bone marrow aspiration smear emperipolesis of hematopoietic cells (cells of myelocytic origin, lymphocytes, and normoblasts) by megakaryocytes was observed (Figs. 1a, 1b). Cells of myelocytic origin were the most comon marrow cell engulfed by megakaryocytes. The patient was treated with antibiotics for otitis media. Megakaryocyte emperipolesis in bone marrow smear and neutropenia were noted to be persistent six weeks after the first marrow.



(a)



(b)

Figs. 1a and b. The phenomenon of emperipolesis with megakaryocytes containing cells of myelocytic origin, lymphocytes, and erythroid precursors.

## Discussion

Emperipolesis is a phenomenon characterized by the temporary presence of one cell within another's cytoplasm, but it differs from phagocytosis in that the engulfed cell remains viable and can ultimately exit from the engulfing cell. Electron microscope findings by Larsen[6] demonstrated that neutrophils engulfed by megakaryocytes had intact membranes. Although all types of marrow cells (myelocytic, erythroid, and lymphoid) have been involved in emperipolesis by megakaryocytes, mature neutrophils are the most common. It is widely accepted that megakaryocytic emperipolesis is possibly mediated by some adhesion molecules[7] and by IgG bound to the surface membrane of hematopoietic cells[5].

Megakaryocyte emperipolesis has been most often reported in association with neoplastic disorders (e.g. lymphoma, Hodgkin's disease, lymphocytic leukemia, myelodysplastic syndrome, myeloma, carcinoma, neuroblastoma), and in a few instances in ITP, iron deficiency anemia, bleeding, and during the administration of rhG-CSF. However, to our knowledge, megakaryocyte emperipolesis in association with CN has not been reported previously. In the present case a diagnosis of CN was made based on recurrent infections starting from the first year of age and persistent neutropenia.

Several possibilities could be considered for the association of megakaryocyte emperipolesis and CN. 1) Megakaryocyte emperipolesis is most often described in association with malignancy, and since CN is regarded as a premalignant condition, emperipolesis should be an expected feature of CN. 2) In our patient neutropenia might be a secondary phenomenon due to the engulfment of myelocytic cells by megakaryocytes. 3) Some serological or cell membrane changes due to frequent bacterial infections associated with chronic neutropenia might be the cause of this phenomenon.

Therefore, we suggest that evaluation of patients with CN is required for a definite conclusion about the relationship between CN and megakaryocyte emperipolesis.

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# Anomalous origin of one pulmonary artery branch from ascending aorta ("so-called hemitruncus"): report of an additional case treated surgically

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SUMMARY: Doğan R, Çeliker A, Farsak B. Anomalous origin of one pulmonary artery branch from ascending aorta ("so-called hemitruncus"): report of an additional case treated surgically. Turk J Pediatr 2001; 43: 257-260.

The aortic origin of one pulmonary artery branch, so-called hemitruncus, is a rare congenital anomaly with poor prognosis. In this report, an additional patient is presented. The patient, a 60-day-old male infant with the right pulmonary artery originating from the ascending aorta was operated successfully. Postoperative catheterization demonstrated normal flow to the right lung and pulmonary artery pressure decreased to normal level.

*Key words: hemitruncus, anomalies-pulmonary artery, abnormalities-lung.*

Origin of a pulmonary artery branch from the ascending aorta (so-called hemitruncus) was first reported by Fraentzel in an adult patient in 1868[1]. Approximately 90 patients with anomalous origin of one pulmonary artery (PA) from the ascending aorta have been described in the literature[2-9]. The malformation is more often recognized in neonates and infants as relentless heart failure. The most prominent clinical feature in patients surviving into adulthood is dyspnea on exertion and recurrent hemoptysis. Early diagnosis and corrective surgery is the treatment of choice to avoid pulmonary vascular obstructive disease (PVOD).

We report an additional case of anomalous origin of one pulmonary artery from the ascending aorta, diagnosed by cardiac catheterization and angiography, who underwent successful hemodynamic repair.

## Case Report

A male infant weighing 4,100 g was born at term following an uncomplicated pregnancy. He initially seemed well, but was taken to another hospital at four weeks of age because of feeding difficulties and dyspnea. He was referred to our hospital at 55 days of age because of congestive heart failure. He was found to be in severe congestive heart failure and was treated with digitalis and diuretics. The precordium was hyperdynamic. A grade 3/6 continuous murmur was heard along the left sternal border. The liver's edge was 4 cm below the right costal margin. The arterial $PO_2$ was 64 mmHg with an oxygen saturation of 72%. Despite medical therapy, the patient's heart failure did not improve.

Two-dimensional echocardiography revealed the origin of the right pulmonary artery from the ascending aorta, patent ductus arteriosus (PDA) and moderate tricuspid regurgitation. Cardiac catheterization (Table I) and angiography (Fig. 1) confirmed the diagnosis. The patient was then transferred to the Cardiac Surgery Department, and the operation was undertaken on the following day. At operation, via median sternotomy, it was observed that the right PA originated from the posterior wall of the ascending aorta. The PDA was exposed and occluded with a snare. By means of standard bicaval cannulation and hypothermic (24 °C) cardiopulmonary bypass, main PA, right PA and ascending aorta were mobilized. First, the aorta was opened transversely on its anterior surface just at the level of the right PA connection. The right PA orifice was found to be slightly stenotic and was excised with a button, containing a part of the posterior aortic wall. The right PA orifice

was enlarged with an anterior autologous pericardial patch to ensure construction of a widely patent tension-free anastomosis. It was then sutured to the main PA, placed posteriorly to the aorta. The aortotomy was closed primarily, and the PDA was divided and oversewn (Fig. 2).

The patient tolerated the operation well. He was discharged on the 9th postoperative day receiving digoxin only. At cardiac catheterization six months postoperatively, the PA pressure was normal and there was no gradient across the anastomosis (Figs. 3, 4). On follow-up 24 months after surgery, he appeared to be a normal, very active boy.

Table I. Preoperative and Postoperative Catheterization Data

| | Pre-op | Post-op (13th month) |
|---|---|---|
| Pressure (mmHg) | | |
| MPA | 76/36 (51) | 27/4 (13) |
| RPA | 66/33 (50) | 26/4 (13) |
| RV | 87 | 27 |
| LV | 91 | 97 |
| Ao | 91/64 (74) | 97/60 (68) |
| Oxygen saturation | | |
| MPA | 53 | 62 |
| RPA | 83 | 84 |
| RV | 44 | – |
| LV | 90 | 97.1 |
| Ao | 75 | 98 |

MPA: Main pulmonary artery. RPA: Right pulmonary artery. RV: Right ventricle. LV: Left ventricle. Ao: aorta. The value in parentheses indicates mean pressure.

