THE TURKISH JOURNAL OF PEDIATRICS

VOLUME: 31 NUMBER: 2 APRIL - JUNE 1989

A joint publication of the Turkish National Pediatric Society and the Turkish and International Children's Center

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This Journal is listed in *Current Contents, Index Medicus, Abstracts on Hygiene and Communicable Diseases, Tropical Diseases Bulletin* and the CAB Abstracts database.

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The Turkish Journal of Pediatrics 31:103 - 112, 1989

COMPUTERIZED TOMOGRAPHY FINDINGS OF THE POSTERIOR FOSSA IN CHILDREN: ETIOLOGY AND CLINICAL CORRELATION*

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Key words: computerized tomography, posterior fossa abnormalities, cerebellum

New developments in the field of radiodiagnostic procedures have brought changing clinical concepts with them. Since the advent of techniques like computerized tomography (CT) and nuclear magnetic resonance (NMR), detailed evaluations of cranial structures have become possible and the scope of observed morphological abnormalities has enlarged. The extent to which these findings are correlated with the clinical picture is a matter of curiosity.

In this study, we reviewed, retrospectively, children who had CT abnormalities confined to the posterior fossa and evaluated their clinical and neurological findings in relation to their appearance on tomography.

Material and Methods

Of the 1105 patients, two days to seventeen years of age, who were examined by cranial CT for various reasons at the Hacettepe University Children's Hospital between June 1986 - June 1988, 93 with posterior fossa abnormalities were reviewed. Twenty-five patients whose hospital records were incomplete, and nine with postoperative tissue defects, were not included. Table I shows the CT results of the 93 cases.

The CT examinations were routinely performed parallel to the orbito-meatal line, with nine mm slice thickness from the foramen magnum to the vertex. A second

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series of CT was performed with intravenous injection of contrast medium. The CT findings were grouped as follows: neoplasms of the brain stem or cerebellum, the Arnold-Chiari malformation, cerebellar hypoplasia, cerebellar atrophy, cerebral and cerebellar atrophy, cerebellar abcess, cerebellar hemorrhage and the Dandy-Walker malformation (Figs. 1-5).

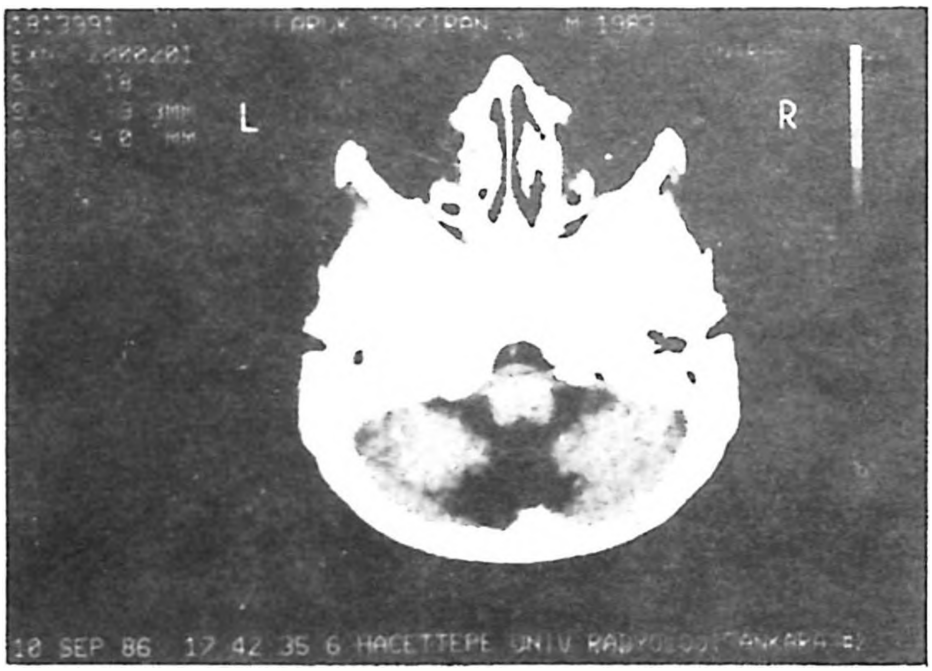

Fig. 1 (a): Cerebellar atrophy.

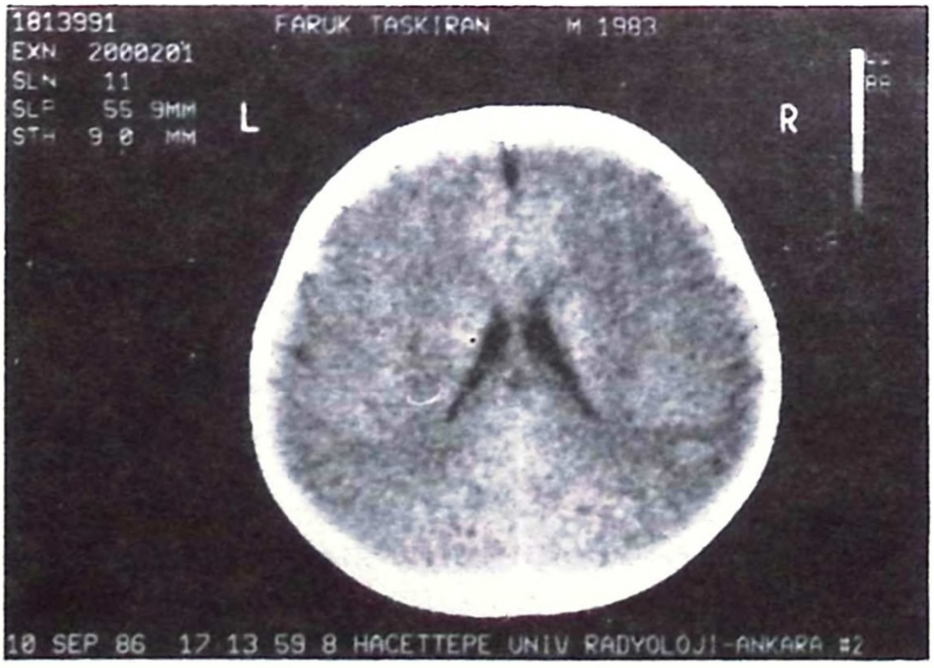

Fig. 1 (b): Compared to normal cerebellum.

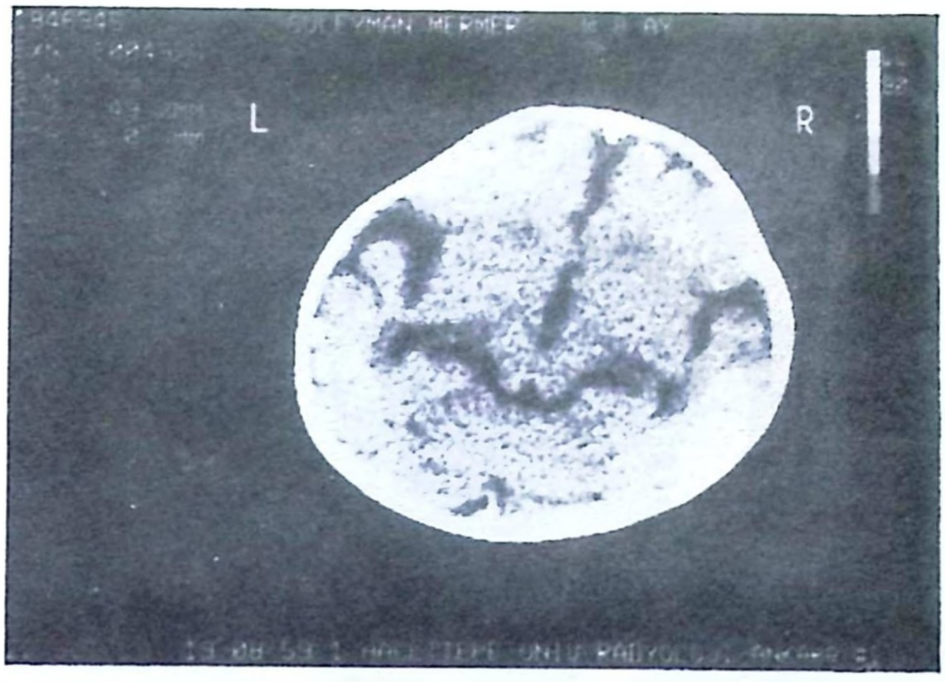

Fig. 2: Cerebral and cerebellar atrophy.

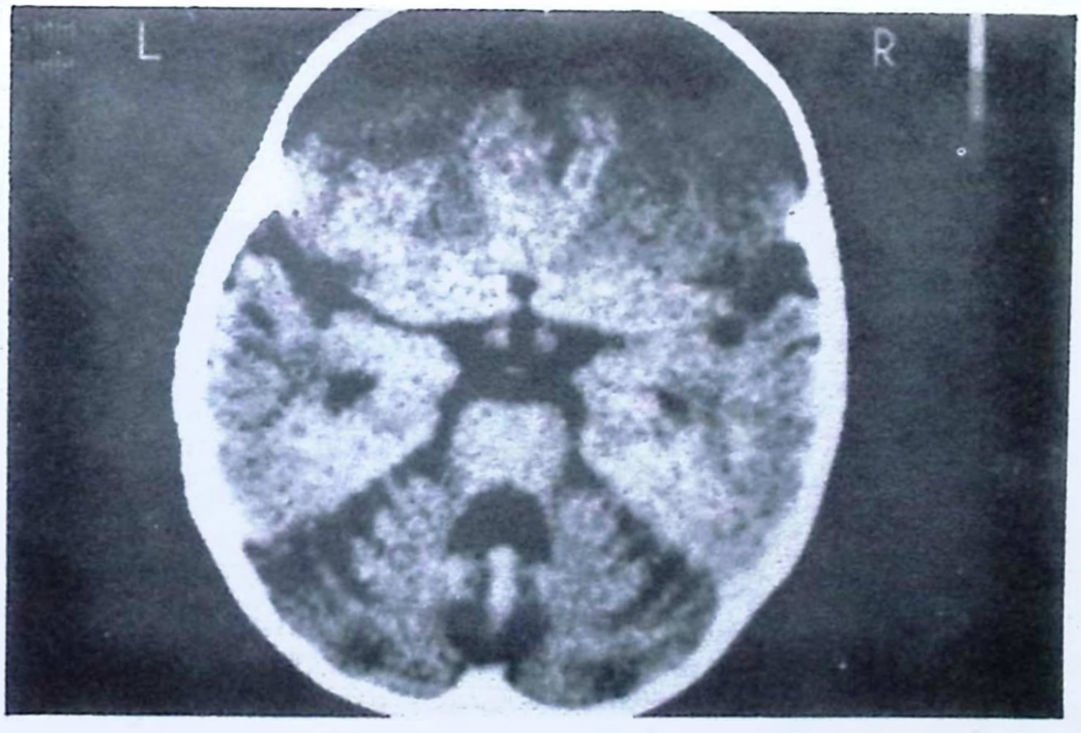

Fig. 3: Small posterior fossa and cerebellar hypoplasia.

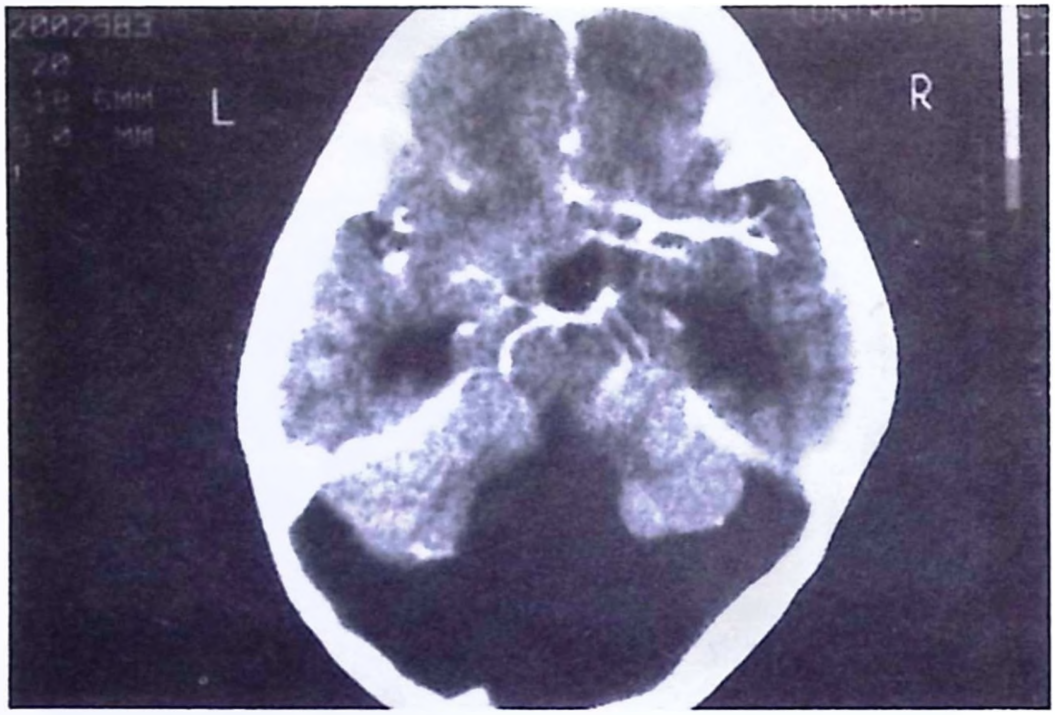

Fig. 4: Dandly-Walker malformation and partial cerebellar agenesis.