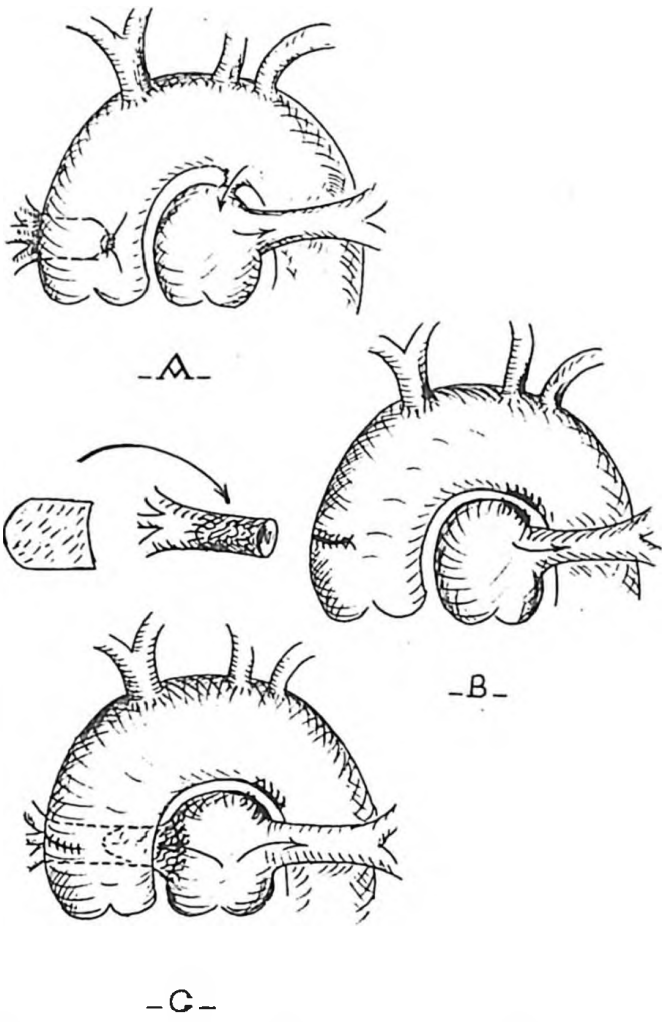
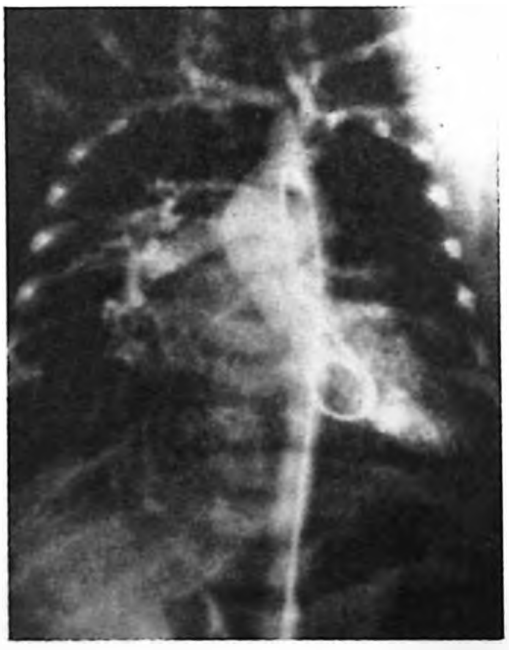
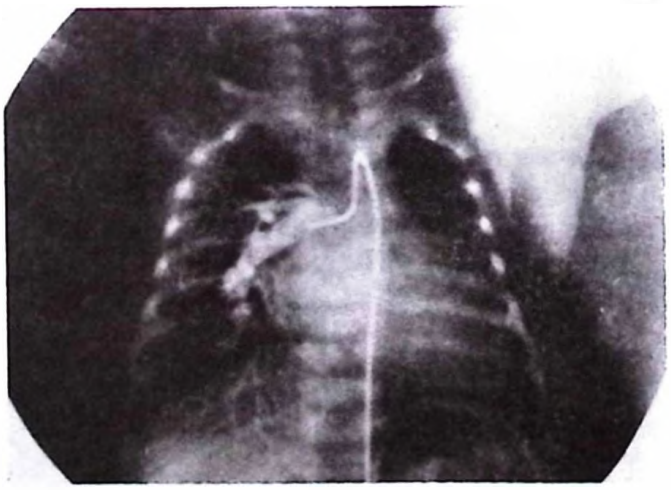



Fig. 2. Operation technique. A: preoperative view. B: the anomalous right PA is detached from the aorta with a portion of aortic wall, and the right PA orifice was enlarged with an autologous pericardial patch. C: the right PA is sutured to the main PA behind the ascending aorta.



(a)



(b)

Fig.1. Preoperative angiogram (A and B) showing anomalous origin of right pulmonary artery (RPA) branch from the ascending aorta.

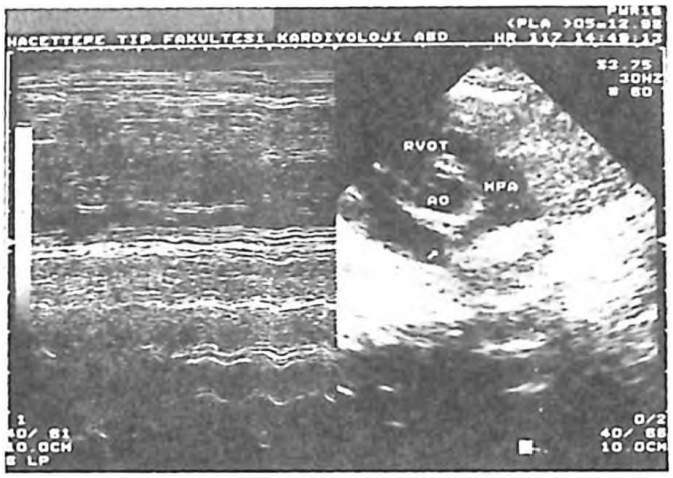



Fig.3. Parasternal short-axis view showing the right ventricular outflow tract (RVOT) and the pulmonary artery branches after correction (MPA: main pulmonary artery, LPA: left pulmonary artery, RPA: right pulmonary artery, Ao: aorta).

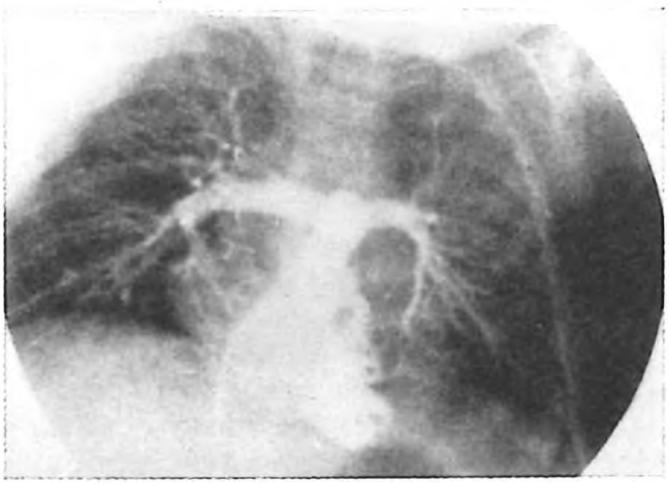


Fig. 4. Postoperative right ventricular control angiogram showing uniform distribution of pulmonary blood flow.

## Discussion

Anomalous origin of one pulmonary artery branch from the ascending aorta, also called hemitruncus arteriosus, is a rare, congenital cardiovascular malformation with poor prognosis if it is not treated surgically in early infancy[3,4,7]. Although it was first described in an adult patient by Fraentzel[1], the anomaly is more often recognized in neonates and infants; only eight patients have been diagnosed during adulthood[6,8,9]. The most common associated anomaly when the right PA is involved is a PDA, which always occurs contralaterally to the anomalous pulmonary artery. In the case of the left PA branch originating from the ascending aorta, tetralogy of Fallot is the most frequently associated malformation[4].

Penkoske and coworkers[4] stated that analysis of the literature on origin of a pulmonary artery branch being from the ascending aorta is difficult, because at least three different cardiovascular malformations have been classified as such name:[1] origin of the right or left PA from the ascending aorta;[2] absence of the proximal portion of either pulmonary artery, with the distal pulmonary artery branch being supplied via PDA;[3] absence of a proximal pulmonary artery branch, the distal pulmonary artery branch being supplied via an aorticopulmonary collateral artery, not via a PDA.

Although diagnosis of the anomaly has usually been made at cardiac catheterization[2-7], echocardiography has also been useful in infants[5,9]. Recently it was reported that the diagnosis could be made by computed tomography[6] or by magnetic resonance imaging[8].

To date, different kinds of procedures have been performed for correction. The first corrective procedure was published by Caro and coworkers in 1957[2]. An Ivalon graft was interposed between the right PA and the main pulmonary artery (MPA) in that case. Unfortunately the patient died after completion of the operation. The first successful operation using the same technique but with a Dacron graft was reported by Armer and coworkers in 1961[10]. In 1967; Kirkpatrick and coworkers[11] reported the first case in which primary anastomosis was performed between the aberrant right pulmonary artery and the MPA. Since than, many patients have undergone surgical correction in relation to their cardiac anomalies in a one-or two-stage fashion with or without the aid of cardiopulmonary bypass and hypothermia.

Because the patients surviving into adulthood are at risk for developing pulmonary vascular obstructive disease, surgical repair should be performed as early as possible in order to prevent death from congestive heart failure or the development of irreversible PVOD[1,2,8,9]. In patients with an anomalous origin of one pulmonary artery branch from the ascending aorta, the pulmonary hypertension in the main pulmonary artery and the contralateral pulmonary artery branch seems to be reversible when correction is performed in infancy[4]. However, in older children and adults, who survive to the operation, pulmonary hypertension may still persist[4,12]. Although the exact mechanism of the persistent pulmonary

hypertension in the MPA and in the protected (contralateral) lung has not been fully explained, a neurogenic crossover from the lung perfused by the aorta to the protected lung has been postulated by Griffiths and coworkers[13].

In our patient, the MPA pressure decreased from 76/36 mmHg to 27/4 mmHg after the correction. In patient with hemitruncus, diagnosis and surgical correction should be performed as early as possible to prevent death from heart failure or the development of irreversible PVOD.

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# Noncompaction of the right ventricle following Senning repair

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SUMMARY: Tavlı V, Kayhan B, Okur FF, Kozan M, Kırman M, Bakiler AR, Tekdoğan M. Noncompaction of the right ventricle following Senning repair. Turk J Pediatr 2001; 43: 261-263.

**A three-year-old boy presented with generalized edema, respiratory distress, prominent right ventricular impulse and hepatosplenomegaly. He had undergone Senning repair at one year of age. On his echocardiography, there were numerous prominent trabeculations and deep intertrabecular recesses measuring approximately 5 mm in depth along the free wall and right ventricular apex. Echogenicity of the endocardial surface was increased suggesting a fibrotic process in progress. Intertrabecular recesses were observed to be filling from the ventricle by color Doppler which is consistent with noncompaction. Various semilunar valve obstructions were shown to be responsible for the persistence of deep endomyocardial spaces surrounded by exeggerated hypertrophy of the trabeculae. This report presents the echocardiographic findings of right ventricular cardiomyopathy associated with dextroposition of the great arteries following Senning operation resembling noncompaction. Thus, this rare entity needs to be clarified regarding morphological criteria in distinction from other cardiomyopathies.**

*Key words: Senning repair, cardiomyopathy, noncompaction.*

Postnatal persistence of spongy myocardium with embryonic blood supply may accompany a number olf congenital defects. Deep intertrabecular recesses and prominent trabeculae are features of the embryonic or spongy myocardium that normally develops into the compact myocardium characteristic of the mature mammalian heart[1-11]. Noncompaction has been reported to occur as a form of hypertrophic or restrictive cardiomyopathy and endocardial fibroelastosis[12,13]. We describe the typical echocardiographic appearance of isolated noncompaction in a postoperative case with the diagnosis of dextroposition of the great arteries.

## Case Report

A three-year-old boy presented with swelling of the face and extremities and respiratory distress. He had undergone Senning procedure at one year of age with the diagnosis of dextroposition of the great arteries. Permanent pacing had been initiated approximately six months after surgery due to persistent dysrhythmias. Following hospital admission, hyperbilirubinemia developed due to hepatitis B virus. When he first presented he was already on digoxin and diuretics. He was tachypneic and in respiratory distress. There was generalized edema with hepatosplenomegaly. Right ventricular impulse was prominent. There was cardiomegaly and right ventricular hypertrophy on his chest X-ray and electrocardiogram (ECG). An echocardiogram was performed with HP-1000 Sonos and 3.5 mHz transducers. There was no obstruction to the pulmonary venous flow. Both ventircles were enlarged. Systolic function was depressed. There were numerous prominent trabeculations and deep intertrabecular recesses measuring approximately 5-7 mm in depth along the free wall and apex of his right ventricle (RV). RV free wall was thickened (Fig. 1). Echogenicity of the endocardial surface was increased, suggesting a fibrotic process in progress. Intertrabecular recesses were observed to be filling from the ventricle by color Doppler, which is consistent with noncompaction. Pulmonary and 1 (+) tricuspid regurgitation were present. The patient died at home shortly after his discharge.

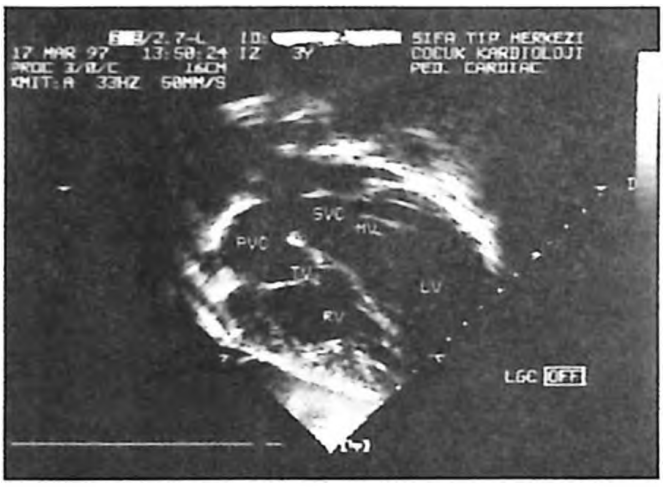


Fig. 1. Two-dimensional echocardiographic appearance of right ventricular cardiomyopathy.

## Discussion

Right ventricular dysfunction may occur in the long-term follow-up of patients undergoing atrial switch[1-5]. In a prospective study, the majority of patients,with transposition of the great arteries who underwent Mustard repair were in NYHA classes I and II at a mean follow-up period of 18 years, with mean RV ejection fraction values of 39%. Wilson et al.[6] reported that only half of the patients were in sinus rhythm; one patient was in complete heart block and the rest were in junctional rhythm. High occurrence of early and late postoperative dysrhythmias is more likely to cause injury to the sinoatrial node and/or its arterial supply than disruption of internodal tracts or damage to the atrioventricular node[6]. This case presented manifested persistent dysrhythmias requiring permanent pacemaker implantation. Neither shunting across the intraatrial repair nor obstruction to systemic or pulmonary venous return was present. However, RV and left ventricular (LV) dysfunction must have led to marked dilatation of both ventricles. It seems likely that one of the problems was the RV fuctioning as the systemic pumping chamber.