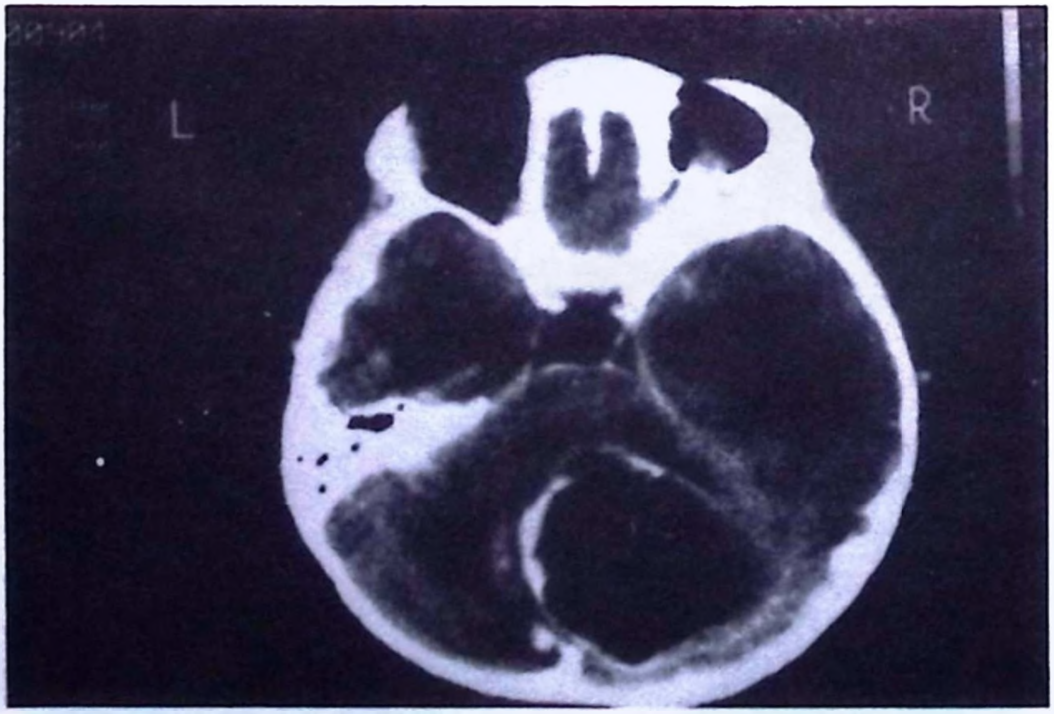

Fig. 5: Cystic astrocytoma in the right cerebellar hemisphere (left contrast substance injection).

TABLE I: CT Findings Related to the Posterior Fossa

	n
–Tumors	21
–brain stem-15	
–cerebellum 6	
–Cerebellar atrophy	13
–Cerebellar hypoplasia	6
–Cerebellar and cerebral atrophy	30
–Cerebellar abcess	1
–Cerebellar hemorrhage	2
–Arnold-Chiari malformation	20

A diagnosis of cerebellar atrophy was based on the visualization of the cerebellar sulci and the enlargement of the cerebellopontine and superior cerebellar cisterns. The term hypoplasia was used by the radiology department if the above findings were accompanied by other malformations on CT or if the clinical course was a non-progressive one starting from birth.

Symptoms, physical findings, developmental status and neurological signs of the patients were noted from hospital records. The patients were considered positive for cerebellar symptoms and signs if at least one of the following features was present: intentional tremor, ataxia, nystagmus, dysarthria, in addition to others (dysdiadochokinesia, etc.).

The clinical diagnoses and, if present, the suspected or definite cause for the patient's clinical condition was also recorded.

Results

The frequency of different CT findings, cerebellar and neurological findings and developmental status of the patients in each group are illustrated in Table II.

The radiological and clinical diagnoses were similar in 95% (20/21) of the tumor group. The CT results were considered unexpected if a discrepancy was present between the CT finding and the primary diagnosis or the reason for performing CT (i.e., if atrophy was observed in a patient investigated for malignant infiltration or cerebellar hypoplasia was found in a child with convulsions). The unexpected findings comprised 70% (30/43) cerebral and cerebellar atrophies, either alone or accompained by cerebral atrophy.

Cerebellar signs were present in 6/6 of the cerebellar tumors, 4/6 of the cases with cerebellar hypoplasia and 7/13 of the cases with cerebellar atrophy; they

TABLE II: Clinical and CT Findings

	Concordance with clinical diagnosis	Cerebellar signs	Other neurological signs	Delayed development
– Tumors				
– Brain stem	15/15	8/15	15/15	–
– Cerebellum	5/6	6/6	2/6	–
– Cerebellar atrophy hypoplasia	10/13	7/13	4(13	9/13
– Cerebellar hypoplasia	4/6	4/6	5/6	5/6
– Cerebral and cerebellar atrophy	3/30	3/30	26/30	19/30
– Cerebellar hemorrhage	1/2	0/2	2/2	–
– Cerebellar abcess	1/1	1/1	1/1	–
– Arnold-Chiari malformation	19/20	–	20/20	20/20

were less frequent in the group with cerebral and cerebellar atrophy (3/30; 10%). The later group presented with other neurological signs (26/30; 86%).

The frequency of delayed development was similar in cerebellar hypoplasia (5/6) or atrophies (9/13) and in cerebral and cerebellar atrophies (19/30).

The conditions leading to or accompanying the CT results are illustrated in Table III. No etiologic relationship between the CT finding and the patient's clinical condition was found in the two cases with hypoplasia, four with cerebellar atrophy and the seven with cerebellar and cerebral atrophy.

TABLE III: Etiology or Associated Condition

Hypoplasia	Cerebellar atrophy	Cerebral and cerebellar atrophy
Dwarfism (1)	Post infection (2)	Postinfection (2)
Arrested hydrocephaly (1)	Diphenylhydantoin (2)	Diphenylhydantoin (5)
Multiple congenital malformation (2)	Radiotherapy (1)	Degenerative (2)
	Ataxia telangiectasia (2)	Birth anoxia (2)
	Spinocerebellar (1) degeneration	Intrauterine infection (2)
	Birth anoxia (1)	Collagen disorder (3)
		Leukemia/lymphoma (3)
		Hepatic coma (1)
		Cyanotic heart disease (1)
		After pseudotumor (1)
		Mitochondrial myopathy (1)
		Unknown (7)

Discussion

Among the new, sometimes incidental findings which are being observed with the introduction of CT, those concerning the posterior fossa attracted our interest by their frequency (84/100 scans), and this observation became the starting point of our study. Similar studies have been done previously with particular emphasis on the enlargements of the cisterna magna[1,2] and the fourth ventricle[3]. It has been reported that solitary enlargements of these structures are not reliable predictors of clinical involvement because of the wide variation in size occurring in normal people, and that the mega cisterna magna and an enlarged 4th ventricle have a constant ratio on routine CT material. For this reason, we did not record these abnormalities when they were isolated but considered them as an indication of the other signs of cerebellar atrophy or hypoplasia.

The visualization of cerebellar sulci and the enlargement of the cerebellopontine and superior cerebellar cisterns may be due to cerebellar atrophy or hypoplasia. A definite discrimination between these diagnoses may be difficult on radiological

findings only. We used the term hypoplasia when other congenital anomalies (arachnoid cysts, hydrocephalus) were present or if the clinical course was consistent with a congenital malformation.

In contrast to the tumor cases, not all of the patients with cerebellar atrophy on CT had clinical signs of cerebellar dysfunction: 11/19 with atrophy or hypoplasia and only 3/30 with cerebral and cerebellar atrophy had cerebellar signs or symptoms. The cerebral and cerebellar atrophy group presented frequently with other neurological findings, particularly pyramidal signs and mental retardation which might have masked the cerebellar dysfunction. Our two cases with hemorrhagic infarcts did not give cerebellar signs and were investigated for altered consciousness or convulsions. The frequency of developmental delay was high among the hypoplasia, atrophy and the Arnold-Chiari groups (Table II).

Cerebellar atrophy may be due to a variety of causes which may be difficult to distinguish. Diphenylhydantoin (DPH) has been frequently reported as an etiological factor[4-6]. Some authors have pointed out that anoxia due to convulsions may be the real cause of, or a contributor to the atrophy[7]. Koller et al[6], who evaluated patients treated with DPH having cerebellar atrophy observed no signs of cerebellar dysfunction on CT. This result which is in contrast to other studies may indicate the state of preclinical DPH-induced cerebellar degeneration. Since our seven cases with atrophy, who had received DPH, had no cerebellar signs either, we can assume that in addition to the cerebellar syndrome associated with cerebellar degeneration, DPH may cause cerebellar atrophy without any clinical findings. Prospective studies indicating the clinical and CT evaluations of DPH-treated patients are needed to show the frequency of these conditions.

Malignant disorders may cause cerebellar atrophy by several mechanisms: the remote effect of cancer, the toxicity of chemotherapeutic agents or of radiotherapy[8-10]. One of our cases had received radiotherapy for a glial tumor of the pons; the other three cases with leukemia or lymphoma had received cytosine arabinoside or cyclophosphamide. However, we believe that chronic malnutrition and anemia, as demonstrated previously, are also important factors in patients with malignancies since cerebral atrophy frequently accompanied cerebellar atrophy in our patients[11].

A specific diagnosis of atrophy could be made in two of our cases with ataxia-telangiectasia, two with postinfectious cerebellar ataxia and in one with spinocerebellar degeneration. Cerebellar hypoplasia has been reported as a nonprogressive, isolated malformation of the brain of autosomal recessive or dominant inheritance or as a feature of some degenerative disorders of early onset[12,13]. Sarnat and Alcala[14] have reported that cerebellar hypoplasia is a clinical syndrome due to fetal exposure to some viruses, toxins, or radiation. In

most of our cases, other congenital malformations (micrognathia, clubfoot, etc.) accompanied the cerebellar hypoplasia.

The patients with cerebral and cerebellar atrophy were a heterogenous group presenting with many different underlying conditions (Table III).

In conclusion, cerebellar abnormalities have an incidence of 84 per 1000 CT scans in our hospital, and the atrophies are the most frequent (45%). Signs of cerebellar dysfunction are more likely to be present if cerebellar atrophy is the only finding; they are infrequent (10%) in patients with cerebral and cerebellar atrophy. A specific cause can be found in cases with cerebellar atrophy (9/13, 69%) or hypoplasia (4/6, 66%) while systemic disorders (8/30, 26%) or unknown causes (8/30, 23%) are responsible for most of the more diffuse atrophies involving both the cerebrum and cerebellum. In this situation, CT is a useful method in detecting the injury. The cerebellum, as the cerebrum, appears to be prone to injury resulting from a heterogenous group of disorders. These disorders frequently give no signs indicating cerebellar involvement. In addition, CT is particularly indicated in children showing one or more cerebellar signs or symptoms since it usually reveals important diagnostic information of these patients.

Summary

Of 1105 childhood cases who were evaluated by computerized tomography (CT) in a two-year interval, 93 who had posterior fossa abnormalities are reviewed. The cerebellar atrophies, either alone or accompanied by cerebral atrophy, were the most common morphological diagnoses. The clinical picture, etiology, and developmental state of the cases are discussed in relation to the CT findings.

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The Turkish Journal of Pediatrics 31:113 - 122, 1989

CHIARI II MALFORMATION: COMPUTED TOMOGRAPHIC EVALUATION*

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Key words: Chiari II malformation, computed tomography

In 1883, Clealand described the morbid findings in a full-term infant with spina bifida, craniolacunia, an elongated brainstem and herniated fourth ventricle through the foramen magnum. In 1891, Chiari reported the anomalies in the pontobulbocerebellar area and classified them into three types. An infant with fourth ventricular and cerebellar herniation was reported by Arnold in 1894. In 1896, Chiari added a fourth type of malformation to the three types of malformations he had previously described-the Chiari II or Arnold-Chiari malformation which is the most common of the four types[1-4].

The Chiari II malformation is characterized by the caudal elongation of the cerebellum and brainstem through an enlarged foramen magnum. There may also be accompanying midbrain, forebrain, and cranial bony deformities, as well as marked hydrocephalus. It must be differentiated from other types of hydrocephalus preoperatively, since the surgical management of the Chiari II malformation may differ from other types of hydrocephalus. The surgical management of the Chiari II malformation consists of cervicomedullary decompression in addition to ventricular shunting.

Several reports about the cranial computed tomography (CT) findings of this malformation have appeared in the literature. With the use of magnetic resonance imaging (MRI), some new features of the malformation, such as increased mamillopontine distance, have been reported[2].

In this article, we analyzed the CT findings in 28 patients with Chiari II malformation in the light of CT and the recently defined MRI characteristics.

Material and Methods

Twenty-eight patients with Chiari II malformation were evaluated. There were 15 males (53.6%), and 13 females (46.4%). The youngest of the patients was ten-days-old, and the oldest was 44-years-old, with the mean age being 7.8 years. The age distribution of the patients was as follows: 12 (42.9%) were less than

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one-year-old, six (21.4%) were 1-5 years-old, three (10.7%) were 6-10 years-old, four (14.3%) were 11-20 years old, and three (10.7%) were more than 21-years-old. In seven patients CT examinations were performed after a ventricular shunt was placed. Two patients had CT examinations both before and after shunting.

All the CT examinations were performed with the third generation Philips Tomoscan-350 scanners in the Radiology Department of the Hacettepe University Children's Hospital. All of the patients had CT scans in the transaxial plane parallel to the orbitomeatal line. Three patients had additional direct coronal and direct sagittal scans taken.

Results

The results of the study are categorized and summarized in Table I.

TABLE I: Computed Tomographic Abnormalities in Chiari II Malformation

Abnormalities grouped by location	Number of patients (Total 28)	Percentage (%)
Cranial bones		
Asymmetry of the cranial bones	16	57.1
Sagittally enlarged foramen magnum	23	82.1
Craniolacunia	18	64.3
Petrous/Clival scalloping	27	96.4
Rhombencephalon		
Fourth ventricle		
Position		
Low	15	53.6
Normal	10	35.7
Size		
Not seen	3	10.7
Small	22	78.6
Normal	3	10.7
Cerebellum		
Enveloping	22	78.6
Upward displacement	22	78.6
Orientation of vermian folias		
Not seen	13	46.4
Transversally	4	14.3
Oblique posteromedially/Sagittally	11	39.3
Mesencephalon		
Tectum		
Pointed	22	78.6
Flattened	6	21.4
Diencephalon		
Third ventricle		
Size		
Normal	6	21.4
Enlarged	22	78.6
Telencephalon		
Lateral ventricles	15	53.6
Normal		
Enlarged		
Asymmetry	2	7.1
Corpus callosum	26	92.9
Partial agenesis	24	85.7
Supracerebellar CSF containing space		
	9	32.1
Tentorium and Falx	8	28.6
Wide tentorial hiatus		
Falx hypoplasia/Interdigitation of gyri		
	17	60.7
	13	46.4

Discussion

The following is a discussion of our findings from 28 cases grouped according to location of abnormality:

Cranial bones

Enlarged foramen magnum: The reports about the size of the foramen magnum in cases with Chiari II malformation are controversial. By using conventional radiologic techniques, Kruyff and Seffs[5] reported enlarged foramen magnum in 71 percent of cases with Chiari II malformation. According to Naidich et al[6], it is difficult to assess the size of the foramen magnum by computed tomography unless the slices are taken in the coronal or sagittal planes[6]. We found that the sagittal diameter of the foramen magnum was larger than normal (more than 40 mm) in 23 (82.1%) of our cases, with the mean value being 42.2 mm.

Scalloping of the petrous bones and clivus: Since the posterior fossa is small in Chiari II malformation, as the cerebellum and hindbrain grow there is erosion of the clivus and the posterior aspects of the petrous bones due to pressure[2,6,7]. On axial CT scans, this is seen as a loss in the normal convexity of the posterior aspects of the petrous bones (flattening), or the concavity of the posterior borders of the petrous bones and clivus (scalloping)[6]. Naidich et al[6], using CT, and Wolpert et al[7], using MRI, reported flattening or scalloping of the petrous bones and clivus in 90% and 79% of their cases, respectively. We observed petrous and/or clival flattening or scalloping in 27 (96.4%) of our cases (Fig. 1).

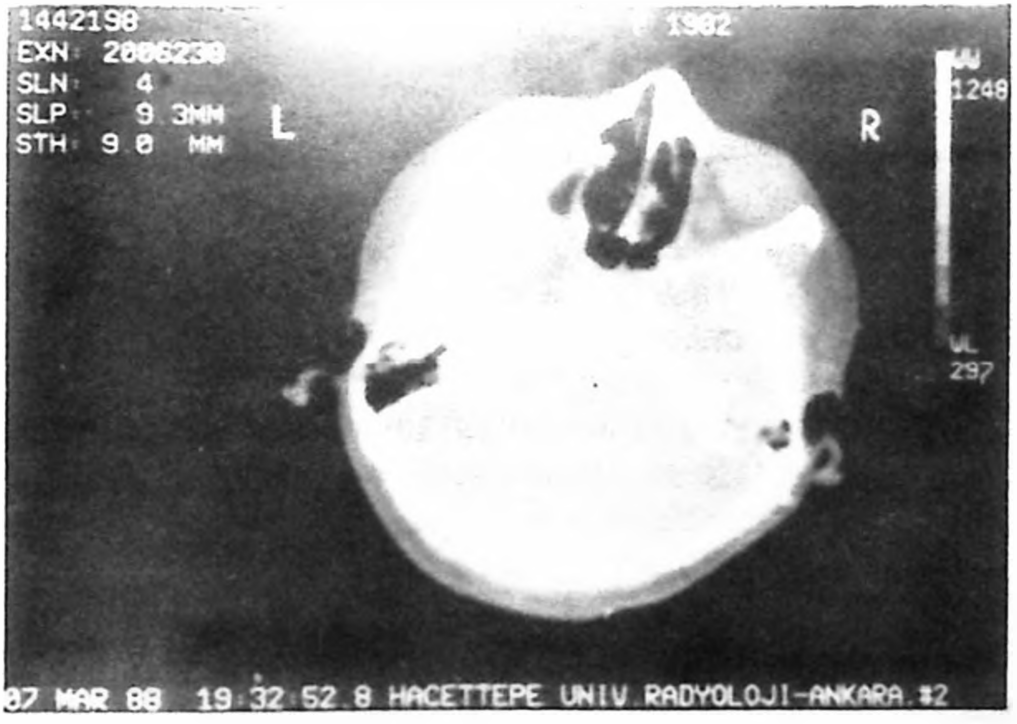

Fig. 1: Convex borders of the posterior aspects of the petrous bones and clivus are noted in this section through the posterior fossa.

Craniolacunia (Luckenschadel): Craniolacunia or lacunar skull, which is caused by calvarial mesodermal dysplasia, is seen as thinnings, pits, or fenestra predominantly involving the inner aspects of the frontal, parietal, or membranous occipital bones[6,7]. The lacunae mostly disappear after six months of age[1,6,7]. We found that craniolacunia was present in 18 (64.3%) of our cases, with seven of them being more than one-year-old (up to 18-years-old).

Asymmetry of the cranial bones: We found that the cranial bones were asymmetric in 16 (57.1%) of our patients. Asymmetric lateral ventricular dilatation was noted in all these 16 patients, and 13 of them also had craniolacunia. Asymmetry of the cranial bones due to asymmetric lateral ventricular dilatation has been previously reported[8]. We believe that the asymmetry of the cranial bones in patients with Chiari II malformation is due to asymmetric lateral ventricular dilatation, with craniolacunia being a contributing factor.

Rhombencephalon

Fourth ventricular size: Elongation and sagittal flattening of the fourth ventricle is the hallmark of the Chiari II malformation[2-4,7-10]. Naidich et al[10] have reported that the fourth ventricle was not seen in 70%, and was narrow in 25% of their cases. We found that the fourth ventricle was not seen in three of our cases (10.7%), and was small in 22 (78.6%). The fourth ventricle was of normal size in the remaining three cases. We were able to identify a small fourth ventricle in more cases than Naidich et al[10], maybe because a high resolution scanner was used on all of our patients which might cause reduced posterior fossa artefacts.

Fourth ventricular position: In the Chiari II malformation, along with the caudal displacement of the brainstem, the fourth ventricle may also be low in position[4]. According to Zimmerman et al[11], failure to demonstrate a fourth ventricle at or above the upper third level of the petrous pyramids indicates pathologic displacement. Elgammal et al[2] have reported that the fourth ventricle was stretched and low in position in 75% of their cases. The fourth ventricle was low in position in 15 of our 25 cases, in whom we managed to identify a small or normal sized fourth ventricle (Fig. 2). The caudal displacement of the fourth ventricle is better evaluated with sagittal MR sections[2,7]. The fourth ventricular size and position can also be assessed by intraoperative ultrasound, and the surgical approach is tailored to the specific abnormality for improving the safety of the procedure[12]. Three major types of fourth ventricular malformation have been identified in preoperative MRI and intraoperative ultrasound studies[7,12].

Cerebellar enveloping: Since the posterior fossa is small, the anterior parts of the cerebellar hemispheres migrate into the prepontine cistern causing envelopment of the brainstem[7,13]. Naidich et al[13], and Wolpert et al[7] reported that the cerebellar enveloping of the brainstem was present in 75% of their cases[7]. Cerebellar enveloping was identified in 22 (78.6%) of our patients (Fig. 3).

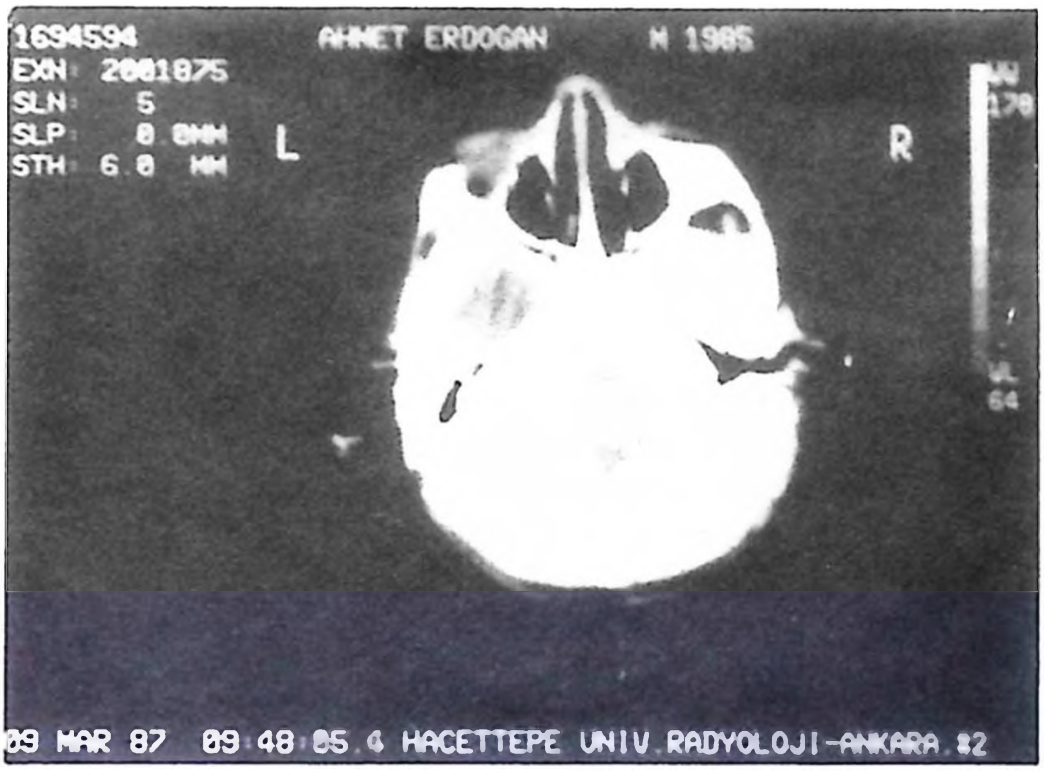

Fig. 2: A narrow fourth ventricle is seen at the level just above the foramen magnum, characteristic of Chiari II malformation.

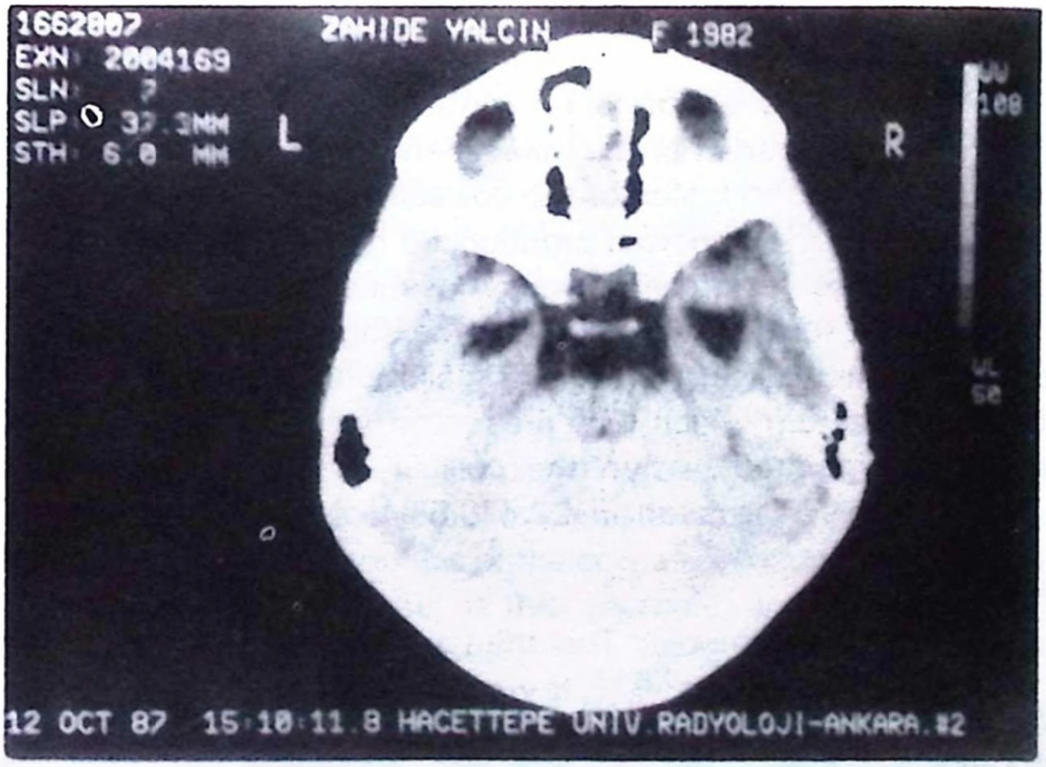

Fig. 3: The anterior cerebellar margins are sharply pointed and overlap the cerebral peduncles on both sides.

Cerebellar vermian folias: In patients with Chiari II malformation, some form of cerebellar dysplasia and disorders of migration were described by Gilbert et al[14]. Wolpert et al[7], mentioned the nonvisualization of orientation in the obliquely posteromedial direction of the vermian folias, and explained this feature by the dorsal angulation and displacement of primary and postlunate fissures. We found that the superior vermian folias were not seen in 13 (46.4%), and were directed obliquely posteramedially or sagittally in 11 (39.3%) of our cases.

Cerebellar displacement: The inability of the small posterior fossa to accommodate posterior fossa contents in Chiari II malformation causes upward herniation of the cerebellum through the wide tentorial incisura[2,7,11,13]. Zimmerman et al[11] reported the CT appearance as a "pseudotumor of the tentorium", and Naidich et al[13] described it as a "towering cerebellum". Transincisural growth of the cerebellum in 43% of Chiari II patients before shunting, and in 76% after shunting have been reported[13]. Upward cerebellar displacement was present in 22 (78.6%) of our cases, and also identified in all the seven patients having ventricular shunts. But recent MR studies indicate that these findings may be related more to the technique of the radiologic examination, than to true upward herniation of the cerebellum[2]. Caudal displacement of the medial posterior cerebrum through the wide tentorial hiatus may allow visualization of a centrally placed cerebellum and a peripherally placed supratentorial brain in axial CT scans[2,11].

Mesencephalon

Tectum: The midbrain is abnormal in virtually every patient with Chiari II malformation[13]. The anomalies of the mesencephalon range from a slight loss of the intercollicular groove, to fusion of the colliculi into an elongated beak-shaped structure[15]. Naidich et al[13], reported pronounced mesencephalic beaking in 81% of their cases. We observed an anomalous mesencephalic tectum in all of our 28 cases. In the mildest form of the anomaly, the sagittal length of the tectum is shortened and the intercollicular groove is shallow. We defined this from as the with a "flattened" tectum which was present in six (21.4%) of our cases. The tectum is termed "pointed" when the colliculi is fused into a beak-shaped structure (Fig. 4). This was seen in 22 (78.6%) of our patients.