Various forms of bizarre trabecular patterns may be noted on angiocardiograms in patients with complex cyanotic congenital heart disease[7-9]. Failure of the normal differentiation of the primitive ventricular wall into the compact myocardium has been proposed in the mechanism of the abnormal patterns seen in some congenital heart diseases. With the advence of noninvasive techniques, a new entity, isolated noncompaction, has been described recently by echocardiography and confirmed pathologically. Diagnostic criteria for isolated noncompaction are prominent trabeculations associated with deep intertrabecular recesses. However, it must be noted that discrete muscle bundles, three or less in number and more than 2 mm in diameter, have been reported in 68% of normal hearts[10]. It was proposed that in isolated noncompaction increased fibrous and elastic tissue on the endocardium and within the intertrabecular recesses may be due to subendocardial ischemia[10]. The arrhythmogenic aspect observed in LV noncompaction has been explained by the morphological appearance of the troughs of the intertrabecular recesses being reminiscent of RV dysplasia. However, in a larger series reported, isolated noncompaction was not considered comparable to arhythmogenic RV dysplasia because the morphologic characteristics of these conditions differ completely[11]. Both studies reported that the intertrabecular recesses showed continuity with the left ventricular cavity. This finding has been depicted as an expression of an arrest of compaction of the ventricular myocardium, more appropriately terming the disorder noncompaction, rather than persisting sinusoids. Abnormal mitochondrial structure and mitochondrial chain abnormalities have been established in noncompaction associated with ventricular septal defects. Isolated noncompaction was reported to present as restrictive cardiomyopathy and endocardial fibroelastosis[12]. The cardiomyopathy observed in this case was distinct from arrhythmogenic RV dysplasia, which is characterized anatomically by patchy or diffuse adipose or fibroadipose substitution of RV myocardium and akinetic areas with discrete wall bulges in the absence of any other identifiable structural heart or pulmonary disease[13]. Neither does it resemble Uhl's anomaly, which is marked by extreme thinning of the RV, which may rarely be seen as an associated pathology in patients with congenital left or right ventricular obstruction and with anomalous origin of the left coronary artery from the pulmonary trunk. Although histopathological examination was not possible in this case, the echocardiographic findings were identical to the features of isolated noncompaction described by Chin et al.[10] Isolated noncompaction has been previously decribed as involving either both ventricles or the LV alone, but never just the RV[11].

To our knowledge, an echocardiographic appearance resembling that of noncompaction as a form of cardiomyopathy of the right ventricle following Senning operation has not been reported to date. This rare entity needs to be clarified regarding morphological criteria to distinguish it from other cardiomyopathies.

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# A case of osteopetrosis with pelvic ectopic spleen: an unusual association

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SUMMARY: Reisli İ, Çalışkan Ü, Taştekin G, Koç H, Açıkgözoğlu S, Aydoğdu-Kıreşi D, Aydın K. A case of osteopetrosis with pelvic ectopic spleen: an unusual association. Turk J Pediatr 2001; 43: 265-268.

A three-month-old girl was admitted to the hospital with a history of pallor. On physical examination, the liver was enlarged and a solid mass was palpated in the left abdomen. Laboratory evaluation revealed anemia and thrombocytopenia. Bone marrow was hypocellular with reduced number of megakaryocytes. Radiographic findings and scintigraphic study of the long bones were consistant with osteopetrosis. In the imaging studies, including ultrasonography, computerized tomography, magnetic resonance imaging and scintigraphic study, an ectopic spleen expanded into the bony pelvis was observed. We report here unique case of infantile osteopetrosis associated with pelvic ectopic spleen.

*Key words: infantile osteopetrosis, ectopic spleen, hypersplenism.*

Osteopetrosis is a rare bone disease characterized by a generalized increase in the density of the skeleton. Because of the defective osteoclast function, normal bone growth and remodeling are impaired. Several forms of the disorder, with different prognoses and modes of genetic transmission, are now recognized[1-3]. Another very rare entity is pelvic ectopic spleen. It occurs as a consequence of the embryonal disturbances in the development of the ligaments connecting the spleen with surrounding tissue[4,5]. We report a case of infantile osteopetrosis associated with pelvic ectopic spleen.

## Case Report

A three-month-old girl was admitted to the hospital with a history of pallor and irritability. Her family history was only significant for consanquinity. On her physical examination, her height and head circumference were below the 3rd percentile, the liver was enlarged, and a solid mass about 13 x 7 cm in diameter, expanding from 1 cm below the left costal margin toward the right pelvic region, was palpated.

Her laboratory evaluation revealed hemoglobin 51 g/L, white blood cell count 11.8 x $10^9$/L and platelet count 31 x $10^9$/L. A peripheral blood smear showed normocytic, mild hypochromic erythrocytes; mild anisopoikilocytosis; basophilic stippling; polychromasia; and numerous myeloid progenitors. The reticulocyte count was 7.1%. Bone marrow aspiration was performed with difficulty and revealed hypocellular, markedly reduced megakaryocytes, and no abnormal cells. The HbA was 93%, HbF 6.2%, and $HbA_2$ 0.8% in the hemoglobin electrophoresis. The results of the serological tests for Toxoplasma, cytomegalovirus, herpes, and syphilis were negative. The level of alkaline phosphatase was increased (1164 U/L), but the other laboratory measurements were normal.

In radiographs of the cranium, chest, pelvis and long bones, there was a generalized increase in bone density, and the demarcation between the cortex and the medullary cavity was lost (Fig. 1). In the scintigraphic scan of the bone [3 mCi Tc-99m methylenediphosphanate (MDP); DUPONT PHARMA], there was generalized intense uptake of radiophosphate in the skeleton with faint visulization of the kidneys (Fig. 2).

In the direct radiographs, there was no spleen shadow in the area where it is normally seen, and in the pelvic region, there was a soft tissue

density pushing the intestines above. In the abdominal ultrasonography, an enlarged liver was observed and the spleen was again not observed in its region; however, a solid mass expanding into the bony pelvis was found in the lower region of the abdomen. In the Doppler ultrasonography, the spleen's arterial blood supply was from the celiac plexus, and its venous outflow was into the portal vein. In computerized tomography, there was an ectopic spleen. This ectopic spleen with its vascular structure was also confirmed by abdominal magnetic resonance imaging (Figs. 3a and 3b). In the scintigraphic examination (2 mCi Tc-99m tin colloid; DUPONT PHARMA), there was an ectopic spleen showing diffuse hyperplasia in the pelvic region (Fig. 4). High-dose methylprednisolone was used for the treatment of anemia and thrombocytopenia, but the patient died on the 13th day of treatment from pulmonary infection.