Diencephalon

Third ventricle/massa intermedia: The third ventricle is reported to be mildly dilated in most Chiari II patients[7,8,10]. It was enlarged in 22 (78.6%), and was of normal size in (21.4%) of the patients. The massa intermedia is reported to be enlarged in 67-90% of Chiari II cases[7,10]. The enlarged massa intermedia was noted in 15 (53.6%) of our cases.

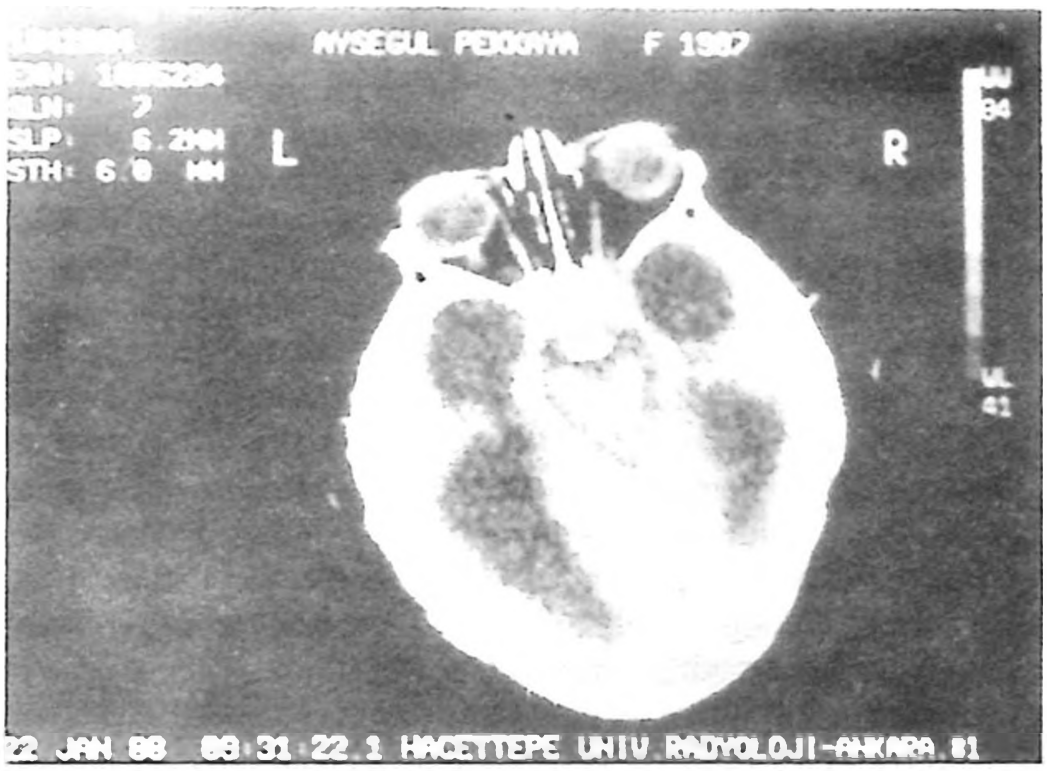

Fig. 4: In mesencephalon, fusion of the colliculi into a beak-shaped structure with posterior elongation is seen. Marked dilatation of the temporal and occipital horns of the lateral ventricles are also noted.

Telencephalon

Lateral ventricles: At necropsy, the lateral ventricles are dilated in 95% of Chiari II cases, and in most cases the dilatation is bilaterally asymmetric[16]. The atria and the occipital horns are more dilated than the frontal horns[16]. Dilatation of the lateral ventricles has been reported in 74% of cases with Chiari II malformation[10]. We observed dilated lateral ventricles in 26 (92.9%) of our cases, and in 24 of them the dilatation was asymmetric. Though the absence, or the fenestration of the septum pellucidum has been reported in necropsy studies, axial CT scans failed to demonstrate this anomaly in 50% of patients[10].

Corpus callosum: We have observed partial agenesis of the corpus callosum in nine (32.1%) of our 28 cases. We believe that the axial CT sections are not very reliable for assessing the dysgenesis of the corpus callosum. Sagittal MR sections better demonstrate the presence of this anomaly, and it was reported to be present in 33-83% of Chiari II cases[7,17].

Supracerebellar CSF containing spaces: A wide subarachnoid cistern above the cerebellum involving, to varying degrees, the quadrigeminal plate cistern, the cistern velum interpositum, the interhemispheric fissure, and the ambient cistern has been reported[2,7]. This may be due to parenchymal loss in the medial posterior aspects of the cerebral hemispheres resulting from pressure atrophy from

hydrocephalus[2]. A relationship between the size of the cistern and the degree of hydrocephalus has been noted. The spaces were compressed or smaller when hydrocephalus was present, and were larger when the ventricles were effectively shunted[2,7]. A large supracerebellar CSF containing space was identified in eight (28.6%) of our cases. We found that the size of the cistern was greater in five patients, in whom the lateral ventricles were compressed due to shunting. In cases with marked hydrocephalus, the cistern could not be identified.

Tentorium and Falx

Wide tentorial hiatus: Widening of the tentorium is seen in axial scans by the appearance of cerebellar tissue extending superiorly without the normal tapering caused by the cerebellar margins of the tentorium[7]. The tentorial margins may also be identified on contrast enhanced scans[6]. Peach[16] has reported the widening of the tentorial incisura, and its low insertion to the occipital bone in 95% of cases coming to necropsy. Wolpert et al[7] have reported the widening of the tentorial hiatus in 15 of their 24 cases. Widened tentorial hiatus was present in 17 (60.7%) of our cases.

Falx hypoplasia/Interdigitation of gyri: Partial absence or hypoplasia of the falx, and fenestrations were reported to be present in all Chiari II cases at necropsy[16]. Interdigitation of the gyri, which indicates falx fenestration has been significantly demonstrated by CT[6]. While Naidich et al[6] reported a 22% rate, Wolpert et al[7] reported that the interdigitation of the gyri was present in nine of their 24 cases. Gyral interdigitations were present in 13 (46.4%) of our cases (Fig. 5).

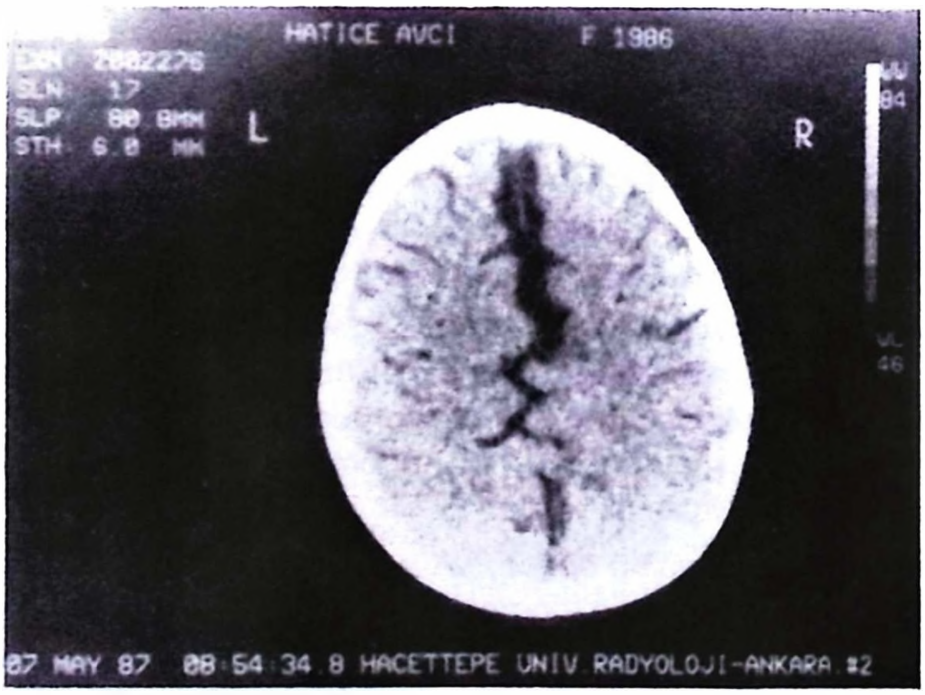

Fig. 5: The fenestration of the falx and the apposition between the gyri of the two hemispheres are noted.

Surgery

Respiratory or swallowing dysfunction associated with poor feeding and failure to thrive is considered an indication for surgery in an infant[12]. In the older child, progressive spasticity and upper extremity weakness are the most common indications for surgery[12]. The treatment of hydrocephalus in Chiari II malformation requires decompressive approaches in the suboccipital and cervical areas in addition to ventricular shunting[18]. Surgery has been designed to decompress the fourth ventricle and spinal cord promoting relief of pressure symptoms resulting from either internal expansion, or dorsal compression of the medulla and the cervical cord[12]. It is important to make a differential diagnosis between the Chiari II malformation and other types of hydrocephalus preoperatively. Although malformations have rich computed tomographic findings, none of them are pathognomonic for Chiari II[6,10,13]. Each may be seen infrequently in other patients with other conditions. But the presence of several of these anomalies together, helps to identify the patients with Chiari II malformation, thus differentiating them from other hydrocephalus cases (non-Chiari hydrocephalus)[6,10,13].

Summary

In this study cranial computed tomographic (CT) features of 28 cases with Chiari II malformation are presented. 26 of these cases had hydrocephalus (92.9%) and the fourth ventricle was either absent or small in 25 (89.3%) of the cases. Caudal displacement of the fourth ventricle was noted in 15 (53.6%) of the cases, and craniolacunia was present in 18 (64.3%) of the cases with seven of them being more than one-year-old (up to 18-years-old).

We found CT to be a safe, non-invasive and effective method of elucidating the types of abnormalities associated with this disorder. Preoperative computed tomographic evaluation of patients with Chiari II malformation helps to differentiatic it from other types of hydrocephalus, thus yielding a change in the operative approach.

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The Turkish Journal of Pediatrics 31:123 - 126, 1989

THE INCIDENCE OF PUBERTAL GYNECOMASTIA IN BOYS LIVING IN THE ANKARA REGION*

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*Atilla Büyükgebiz MD****

Key words: gynecomastia, puberty, Turkish population

Gynecomastia, or the occurrence of mammary tissue in the male, is a common condition. During pubertal development, approximately two thirds of boys develop varying degrees of subareolar hyperplasia of the breasts. Tenderness of the breast is frequent but transitory. Spontaneous regression may occur within a few months; it rarely persists one year or more[1-5]. The incidence of this condition is not clearly defined in Turkish pubertal boys because studies of pubertal gynecomastia are very limited in number[6]. The aim of this cross-sectional study is to find the incidence of pubertal gynecomastia among healthy young boys in Ankara.

Material and Methods

The study consisted of 646 Turkish boys from the Ulus Social Security Hospital in Ankara. Since they came to the hospital presenting with simple complaints, the subjects were in good health and had no physical abnormalities. Their ages ranged from ten to 16 years. All of the boys were from the lower socioeconomic sector of the population. Physical examinations were carefully performed to determine the stage of pubertal development, and the presence and degree of gynecomastia. Genital development and pubic hair growth were classified into five different stages, as described by Marshall and Tanner[7], and Winter[8].

The degree of gynecomastia was evaluated by measuring the diameter of breast tissue[1]. The size of these subareolar masses were estimated and rated on a scale of 1+ to 4+ separately in each breast: A small disk limited to the subareolar area and not reaching the margins of the areola (about 0.5 cm in diameter) was rated 1+, reaching the margins of the areola, but not beyond (up to 1.5 cm in diameter) 2+, no more than 5 mm beyond the margins 3+, and more than 5 mm beyond the margins of the areola 4+.

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Results

The incidence of gynecomastia among pubertal boys according to pubertal stages and their ages are summarized in Tables I and II. A marked increase from 9.2 percent at Pubertal Stage 2 to 60.2 percent at Pubertal Stage 4 in the incidence of gynecomastia was observed. After Stage 4, the incidence appeared to drop to 28.2 percent at Pubertal Stage 5 (Table I).

TABLE I: The Incidence and Degree of Gynecomastia in Pubertal Stages

Pubertal stage	Total number of cases	Number of cases with gynecomastia	Number of cases in each gynecomastia degree			
			1 +	2 +	3 +	4 +
2	195	18 (9.2%)	8	7	3	–
3	208	89 (42.7%)	26	52	7	4
4	151	91 (60.2%)	21	49	15	6
5	92	26 (28.2%)	2	18	5	1
Total	646	224 (34.6%)	57 (25.5%)	126 (56.2%)	30 (13.4%)	11 (4.8%)

A gradual increase was seen from 8 percent at age 11.5 years to 43.8 percent at age 13.5 years. Peak incidence of 61.1 percent occurred in the 14-year-old age group. After the age of 14 years, the incidence gradually decreased (Table II). 80.4 percent of the cases were bilateral. Unilateral cases consisting of 19.6 percent did

TABLE II: The Incidence of Pubertal Gynecomastia in Boys Aged 10-16 Years

Age (yrs)	Number of cases	Number of cases with gynecomastia
10	7	–
10.5	10	–
11	26	–
11.5	25	2 (8.0%)
12	49	13 (26.5%)
12.5	80	23 (28.7%)
13	88	39 (44.3%)
13.5	89	39 (43.8%)
14	72	44 (61.1%)
14.5	74	35 (47.2%)
15	43	20 (46.5%)
15.5	41	7 (17.0%)
16	42	2 (4.7%)
Total	646	224 (34.6%)

not show a statistical difference on the right or left side (10.1 percent and 9.5 percent, respectively; $p > 0.05$). In 56 percent of the cases, the degree of gynecomastia was rated as 2+, while in only 4.8 percent of the cases it was 4+ (Table I).

Discussion

Gynecomastia may appear at different stages of life due to various reasons[1,3,4,9,10]. It is a physiological event in puberty. A large percentage of boys develop some degree of gynecomastria during pubertal developmental and it often occurs bilaterally[1-5]. Although, it has been suggested that this condition is usually associated with a decreased testosterone/estradiol ratio, presumably resulting from a transient imbalance in testosterone-estrogen production and with a variation in prolactin secretion, several studies show that plasma estrogen, testosterone, luteinizing hormone and follicle-stimulating hormone levels do not differ in boys with or without gynecomastia at the same stage of puberty. The serum prolactin level is not elevated in pubertal gynecomastia[2,3,11-14].

In this study, the incidence of gynecomastia during puberty was 34.6% at various pubertal stages and ages, with a peak of 60.2 percent at Pubertal Stage 4 and 61.1 percent at 14 years of age. Nydick et al[1] found the incidence of gynecomastia to be 38.7% in puberty with a peak incidence of 64.6 percent at age 14 years. It has also been reported that the incidence was 67 percent in a longitudinal study by Lee[2]. Neyzi et al[6] studied the incidence of pubertal gynecomastia in 1,530 schoolboys in İstanbul in 1975. By considering the presence of firm subareolar mammary tissue as evidence of gynecomastia, they found the incidence to be seven percent, and could not see a significant difference in the incidences between four socioeconomic groups. We believe that in determining the incidence of pubertal gynecomastia, pubertal staging is more useful than age groups.

In our study, and in that of Nydick et al[1] approximately, one-fifth of the boys were found to have unilateral gynecomastia. In the cases studied by Nydick et al[1], 23 percent were unilateral with 15 percent on the right and eight percent on the left side, but no explanation for the increased incidence of gynecomastia on the right side could be deduced. In our series, 19.6 percent of the cases were unilateral and there was no difference with regard to right and left involvement.

Summary

The incidence of pubertal gynecomastia was determined in 646 Turkish boys in Ankara. A marked increase in the incidence was observed at Pubertal Stage 4 (60.2%) and age 14 years (61.1%). The incidence of gynecomastia during puberty at various pubertal stages and ages was 34.6%. Although the incidence of unilateral gynecomastia was 19.6%; there was no difference between right or left involvement.

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The Turkish Journal of Pediatrics 31:127 - 135, 1989

LEUKOCYTE PHAGOCYTOSIS DURING CARDIOPULMONARY BYPASS IN ADOLESCENTS*

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Key words: cardiopulmonary bypass, polymorphonuclear leukocytes, phagocytosis, infection, adolescent

It is generally recognized that in patients undergoing extracorporeal circulation the immune defence system is temporarily impaired. The decrease in host resistance against invading or endogenous microorganisms can lead to postoperative infections. In patients undergoing operations involving cardiopulmonary bypass (CBP), infection is higher than in closed heart surgery, and other major surgical procedures[1,2]. The higher infection rate has been suggested to be the result of CPB. Cardiopulmonary bypass is associated with hemolytic anemia, denaturation of circulating blood proteins, and reduced levels of complement and immunoglobulins[1,3,4,5]. Therefore, we planned to investigate the effect of CPB on leukocyte phagocytosis in the adolescent. A recent study involving infants has demonstrated a decreased polymorphonuclear leukocyte (PMNL) function, resulting from immature capacities[6]. Studies performed in adults using different methods have shown contradictory results in this field[7-9].

Although in adolescents, the leukocyte functions have completed their maturity, increasing levels of sex hormones cause total body epithelium to change, and there is a rise in susceptibility to infections when compared to adults[10]. As a result, the effects of operations involving CPB on PMNL phagocytic function may differ from those in adults. Since, as far as we know, no other study has been reported in adolescents, this investigation was undertaken to define the effect of operations involving CPB on phagocytic functions of PMNL in adolescents undergoing complete repair of congenital or acquired heart defects.

We decided to undertake this study, using for the first time in this field a radioactive method which had previously been used in the identification of bacteria and is based on the principle that their presence can be determined by their metabolic activity[11]. Almost all aerobic bacteria which use various carbohydrates release CO_2 as a final froduct[11]. Previously, De Land and Wagner[11] added

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Presented at the Pediatric Cardiology and Cardiac Surgery Symposium, Hacettepe University Faculty of Medicine, Ankara, 28-30 April, 1988.

^{14}C-uniform glucose, and later Levin et al[12] used a mixture of ^{14}C-format and ^{14}C-uniform glucose as an energy source in the medium. Thus, they proved that the growth of aerobic bacteria could easily be observed in a short period of time. Subsequently, this method had been employed to determine whether or not biological life existed on the planet, Mars[12].

Material and Methods

Fifty adolescents in which absolute PMNL counts and phagocytosis were assessed were included in this study. They were divided into two groups. The first group consisted of thirty adolescents between 13-19 years of age who had undergone open-heart surgery because of congenital and rheumatic valve disease. The second group, the control group, consisted of twenty adolescents undergoing closed heart surgery.

Anesthesia was induced by use of intramuscular ketamine hydrochloride 5 mg/kg with atropine sulphate and was maintained with fentanyl citrate 50 µg/kg. Muscle relaxation was induced with pancuronium bromide. Ventilation was accomplished by an air/oxygen mixture. In the open operations, heparin 300 U/kg was administered before CBP. Cardiopulmonary bypass was performed with a roller De Bakey pump, nonpulsatile perfusion and a disposable bubble oxygenator (Rygg-Kyvsgaard), with a built-in heat exchanger. The pump was primed with electrolyte solution and complete hemodilution was applied. No blood was used during the operation. None of the patients received preoperative medication and no antibiotics were administered pre-or postoperatively to the patients or to the pump prime during this study. In control cases, closed heart surgery was performed.

The following assays were performed to examine each step in the process. Absolute PMNL count and their phagocytic functions were assessed. Total white blood cell counts were determined by a coulter counter and absolute values for PMNL counts were obtained from Wright-stained smears from the same sample and read by an observer who was unaware of the timing of the sample. The counts were corrected for hemodilution by means of the hemoglobin (Hb) concentration.

$$\text{corrected absolute PMNL counts} = \frac{\text{sample PMNL counts} \times \text{control Hb}}{\text{sample Hb}}$$

At least two samples were analyzed at each blood flow.

The following assays were performed to determine phagocytic functions of PMNL.

Blood collection: A total 15 ml of heparinized venous blood was collected from each patient prior to bypass, within the first three minutes on bypass, off bypass and three days post bypass; in control cases the collection occurred before and after the operation. Blood samples were placed in three groups of specially vacuumed tubes.

Preparation of bacteria: *Staphylococcus aureus* coagulase positive and catalase positive were used (*S. aureus* 502A). A stock culture of *S. aureus* 502A, stored at-70°C in trypticase soy broth with 20% glycerol was thawed and incubated for 18 hours at 37°C. The culture was centrifuged and washed with Hanks balanced salt solution and adjusted to $2\text{-}5\times10^8$ bacteria per millimeter.

Preparation of radioactive material: The radioactive substances, ^{14}C-uniform-glucose and ^{14}C-format mixture which have 3 mCi/ml radioactivity were specifically selected. We used 0.2 ml of this radioactive solution which had 1 mCi per millimeter.

Blood samples, bacteria and radioactive substances were placed in three groups of specially vacumed tubes as follows:

Material	Group I	Group II	Group III
Blood samples (leukocytes)	5 ml	5 ml	5 ml
Bacteria	0.5 ml	–	0.5 ml
Radioactive substance	0.2 ml	0.2 ml	0.2 ml

Tubes in Group I contained leukocytes of patients, bacteria, and a mixture of ^{14}C-format in which the leukocyte function was assessed. The tubes in Group II contained only leukocytes and radioctive substances which indicated whether or not the blood samples of the patient and the intravenous infusion liquids had been contaminated with bacteria. The tubes in Group III were primarily frozen at −20°C and later thawed at room temperature. Thus, the leukocytes in the blood sample were broken down. This group of tubes indicated whether or not the bacteria were alive. Tubes in Groups II and III were control tubes of Group I and of the method which was used. The tubes in Groups I, II and III were placed in a special mixture-heater machine whose temperature was stable at 37°C. Thus, optimal conditions were obtained so that the bacteria could easily reproduce. The $^{14}CO_2$ level which is produced as a result of the bacteria reproducing was counted with a special "Bacted" machine. It has been established that the volume counted is satisfactory within a 12-hour period. The $^{14}CO_2$ volume which is obtained in the medium is assessed as vol/min. It has been demonstrated that bacteria in the

medium is unable to reproduce in cases where the $^{14}CO_2$ volume is low. This shows that the leukocyte phagocytosis is effective. In cases where the $^{14}CO_2$ volume is high, the bacteria in the medium is found to multiply rapidly and leukocyte phagocytosis is inhibited.

Results

The effect of CPB on the absolute PMNL count is presented in Fig 1 a. Initially, the absolute PMNL count was 3.81 ± 0.43 /mm^3, and had decreased on bypass and off bypass periods; it exceeded the baseline level significantly on the third post bypass day ($p < 0.05$). The values in closed heart surgery did not show any significance ($p > 0.05$; Fig. 1 b).

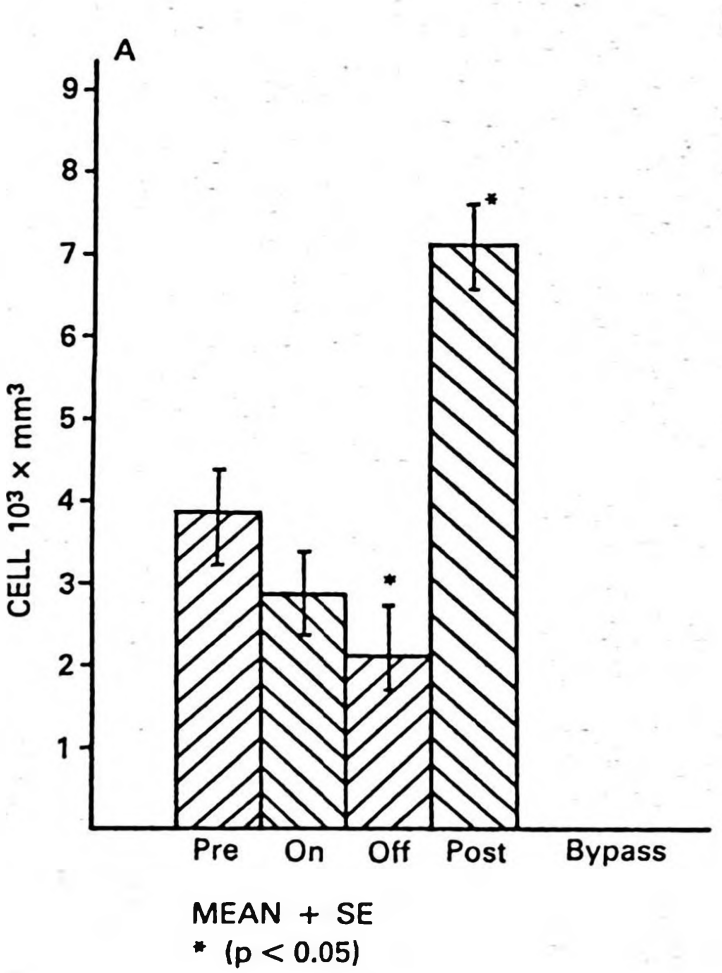

Fig. 1 a: Effects of CPB on absolute PMNL count; it dropped in the on and off bypass periods, and then increased approximately two-fold in the post bypass period.

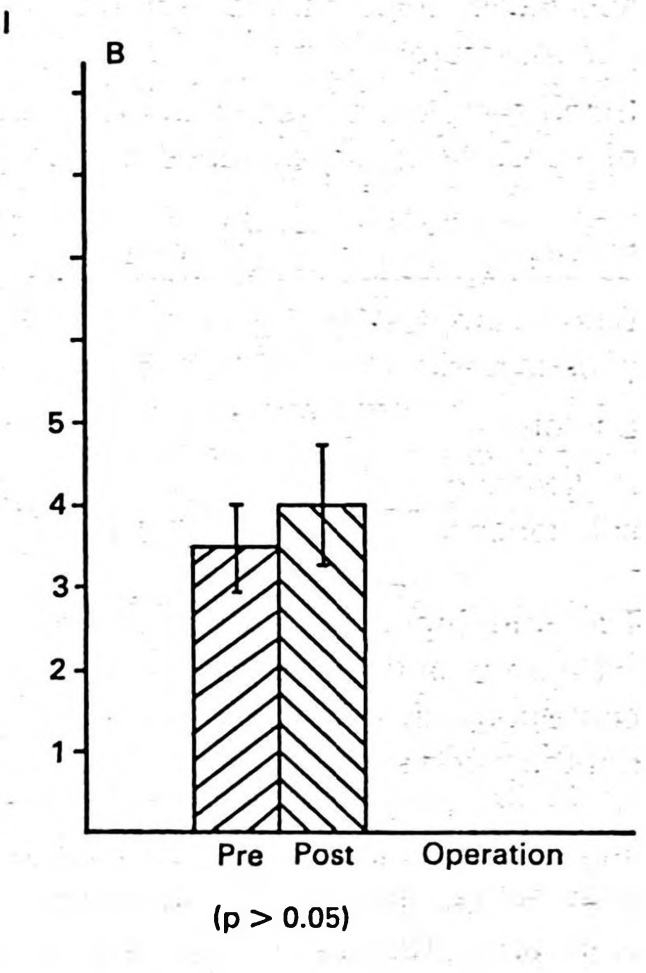

Fig. 1 b: Effects of closed operations on absolute PMNL count.