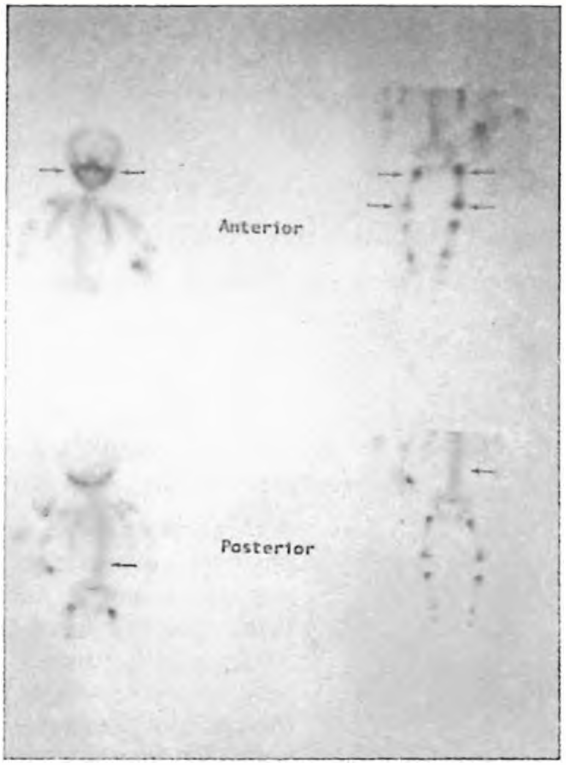


Fig. 2. Scintigraphic study of the bone: Tc-99m MDP scan shows a generalized intense radiophosphate accumulation in the skeleton (anterior) with faint visualization of the kidneys (posterior).

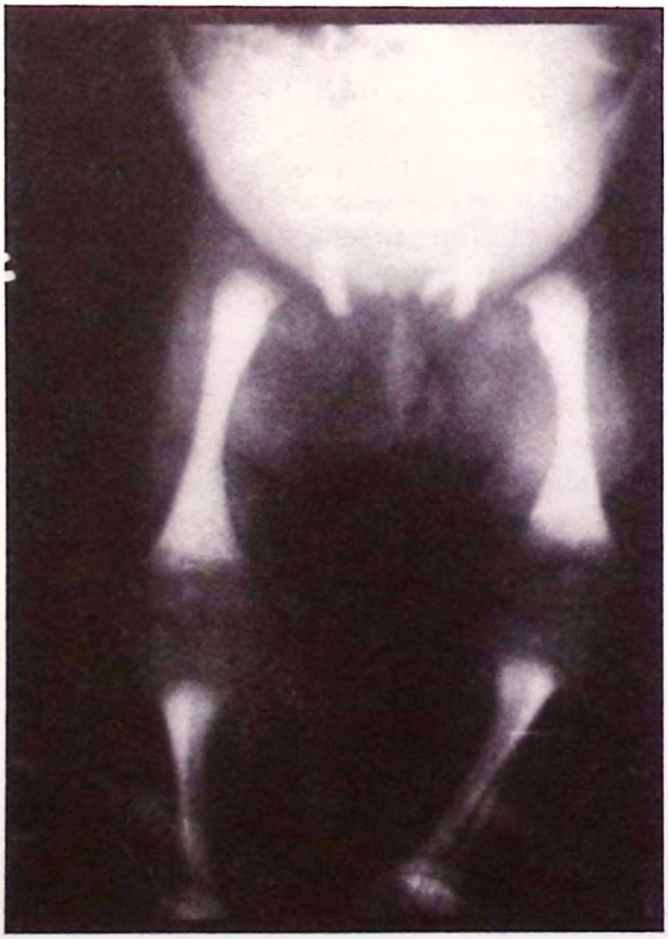

Fig. 1. Generalized increased density of the long bones and loss of demarcation between the cortex and medulla.

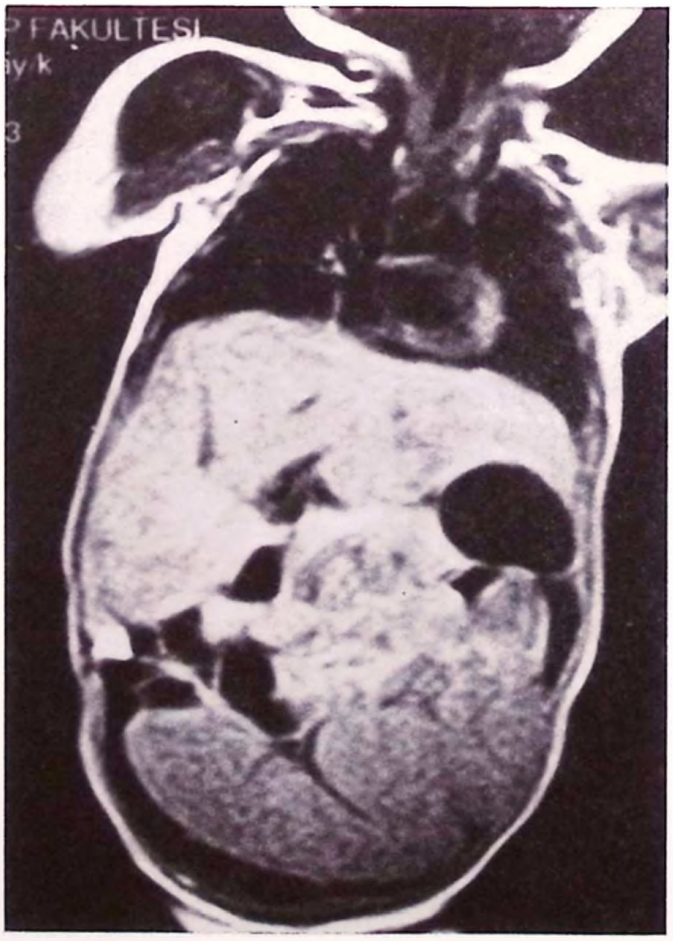


Fig. 3a. Pelvic ectopic spleen and its vascular structure in magnetic resonance imaging (coronal section).

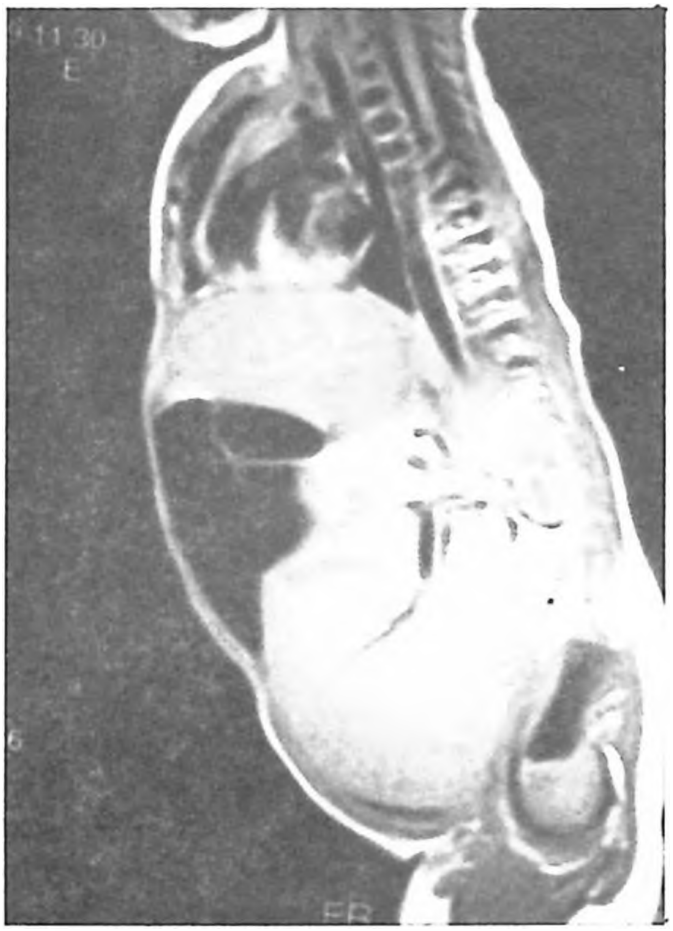

Fig. 3b. Pelvic ectopic spleen and its vascular structure in magnetic resonance imaging (sagittal section).