In the open operations the phagocytic function of PMNL is shown in Table I. The tubes in Group I show the $^{14}CO_2$ volume indicating phagocytosis of PMNL to be normal before the operation. However, the phagocytic function began to alter on

TABLE I: $^{14}CO_2$ Values (cc/min) in Patients Undergoing Open-Heart Surgery (n: 30)

	Pre-Bypass			On Bypass			Off Bypass			3 days Post-Bypass		
Group	I	II	III	I	II	III	I	II	III	I	II	III
Mean±SD	0	0	850±20.4	8.4±2.3	0	780±18.2	254±22.8	0	625±28.4	7.8±0.6	0	930±31.8

$p < 0.05$ $p < 0.05$

bypass. Immediately off bypass the same activity was significantly decreased as compared with the beginning on bypass ($p < 0.05$). The low $^{14}CO_2$ volume in Group tubes I on the third post bypass day showed that the growth of bacteria was inhibited because of active phagocytosis. The $^{14}CO_2$ volume in Group tubes II had been zero before surgery, at the start on bypass, off bypass and in the post bypass period. This result demonstrated that the patient's blood and the perfusion system used in the operation had not been contaminated with bacteria. Due to the fact that the results obtained in Group II tubes yielded a value of zero with regard to $^{14}CO_2$ for each period, no statistical comparison was made. We obtained a rather higher volume of $^{14}CO_2$ in the third group of tubes during the four periods of study (pre-bypass, on bypass, off bypass and post bypass). Indicating that the bacteria were alive and that they could easily multiply. This leads to the conclusion that no technical fault was found in the method used. For this reason, we felt that there was no need for a statistical study involving Group III which constituted the control tubes of the perfusion system as well as of the method.

In control cases who underwent closed heart surgery, the phagocytic function of PMNL is shown in Table II. The tubes in Group I show the volume of $^{14}CO_2$ which indicates the PMNL phagocytosis to be at a normal level in the pre-and postoperative periods.

TABLE II: $^{14}CO_2$ Values (cc/min) in Patients Undergoing Closed Heart Surgery (n: 20)

	Preoperative			Postoperative		
Groups	I	II	III	I	II	III
Mean±SD	0	0	680±4.81	7.3±1.21	0	6.20±5.24

As a result of this study it has established that the absolute PMNL count as well as the phagocytic functions were significantly decreased in off bypass adolescents who had undergone CPB as compared to the cases who had undergone closed heart surgery. This decrease in PMNL phagocytic causes adolescents to be susceptible to infection after open heart surgery. Indeed, of the thirty adolescents, fourteen had various types of infections in the postoperative period. The majority of the cases (nine) had genitourinary tract infections but there were also three pulmonary and two wound infections. Another point of interest found in this study was that in the cases in which a clinical infection picture was seen after surgery, there was a longer duration on bypass and a higher inhibition of leukocytic phagocytosis. The correlation between the duration on bypass and the $^{14}CO_2$ volume related to the inhibition of leukocyte phagocytosis could be shown as a trend (Fig. 2).

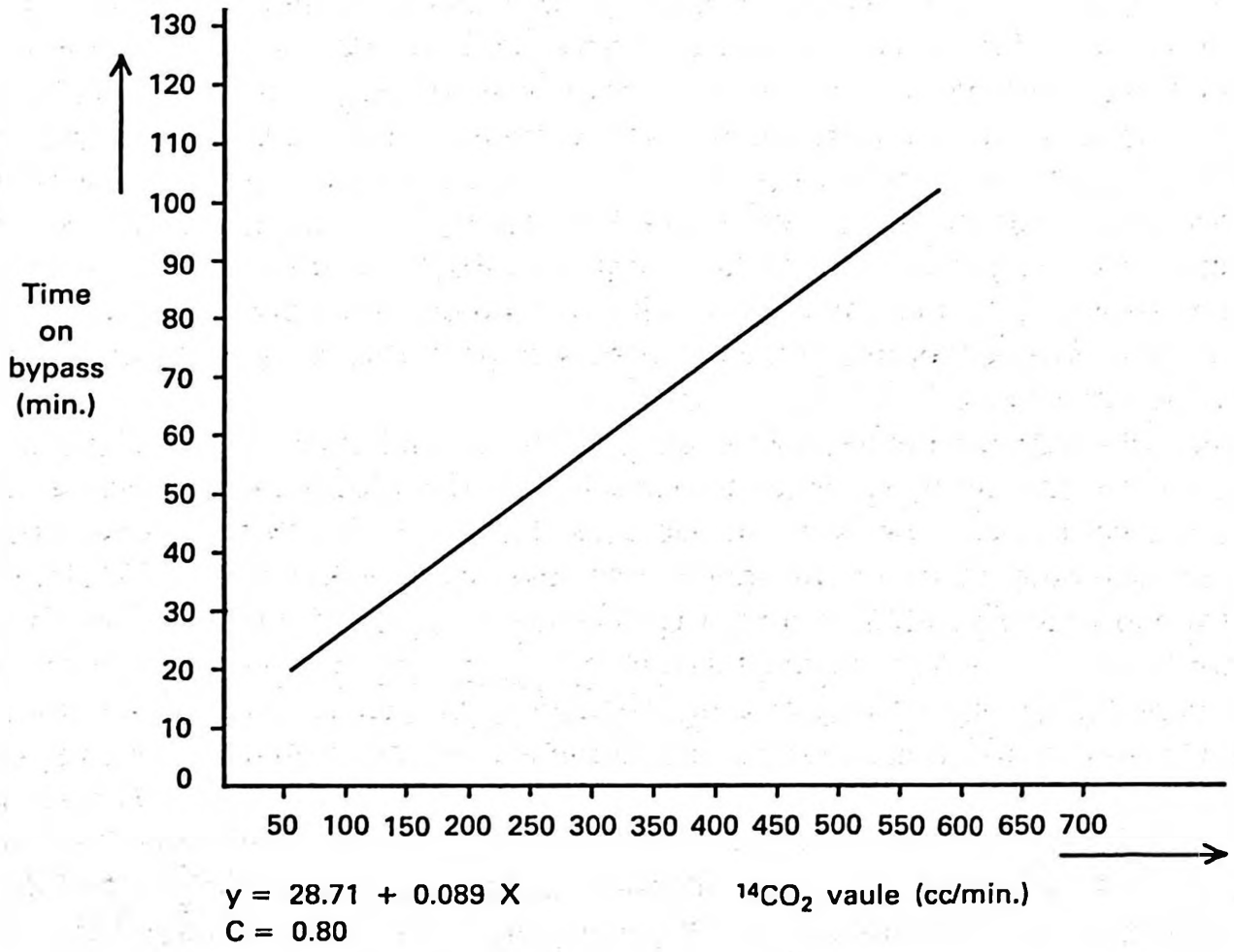

Fig. 2: Correlation between the duration of bypass and $^{14}CO_2$ values with relation to the inhibition of leukocytic phagocytosis.

Discussion

The phagocytic function of leukocytes has an important effect on the defence mechanism of the body[1]. There have been contradictory opinions related to the function of leukocytes during operative procedures involving cardiopulmonary bypass[7-9]. However, in these studies various methods have been used in evaluating the function of leukocytes[7-9]. In this study we have assessed the phagocytic function of leukocytes by using a radioactive method which differs from other studies in this field[11]. In the method we used it is unnecessary to obtain the leukocytes from the blood medium[12]. Furthermore, only a 12-hour period is sufficient for the growth of bacteria whereas 72-96 hours are required in some other methods[3]. It is also possible to complete the experiment by measuring the $^{14}CO_2$ volumes every hour without cancellation of the medium. Thus, this method can easily and simply be applied in this field. In our study it has been shown that the phagocytic function of leukocytes were normal at the beginning of the operation, then, with the start of perfusion, gradually diminished.

Although, the phagocytic functions of leukocytes decreased significantly off bypass, these functions returned to normal in three days. However, similar studies in adults have shown contradictory results[6-9,11-17]. For instance, Lunström et al[13], have reported a decrease in phagocytosis which lasted up to 8 days after CPB, although no information was reported regarding the anesthesia or CPB techniques. In contrast Kaplan et al[8], and Ros et al[14] in their studies have reported no change in phagocytosis in adults undergoing CPB. In our opinion, their findings can be explained by the transfusion of fresh blood elements during perfusion. In our system, we neither used blood elements in the perfusion system nor we did transfuse any blood.

In another study, Silva et al[9], who evaluated PMNL in adults following CPB using nitroblue tetrazolium dye reduction, found that the dye reduction was decreased. This finding implies a decrease in bactericidal capacity, which agrees with our results. The other studies performed in this field by Bubenik et al[15] and Mayer et al[16] found a change attributed to a CPB-induced defect of the PMNL in adult patients with decreased phagocytosis. However, our method differs from those mentioned above in that we could not see a defect in our patient. In their study, Van Oeveren et al[17], measured the opsonic activity of serum after CPB with an oil red uptake assay, a method not entirely comparable to our technique. Consequently, they found that there was a decrease in phagocytosis, which agrees with our study. A recent study involving infants has demonstrated a decrease in PMNL functions, which are immature at birth[6]. In our study, as compared to others, no antibiotics were added to the perfusion system nor were they given to the patient prior to surgery. This has proven to be assuring with regard to our findings. We have demonstrated that the influence of surgery involving cardiopulmonary bypass has an adverse effect on polymorphonuclear leukocyte phagocytosis. Another point of interest is that in the cases in which postoperative infections occurred there was a longer duration on bypass and a higher inhibition of leukocytic phogocytosis. This decrease in the PMNL phagocytic functions might be due to the decrease in the absolute PMNL count when on and off bypass and the deleterious effect of CPB in which the blood components are subjected to mechanical trauma as well as the drugs used in the perfusion system.

Summary

This study was performed to determine the absolute PMNL count as well as phagocytic functions in adolescents who had undergone CPB; a radioactive method was used for the first time in this field. Although CPB causes a decrease in the absolute PMNL count when the subject is off bypass, this value exceeded the baseline level within three days. A day prior to surgery PMNL phagocytosis was found to be normal and was unaffected within the first minutes on bypass. Whereas, PMNL phagocytosis decreased significantly.off bypass. However, the

decrease was transient and returned to normal within three days. Another interesting finding obtained as a result of this study was that in the cases in whom the clinical infection picture was seen, the patient had a longer duration on bypass and a higher inhibition of leukocyte phagocytosis. The correlation between the duration on bypass and inhibition of leukocyte phagocytosis could be shown as a trend. Thus it may be concluded that the longer the on bypass period the higher the inhibition of leukocytic phagocytosis and the higher the infection rate in the postoperative period.

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The Turkish Journal of Pediatrics 31:137 - 143, 1989

THE EFFECT OF D-PENICILLAMINE IN THE DEVELOPING RAT CEREBELLUM*

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Key words: cerebellum, copper, D-penicillamine, rat.

Copper deficiency produces a variety of clinical effects in animals and man which is not surprising in view of its known roles in the structure and function of a number of enzymes including cytochrome oxidase (electron transport), superoxide dismutase (free-radical detoxification), tyrosinase (melanin production), dopamine beta-hydroxylase (catecholamine production), lysyl oxidase (cross-linking of collagen and elastin), ceruloplasmin (ferroxidase, transport), and unidentified copper enzyme (cross-linking of disulphide bonds of keratin)[1,2]. Copper deficiency in grazing animals is responsible for the condition termed enzootic neonatal ataxia in lambs, and copper deficiency resulting in neurological abnormalities in neonates has been experimentally produced in laboratory animals[3].

The simularities between Menkes' syndrome and the copper deficient rat includes slow growth, abnormal behavior, a decrease in myelin, a reduction in cytochrome oxidase and presumably less brain copper[3,4]. In this study we evaluate the effects of D-penicillamine, a well-known copper chelator, in the cerebellar maturation of the offspring of pregnant rats.

Material and Methods

Albino pregnant rats with a mean weight of 250 g (ranging from 220 to 300 g) were used in this study. Their gestational ages were determined by the presence of a vaginal plug on the first day of gestation, and abdominal palpation after the tenth day.

Ten animals received D-penicillamine (DPA) in their drinking water in a daily dose of 300 mg (low-dose) or 400 mg (high-dose) during their last six days of gestation and four rats were selected as controls and received no drug. On the 20-21th day of gestation, the fetuses were delivered by cesarian section in four animals of the

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study group (two high-dose and two low-dose) and two of the controls. The remaining two animals received high-dose DPA during their gestation, and two controls were given a normal diet which contained no DPA for three weeks after delivery. At the end of this period, their offspring were sacrificed and evaluated in the same manner as the newborn animals.

The animals were weighed and then killed by decapitation. The cerebellum was separated from the rest of the brain and bisected along the transverse line across the widest diameter. After weighing, the cerebellar tissue was embedded in paraffin blocks stained with hemotoxylin-eosin and examined by means of light microscopy.

A new scoring system was developed to determine the maturation and degeneration of the cerebellum which was based on the thickness of the granular layer, number and disarrangement of Purkinje cells and the heterotopic granular cells in the molecular layer (Table I, Figs. 1-4).

The results were evaluated statistically according to Student's *t* test or the Kruskall-Wallis analysis.

TABLE I: Staging System for Cerebellar Degenerative Changes

Criteria	Score*
1. Reducing thickness of granular layer	0, +, ++, +++
2. Reduced in number of Purkinje cells	0, +, ++, +++
3. Disarrangement of Purkinje cells and heterotophic granular cells in the molecular layer	0, +, ++, +++

* Score was given "from no change to severe pathological changes" as 0, +, ++, +++

** The scores in positive values for three scores was summed arithmetically and the calculated value was used to evaluate the staging as follows:

Total score	Stage
0 - 2	0
3 - 5	1
6 - 8	2
⩾ 9	3

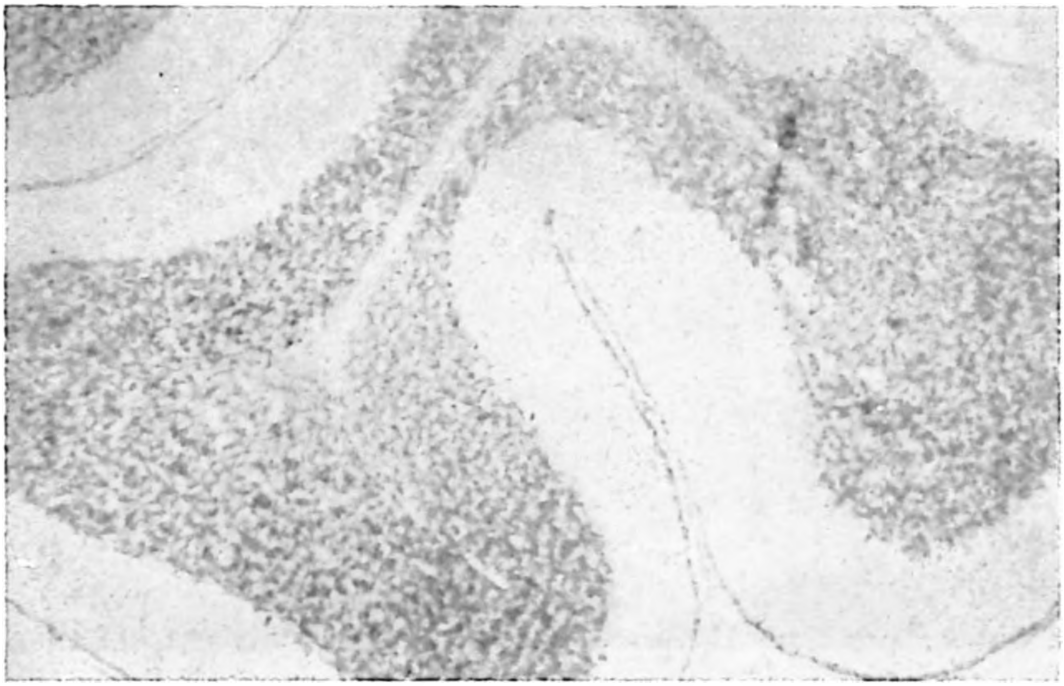

Fig. 1: Normal cerebellum (Stage 0).