Fig. 4. Pelvic ectopic spleen in scintigraphic study.

## Discussion

Osteopetrosis appears with mild or severe clinical forms. The mild type was originally described in 1904 by Albers-Schönberg with autosomal dominant inheritance. Conversely, the autosomal recessive type of osteopetrosis is the most severe, and is termed the "malignant" form. In addition to these two forms, an autosomal recessive form of intermediate severity is recognized[2,3]. The autosomal dominant type is seen in older children and adults. It is often asymptomatic, but may be associated with pathologic fractures, mild anemia and cranial nerve paralysis. The autosomal recessive form of osteopetrosis, or infantile osteopetrosis, typically appears in infancy and the patients die in early childhood. The clinical manifestations of infantile osteopetrosis include failure to thrive, hepatosplenomegaly, severe anemia and cranial nerve dysfunction. The volume of the bone marrow is reduced by progressive obliteration of the marrow space by the increased mass of sclerotic bone, which makes bone marrow aspiration difficult. Hypersplenism eventually develops and leads to pancytopenia[1-3]. Our patient was accepted as infantile osteopetrosis with hypersplenism based on the severe clinical manifestations in early infancy and laboratory findings.

A pelvic ectopic spleen was another interesting finding in our patient. It is an extremely rare entity and should be considered in the differential diagnosis of abdominopelvic masses. Radiological and scintigraphic studies can be used to locate and identify these conditions[4-7]. After ultrasonography, computerized tomography, magnetic resonance imaging and scintigraphic study, we determined the localization, vascularization and function of the pelvic mass and confirmed the diagnosis of pelvic ectopic spleen.

The association of infantile osteopetrosis and pelvic ectopic spleen has not been reported in the literature prior to this case report.

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# Thoracoschisis associated with diaphragmatic hernia in a 31-week-old stillbirth

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SUMMARY: Derbent M, Balcı S. Thoracoschisis associated with diaphragmatic hernia in a 31-week-old stillbirth. Turk J Pediatr 2001; 43: 269-271.

Thoracoschisis is a very rare congenital anomaly and is frequently found with other congenital defects the of limbs and the abdominal wall as a part of limb-body wall complex (LBWC). Early vascular disruption, amnion rupture and intrinsic embryonic maldevelopment are related to the pathogenesis of this complex.

We present a case of thoracoschisis with ipsilateral diaphragmatic hernia. This case had none of the associated anomalies which are seen in LBWC. By ultrasonography performed at 31 weeks' gestation the fetus was misdiagnosed as gastroschisis. In this report we discuss the pathogenetic mechanism of LBWC and our case.

*Key words: thoracoschisis, gastroschisis, prenatal ultrasonographic diagnosis, limb-body wall complex.*

Thoracoschisis is a very rare congenital anomaly characterized by the herniation of the lung through a defect of the thoracic wall. Most previously reported cases of thoracoschisis and thoraco-abdominoschisis are found in association with other anomalies, most frequently exencephaly/encephalocele with or without cleft lip and/or limb defects, although other defects can also be present[1,2]. Three pathogenic mechanisms have been proposed for this disorder: amnion rupture, vascular disruption and embryonic malformation[3]. Recently it has been hypothesised that limb-body wall complex (LBWC) is a very heterogeneous group of disorders. Some cases show amniotic bands while others demonstrate evidence of vascular disruption or early embryonic maldevelopment[4].

Here we present the clinical, radiological and postmortem findings of a case of thoracoschisis without any other components of the LBWC, and we emphasize the importance of the differential diagnosis between gastroschisis and thoracoschisis by prenatal ultrasonography.

## Case Report

A 25-year-old healthy primigravida, a medical doctor working as a general practitioner, was first examined in the 17th week of gestation. Her history revealed a normal pregnancy to that stage. The woman was married to a 28-year-old man, and the couple was nonconsanguineous. Routine obstetric ultrasonography at week 17 was normal. However, ultrasonography at week 31 showed that part of the fetal intestine and almost all the liver were herniated through an abdominal wall defect (Fig. 1). The diagnosis of gastroschisis was made at another hospital. The woman was then referred to our center. The high level of alpha-fetoprotein (410 ng/ml) in the maternal serum at the same week of the diagnostic ultrasound exam was consistent with the fetal morphological findings. There was no history of drug ingestion during pregnancy.

A few days later, the fetus died in utero and labor was induced with an oxytocin infusion. Postmortem examination revealed a female fetus whose weight and length were 1,850 g and 45 cm, respectively. The liver and parts of the intestine and colon were herniated through a right thoracic defect of 4 x 3 cm. The margins of the defect were smooth. Otherwise, the general physical examination was normal (Fig. 2). A total body X-ray showed incomplete formation of the right ribs toward the ventral surface of the chest (Fig. 3). The second and fourth ribs, which exhibited the defect, were separated

cranially and caudally, respectively, in a configuration that allowed the viscera to prolapse. All the other parts of the skeleton and a cranial computed tomography scan were normal. There was also a right-anterolateral diaphragmatic defect of 2 x 3 cm. Unfortunately, no information was available regarding the fetal membranes. The fetus had no adherent bands or membranes. All other pathological exam findings were normal. Microscopic examination of the herniated liver and intestines revealed coagulation necrosis. The placenta was normal with a paracentrally located cord. Efforts to obtain a peripheral blood culture for chromosomal analysis were unsuccessful, but both parents' karyotypes were normal.

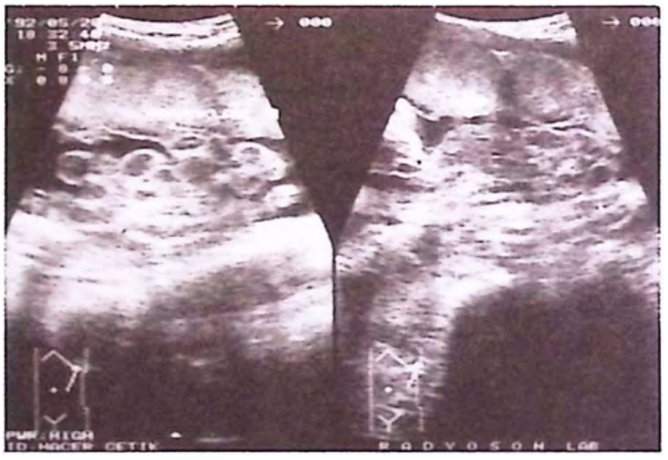

Fig. 1. The ultrasonographic appearance of the fetus demonstrated herniated fetal intestinal loops and the liver.

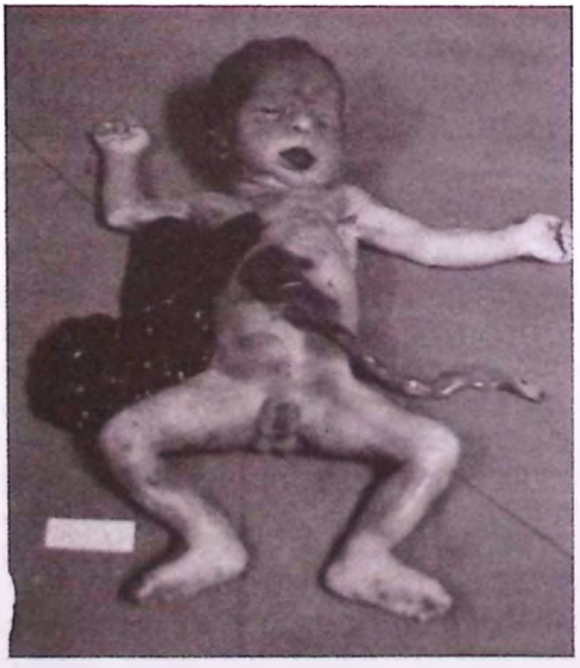

Fig. 2. Macroscopic appearance of the fetus showed no external malformation except right thoracic defect.

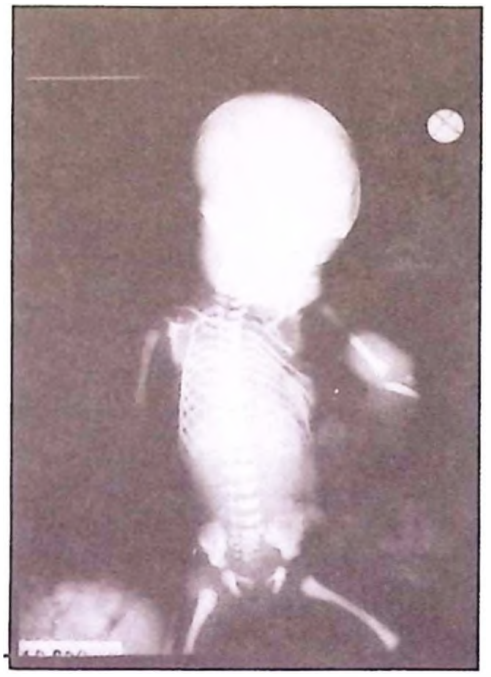

Fig. 3. Postmortem X-ray of the case showed incomplete formation of the right ribs.

## Discussion

Thoracoschisis is a very rare congenital anomaly that involves herniation of the lung through an opening in the thoracic wall[1]. Most cases of thoracoschisis reported in the literature are associated with other anomalies such as exencephaly/encephalocele with or without cleft lip and palate, and congenital amputation of the extremities or fingers, which are components of the limb-body wall complex[1-3]. LBWC refers to a variable spectrum of congenital defects that includes abdominal and/or thoracal wall defect with limb and visceral anomalies. There are three main pathogenetic mechanisms related to this complex: amnion rupture, vascular disruption and embryonic maldevelopment[4]. Van Allen et al.[2] proposed LBWC resulted from vascular disruption. Vascular disruption refers to structural anomalies resulting from damage to or interruption of normal embryonic or fetal development of the arteries and veins. The types of structural anomalies that result from vascular disruption are determined by the timing in gestation, and the severity and location of tissue damage[3]. Higginbottom et al.[5] hypothesized that these cases were due to early amniotic rupture and they named the defect Amniotic Band Disruption Sequence. Amnion Rupture Sequence is a disruption complex characterized by rupture of the amnion with secondary effects on the fetus

producing malformations due to interruption of normal morphogenesis, deformations due to distortion of established structures, or mutilations of structures already formed[5,6]. But these theories cannot explain the severe visceral and placental anomalies seen in LBWC. Alternatively, Russo and others[7] have presented evidence that some cases of LBWC result from primary embryonic maldevelopment. Recently, Craven et al.[4] have hypothesized that there are subsets of LBWC that have similar structural abnormalities and a common pathogenesis. They reported five cases of LBWC. Perinatal autopsies of these cases suggested that a primary malformation had occurred. They proposed that these cases represented a pathogenetic subgroup of LBWC.

It has been suggested that vascular disruption is a possible cause in the pathogenesis of amnion disruption sequence, LBWC, gastroschisis, structural anomalies of the limbs, and the Poland, Moebius, and Klippel-Feil sequences[3]. The type of the anomaly is thought to depend on the severity or location of the vascular disruption and on the stage of pregnancy. For instance, while disruption of the embryonic capillary plexus might cause early amnion disruption sequence and limb reduction anomalies, structural anomalies such as Poland, Moebius, and Klippel-Feil sequences are thought to be due to premature ablation of embryonic vessels[3]. The Poland anomaly is a congenital chest wall deformity that involves unilateral aplasia or hypoplasia of the pectoralis major and/or minor muscles, absence or hypoplasia of the nipple and breast, and deformity or absence of ribs and/or hands. The subclavian artery supply disruption sequence has been suggested as a factor in the pathogenesis of the Poland anomaly[8]. Gastroschisis, which generally appears as an isolated anomaly, or infrequently together with certain anomalies related to the intestines, has been attributed to the ablation or occlusion of the omphalomesenteric artery[3,9].

The relatively localized anomaly in our fetal patient may also have been caused by an embryonic or fetal vascular disruption. Based on the laterality of the defect and the lack of any associated anomaly other than an ipsilateral congenital diaphragmatic hernia, we believe that the pathogenetic mechanism behind the problem in this fetus was similar to that behind gastroschisis. Specifically, we conclude that this case of thoracoschisis with congenital diaphragmatic hernia was caused by premature ablation or occlusion of a specific artery.

This case also illustrates the importance of differentiating thoracoschisis from gastroschisis on ultrasonography. When the intestinal loops appear as cystic structures in the amniotic fluid, the diagnosis of gastroschisis is made easily by prenatal ultrasonography[10]. However, our case involved thoracoschisis with congenital diaphragmatic hernia, which can produce images similar to those of gastroschisis. Also, most reported cases of thoracoschisis have been associated with other anomalies. This differential diagnosis is important with regard to genetic counseling and appropriate postnatal management of the fetus.

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# Bilateral subpleural ectopic brain tissue in a 23-week-old fetus

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SUMMARY: Balcı S, Nabaei ShM, Özaltın F, Önol B. Bilateral subpleural ectopic brain tissue in a 23-week-old fetus. Turk J Pediatr 2001; 43: 273-275.

Bilateral lesions were seen in the subpleural region in a 23-week-old aborted male fetus. This fetus was not macerated and showed no central nervous system abnormality on physical examination and vertebral magnetic resonance imaging (MRI). Postmortem examination revealed bilateral, paravertebral, subpleural, circumscribed, yellowish-white, fluent lesions 2.5 x 1 x 1 cm in size. These lesions were localized on the upper part of both lungs and there was no other internal malformation. Histological examination of lesions showed adult neurones and well-differentiated neural tissue with white and gray matter, choroid plexus, ependymal structures and, rarely, some peripheral neural cells in addition to immature neuroectodermal cells. These cells were more mature than those in the brain tissue.

*Key words: ectopic brain tissue, lung, triple test.*

Central nervous system heterotopia in the lung is a rare abnormality and is commonly associated with encephalocele[1-3], anencephaly[4-9], hemicephaly[10], and rarely, no central nervous system abnormality[11,12]. The etiology of intrapulmonary neuroglial heterotopia is still obscure. Several hypotheses have been proposed, such as aspiration and implantation of detached neural fragments within the amniotic fluid[6,7], defects of neural crest migration[3,6], vascular embolization and implantation of neural tissue following central nervous system trauma[4], and primitive mesenchymal differentiation into neuroglia[11]. The purpose of this paper is to present an unusual case with bilateral, subpleural, well-differentiated neural tissue in a non-macerated fetus that differs from other cases in the medical literature.