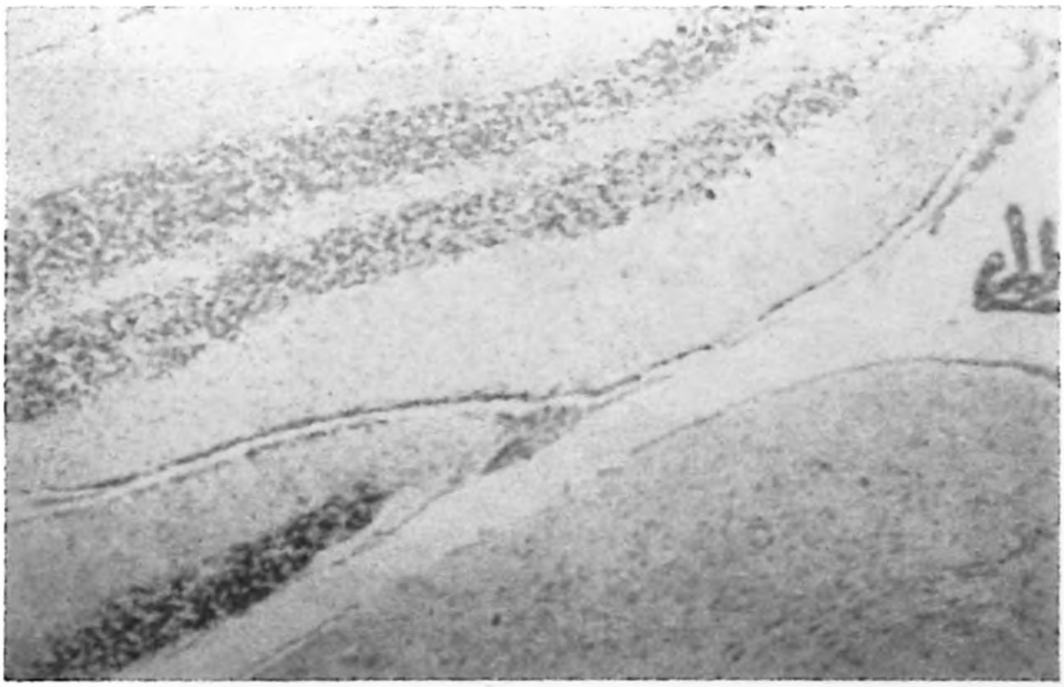

Fig. 2: Moderately cerebellar degeneration (Stage 2).

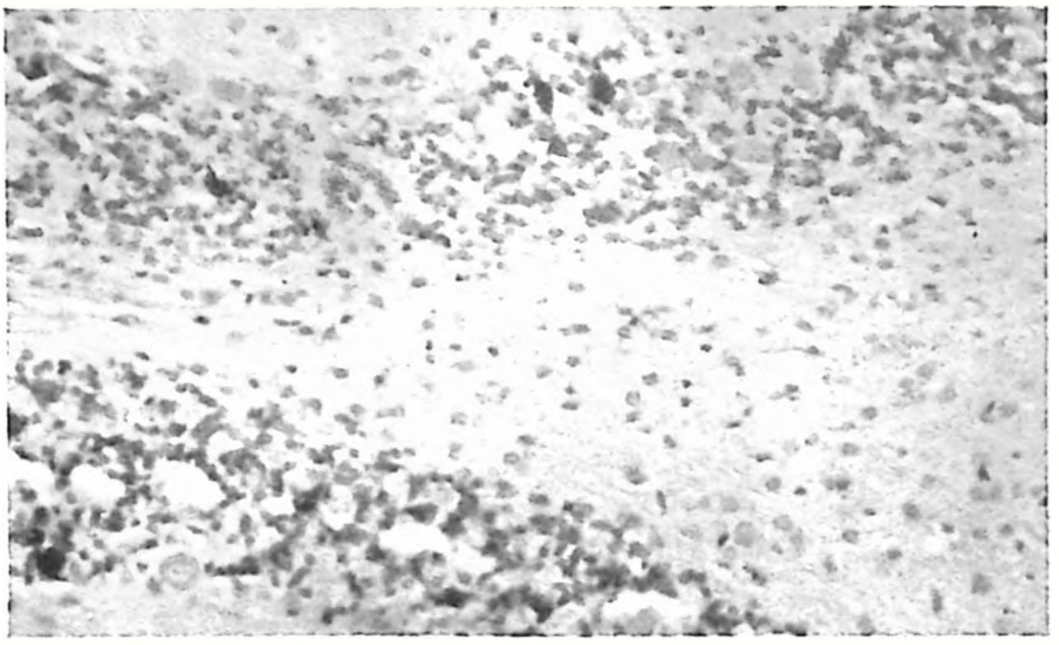

Fig. 3: Histological appearance in high magnification in Stage 2: Reducing in the thickness of granular layer and number of Purkinje cells, disarrangement of Purkinje cells, and heterotupic granular cells in the molecular layer.

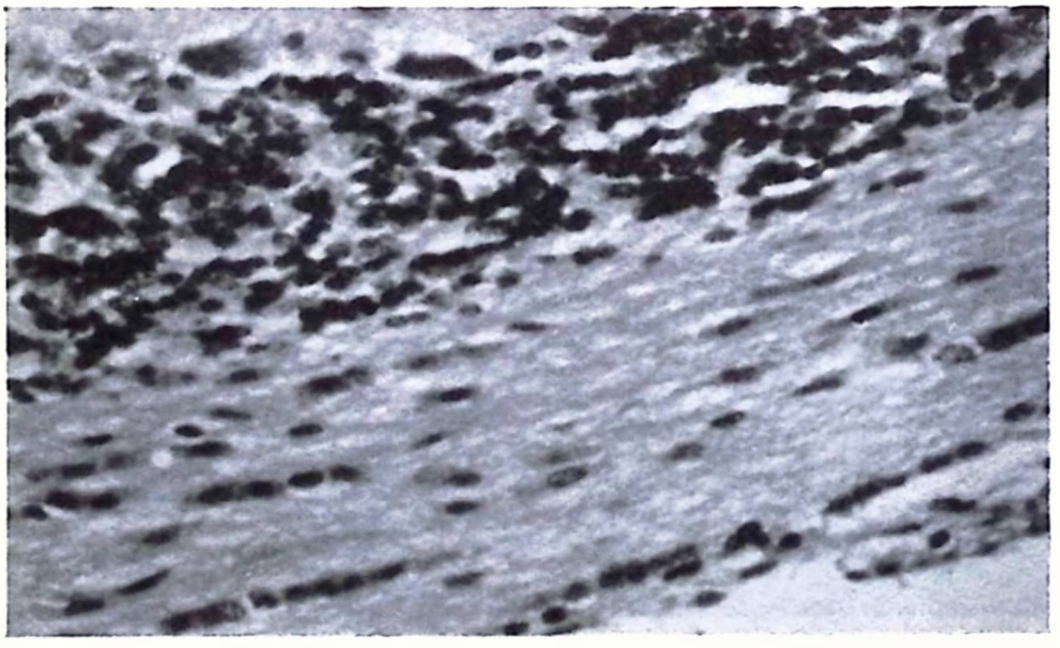

Fig. 4: Severe cerebellar degeneration (Stage 3): Reducing in the thickness of granular layer and marked loss of Purkinje cells.

TABLE II: Cerebellar Findings in the Offspring of Rats

	At birth			At the third week	
	Group I	Group II	Group III	Group IV	Group V
D-penicillamine treatment during gestation	No	Low-dose	High-dose	No	High-dose
Maternal values*					
Serum copper (µg/dl)	95 and 89	83 and 84	71 and 78	92 and 88	93 and 85
Serum zinc (µg/dl)	108 and 113	111 and 114	106 and 113	112 and 114	118 and 113
Serum ceruloplasmin (IU)	41 and 46	36 and 38	31 and 29	44 and 41	47 and 44
Body weight (mg)	9537 ± 390 (n: 7)	8378 ± 483 (n: 10)	4897 ± 579 (n: 8)	13034 ± 303 (n: 8)	1225 ± 418 (n: 7)
CW/BW (%)**	0.36 ± 0.04 (n: 6)	0.35 ± 0.05 (n: 10)	0.27 ± 0.03 (n: 7)	1.05 ± 0.04 (n: 8)	1.03 ± 0.03 (n: 7)
Score for cerebellar degenerative changes***	0 (n: 6)	0.4 ± 0.1 (n: 10)	2.5 ± 0.3 (n: 7)	0 (n: 8)	0 (n: 7)

* At the end of gestation, or at the end of the third week after delivery.
** Cerebellar weight / Body weight (mg) X 100
*** According to Table I.
Statistical comparisons:
Body weight: I-II, I-III, II-III $p < 0.001$, IV-V $p > 0.05$.
CW / BW : I-III, II-III $p < 0.001$, I-II, IV-V $p > 0.05$.
Score : I-III, II-III $p < 0.001$, I-II $p < 0.05$, IV-V $p > 0.05$.

Results

Pups of the DPA treated mothers showed a greater decrease in body weight. Compared to the controls their hair was short, sparse, easily pulled out and of coarse texture. They were less active in general, but became hyperirritable when stimulated. Pups of the DPA-treated mothers also showed an appreciable decrease in the size of their cerebellum. Histological examination revealed a highly significant decrease in myelination, reduction in the thickness of the molecular layer and the number of Purkinje cells. It was observed that heterotopic granular and Purkinje cells in the molecular layer were much more pronounced in these animals (Table II). A postnatal DPA-free diet given to the lactating mothers appeared to have a significant effect in largely reversing the hypomyelination and other pathological findings (Table II).

Discussion

Menkes' syndrome is a sex-linked recessive disorder in male infants, which results in growth retardation, "steely" or kinky hair (pili torti), depigmentation of the skin, and focal cerebral and cerebellar degeneration[4]. Numerous lines of evidence suggest that Menkes' disease is derived from an intracellular defect of copper utilization, which may sequester copper in an abnormal form. The distribution of copper in various tissues of these patients is abnormal, with intestine and kidney having elevated concentrations, and brain and liver being depleted. Copper-dependent enzymes may not be synthesized in tissues from these patients even when tissue copper is elevated[2].

In most patients Menkes' syndrome has not been diagnosed before six to eight weeks of age, when developmental failure and other clinical features become apparent, and low copper levels are found. But early postnatal diagnosis of Menkes' disease may be possible, since hypothermia, lethargy and hyperbilirubinemia as well as the characteristic hair, may be present in the neonatal period. Parenteral copper therapy does not seem to prevent cerebral damage, even when initiated in neonates. Postnatal therapeutic failures may be due to difficulties in maintaining high circulating levels of copper in the first months of life and/or to irreversible cellular damage[1,5]. Copper deficiency may also be seen in very low birth-weight preterm infants who are being fed with parenteral or artificial nutrition[6].

The result of this study which is contrary to a previous study[3] carried out on rats demonstrates that even though copper replacement was begun before the onset of myelination in the cerebellum, whose myelination and neuroglial proliferation occurs primarily postnatally in the first three weeks (at a much earlier developmental stage than that of the human infant), it did completely restore the rate of cerebellum growth and myelin deposition to normal.

DPA is an amino acid, dimethylcysteine penicillin derivative. It chelates metals, particularly copper and was introduced as therapy for hepatolenticular degeneration (Wilson's disease) 30 years ago, because it is stable, extremely soluble and is excreted in the urine. DPA is a teratogenic drug. It has been shown that feeding DPA to pregnant rats throughout gestation causes fetal resorption and congenital abnormalities. Although DPA may cause a decrease in the copper and zinc levels in maternal and fetal tissues, the addition of copper to a DPA-containing diet significantly reduced the frequency of malformed fetuses, supporting the hypothesis that DPA teratogenicity is primarily due to induced copper deficiency[7]. Thus, we can conclude that the result obtained in this study was due to copper deficiency rather than the DPA treatment.

Summary

The effect of D-penicillamine (DPA), a copper chelator, on the cerebellar maturation of the offspring of pregnant rats is evaluated. Pups of the mothers which received DPA in a daily dose of 300-400 mg during their last six days of gestation, showed an appreciable decrease in body and cerebellum weights, and cerebellar degenerative changes on histological examination. A postnatal diet DPA-free given to lactating mothers appeared to have a significant effect in reversing the cerebellar degenerative changes in their offspring.

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The Turkish Journal of Pediatrics 31:145 - 149, 1989

EFFECTS OF VERAPAMIL, PAPAVERINE, SODIUM NITRITE, AND HYDRALAZINE ON ETHYL ALCOHOL-INDUCED CONTRACTION OF THE ISOLATED HUMAN UMBILICAL ARTERY*

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Key words: umbilical artery, ethyl alcohol, verapamil, papaverine, sodium nitrite, hydralazine.