## Case Report

A 40-year-old pregnant woman was admitted to the hospital because of Down syndrome risk due to high triple test (1/80): (alpha fetoprotein 47 ng/ml (1.2 MoM), human chorionic gonadotropin 25 IU/ml (1.22 MoM), and urinary estriol 1 ng/ml (0.59 MoM) at 18 weeks' gestational age. There was a first-degree consanguinity between parents in family history. The spastic second child died at one year of age and two other siblings were healthy. The woman suffered from mitral insufficiency due to rheumatic heart disease and was under treatment (digoxin, dipyridamole, benzathine penicillin G/per month). Cloudy amniotic fluid was obtained from amniocentesis that was performed at 19 weeks' gestational age but the growth of cells was unsuccessful. For that reason chordocentesis was performed at 23 weeks' gestation, and the chromosome analysis was found normal, 46 XY. Unfortunately, spontaneous abortion occurred three weeks after chordocentesis. Weight and length of the aborted fetus were 410 g and 30 cm, respectively. The placenta was 120 g. The general appearance was completely normal except for a dimple sized 0.2 cm on the nose. Postmortem examination revealed bilateral, intrathoracic, paravertebral, subpleural, circumscribed, yellowish-white, fluent lesions sized 2.5 x 1 x 1 cm. These cystic lesions were localized on the upper part of both lungs and there was no another internal malformation (Fig. 1). Histological examination of cystic lesions showed mature neurones, well-differentiated neural tissue with white and gray matter, well-organized cerebral cortex, choroid plexus, ependymal structures (the cysts were not lined by ependyma) and, rarely, some peripheral neural cells in addition to immature neuroectodermal cells (Fig. 2-4). These cells were more mature than those in the brain tissue. Brain and cerebellum were of normal morphology for

age and there was no abnormality in connection between basal parts of the brain and occipital foramen. Likewise, postmortem vertebral X-ray and magnetic resonance imaging (MRI) were also free of any defect.

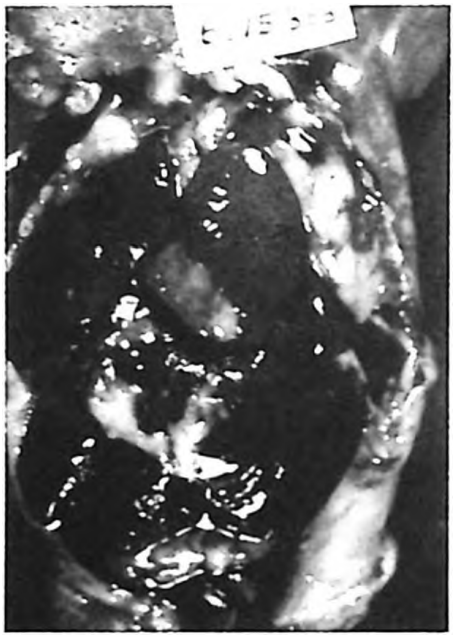

Fig. 1. Bilateral, intrathoracic, paravertebral, subpleural, circumscribed, yellowish-white, fluent lesions sized 2.5 x 1 x 1 cm. These lesions were under the parietal pleura and there was no association with the pulmonary parenchyma. No internal malformation was noted.

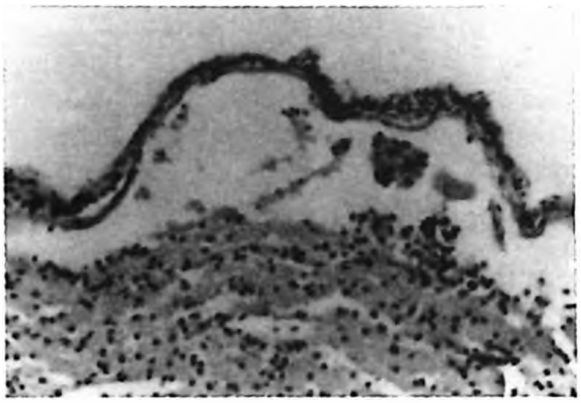

Fig. 2. Necropsy taken from the mass demonstrating arachnoidal membrane (Olympus BH-2, HEx100).

been reported; its etiology is still obscure. Several hypotheses have been proposed, such as aspiration and implantation of detached neural fragments within the amniotic fluid, defects of neuronal migration, vascular

Fig. 3. Necropsy taken from the mass demonstrating choroid plexus (Olympus BH-2, HE x 200).

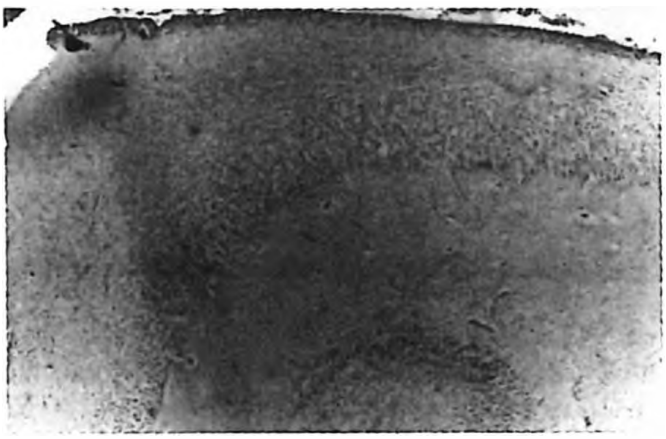

Fig. 4. Ependymal structures and a well-organized neural tissue. Ammon's horn-like appearance was noted (HEx400).

## Discussion

The occurrence of brain tissue outside the cranial cavity is exceedingly rare. It is seen most frequently in central nervous system defects such as encephalocele[1-3], anencephaly[4-9], hemicephaly[10] and, rarely, with no central nervous system abnormality[11,12]. To date, 18 cases with intrapulmonary neuroglial heterotopia have

embolization and implantation of neural tissue following central nervous system trauma, and primitive mesenchymal differentiation into neuroglia. Embolization of brain tissue has been well documented after severe head trauma in adults and children. Hauck et al.[13] observed embolic cerebellar tissue in the pulmonary and coronary arteries of a male infant. Likewise, van

Noort and de la Fuente[14] reported primitive neuroectodermal tumors in macerated fetuses. The authors produced a similar lesion in a 12th week fetus by experimental compression of the skull and suggested that these tumors in macerated fetuses should be considered an artifact[14]. However, in our patient, there was neither maceration nor findings of trauma. Vertebral X-ray and MRI were also normal without any defect. The hypothesis of aspiration of neural tissue from amniotic fluid was unlikely in our case because other cases in literature all had central nervous system defects except for two cases[12,13]. Unilateral development of a teratoma is certainly possible. Moreover, intrapulmonary teratomas have been observed mostly in young adults and older individuals[15] and only rarely in infants[16]; all appeared as a distinct tumor. Valdes Dapena and Arey[17] showed a glial nodule in the lungs of a 51-year-old man with no apparent skull malformation, which was interpreted as an embryoma. Presence of mature neurones, well-differentiated neural tissue with white and gray matter, well-organized cerebral cortex, choroid plexus, ependymal structures and, rarely, some peripheral neural cells in addition to immature neuroectodermal cells suggested to us primitive mesenchymal differentiation was likely possible in the etiology. Until the mechanisms of cellular differentiation are better understood, these cases will remain in question. Further observations will enlighten the etiology of these rare abnormalities.

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