The effects of vasoconstrictor agents such as serotonin[1,2], noradrenaline[3], bradykinin, histamine, some prostaglandins, KCl[4] and some sympathomimetic drugs having a beta-mimetic effect such as adrenaline and isoprenaline[5] on human umbilical arteries have been studied. There have been relatively few investigations regarding the pharmacodynamic effects of ethyl alcohol on the same arterial bed[6,7].

It is well-known that chronic ingestion of alcohol during pregnancy may result in the fetal alcohol syndrome characterized by prenatal and postnatal growth retardation, central nervous system abnormalities and facial dismorphology in the fetus[8-11]. It has been affirmed that the impairment of essential amino acids and oxygen transport to the fetus result in this syndrome[12,13]. However, it has been demonstrated in a recent study that when a high dose of alcohol is infused into a monkey, the umbilical arteries temporarily contract, and the umbilical circulation becomes insufficient leading to severe hypoxia in the fetus[14]. Besides, it has also been demonstrated by Altura et al[7], that in vitro ethyl alcohol has a vasoconstrictor effect on the umbilical arteries. In order to eliminate this vasoconstrictor effect, they studied the effects of some antagonists such as phentolamine, methysergide, pyrilamine, metiamide, atropine, propranolol and indomethacin and proved that they are ineffective. In this study, various antagonists such as verapamil, papaverine, sodium nitrite and hydralazine have been used to inhibit ethyl alcohol-induced contraction of human umbilical arteries in vitro.

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Material and Methods

We used umbilical arteries isolated from cords obtained from the Konya Maternity Hospital in this study. The cords from caesarean sections and anesthetized cases were not utilized. Precautions were taken to eliminate cords belonging to subjects exhibiting eclampsia, hypertension, diabetes mellitus, Rh factor incompatibility and from mothers on medication (antihistamines, meperidine, adrenergic blockers, anticholinergics) during their last two months of pregnancy. The vessels were dissected free of connective tissue and cut spirally into strips approximately 2-3 mm in width and divided into segments measuring 20-25 mm in length. Each strip was mounted vertically in an organ bath containing 25 ml of Krebs-Henseleit solution. The resting tension was adjusted to 1 g and the segments were allowed to relax for a period of two hours during which the bathing fluid was changed every 15 minutes. The solution was maintained at 36-38°C and bubbled with a gas mixture containing 95% oxygen and 5% carbon dioxide. Responses to drugs were isometrically recorded by means of a transducer (Harvard Universal Oscillograph). At the end of the resting period, the preparations were treated with a high K^+ (80 mM) solution obtained by replacing 80 mM NaCl with an equimolar quantity of KCl. The tissue was relaxed by washing with fresh solution. Following this process, a cumulative dose-response curve to ethyl alcohol was obtained, and the tissue was washed again. The same procedure was repeated in the presence of 10^{-6} M concentration of antagonists. An antagonist was incubated for 30 minutes at a given concentration, and only one antagonist was tested on each strip. The responses to ethyl alcohol before and after the addition of antagonists were considered the percentage value of KCl-induced contraction. Maximum relaxations caused by antagonists and EC_{50} values (the concentration producing 50% of the maximum response) of ethyl alcohol were also calculated. A Krebs-Henseleit solution of the following composition (mM) was used: NaCl 118, KCl 4.70, $CaCl_2$ 1.60, $MgSO_4$ 1.20, $NaHCO_3$ 24.90, KH_2PO_2 1.20, and glucose 11.10.

The following drugs were used: ethyl alcohol (Merck), verapamil (Knoll), sodium nitrite, papaverine (Sigma) and hydralazine (Ciba-Geigy). A solution of each antagonist was prepared with distilled watar. All doses of the drugs were calculated in terms of the base weight. The results were expressed as means ± SEM. Significance of differences was calculated by Student's *t* test[15]. P values less than 0.05 were considered to be significant.

Results

Ethyl alcohol caused concentration dependent contraction of the isolated human umbilical artery. A 2000 mg/dl concentration of ethyl alcohol produced maximum contraction which was 64.8 ± 3.08% of 80 mM KCl-induced response (Fig. 1).

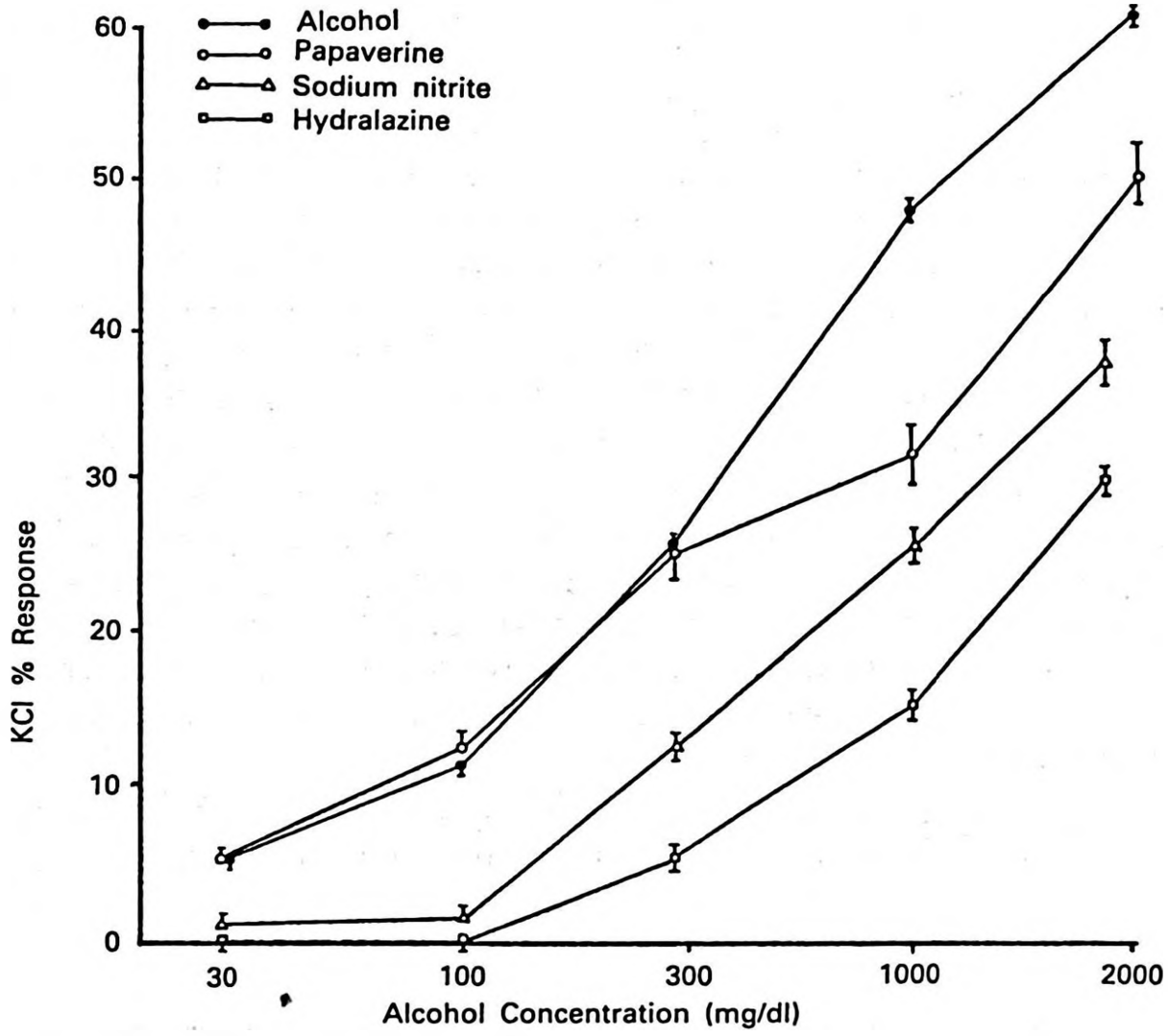

Fig. 1: Contractions produced by ethyl alcohol in the human umbilical artery and antagonistic potency of some vasodilator agents.

When 10^{-6}M verapamil was added to the bath, maximum contraction induced by ethyl alcohol and the control EC_{50} value did not change significantly. On the other hand, the same concentration of papaverine, sodium nitrite and hydralazine reduced the maximum response to alcohol and increased the control EC_{50} values significantly ($p < 0.05$; Table I).

TABLE I: The EC_{50} Value of Some Vasodilator Agents

	Control	10^{-6} M Antagonist	n
Verapamil	720 ± 3.24	700 ± 5.38	19
Papaverine	700 ± 9.68	1000 ± 9.51*	11
Sodium nitrite	380 ± 2.58	1200 ± 9.19*	13
Hydralazine	400 ± 4.54	1900 ± 9.41*	12

* Significantly higher than the control ($p < 0.05$)

Discussion

In this study ethyl alcohol produced dose-dependent contractions of the isolated human umbilical artery. This effect had previously been shown by Alture et al[7]. In his study, various receptor antagonists such as phentolamine, methysergide, pyrilamine, metiamide, atropine and propranolol were used in order to inhibit the contractile, response, however, these drugs were determined to be ineffective. Moreover, indomethacin, a prostaglandin synthesis inhibitor was proved to be ineffective. According to these findings, authors have claimed that activation of these receptors and also prostaglandin synthesis do not play a role in ethyl alcohol-induced contractions.

In the present experiment, smooth muscle relaxants such as papaverine[16], sodium nitrite and hydralazine[17] have inhibited the contractions produced by ethyl alcohol, although verapamil[18], a calcium channel-blocker, has been observed to be ineffective. The ineffectiveness of verapamil has shown that alcohol-induced contractions of the human umbilical artery is not mainly dependent on extracellular Ca^{++}, and that probably an intracellular mechanism may play a role in this response.

In conclusion, smooth muscle relaxing drugs may be effective in eliminating an alcohol-induced vasospastic effect in the human umbilical artery.

Summary

In this in vitro study, the vasodilator effects of certain drugs such as verapamil, papaverine, sodium nitrite and hydralazine on ethyl alcohol-induced contractions were investigated in the isolated human umbilical artery. Ethyl alcohol caused dose dependent contractions in this tissue. Papaverine, sodium nitrite and hydralazine were found to be effective.

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The Turkish Journal of Pediatrics 31:151 - 154, 1989

A CASE OF PARATHYROID ADENOMA WITH BROWN TUMORS DIAGNOSED BY ^{201}THALLIUM – ^{99m}TECHNETIUM SUBTRACTION SCINTIGRAPHY*

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Key words: parathyroid adenoma, radionuclide imaging, Brown tumor, ^{201}thallium-^{99m}technetium subtraction scintigraphy

The preoperative localization of enlarged parathyroids which is the most important step in the surgical approach to primary hyperparathyroidism has always presented difficulties. Numerous diagnostic procedures have therefore been proposed, including scintigraphy. Since first described by Ferlin et al[1] in 1981, ^{201}thallium-^{99m}technetium subtraction scintigraphy has become a reliable method for localizing parathyroid adenomas. Young et al[2] (1983), Percival et al[3] (1985), Skibber et al[4] (1985), and Blake et al[5] (1986) have reported that the ^{201}thallium-^{99m}technetium subtraction scintigraphy technique successfully localizes the vast majority of parathyroid adenomas.

Case Report

A 15-year-old girl was admitted to Hacettepe University Hospital presenting with swelling of the extremities and disturbance of gait. Physical examination revealed swellings on the chin, left wrist, knees and ankles. Since bone radiographs demonstrated disseminated lytic lesions, primary hyperparathyroidism was suspected.

Laboratory studies revealed a serum calcium level of 13.1 mg/dl and a serum phosphorus level of 3 mg/dl. A 24-hour urine sample collected for calcium determination yielded a value of 39 mg/dl. The C-terminal parathyroid hormone level was 9.54 ng/ml. Biopsy findings revealed Brown tumors. Whole-body ^{201}thallium-^{99m}technetium subtraction scintigraphy was performed as described by Young et al[2] with some modifications. Thyroid scintigraphy revealed a normal-sized thyroid with smooth borders. Subtraction scintigraphy demonstrated a focal 2.3 × 3.5 cm area of increased ^{201}thallium uptake localized below the inferior pole of the right lobe of the thyroid. Focally increased ^{201}thallium uptake

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was detected on both parietal bones, right corpus mandibulae, right iliac wing, distal femur, left proximal and distal tibiae, right distal tibiae, 5th metatarsal bones of the left foot and on the left wrist (Figs. 1-3).

A parathyroid adenoma was found during surgery which was located below the inferior pole of the right lobe of the thyroid. A bone biopsy was performed on two of the lytic sites, illustrated on the radiographs, and the histopathological diagnosis was Brown tumor.

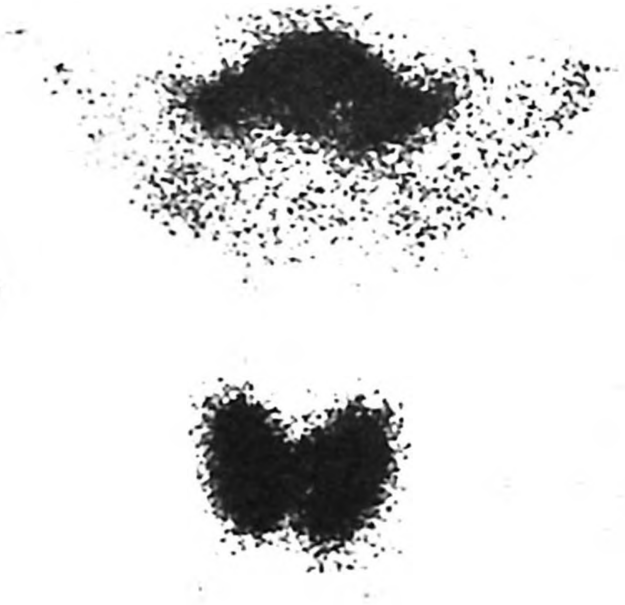

Fig. 1: ^{99m}Tc pertechnetate thyroid scan: Normal thyroid gland with smooth borders.

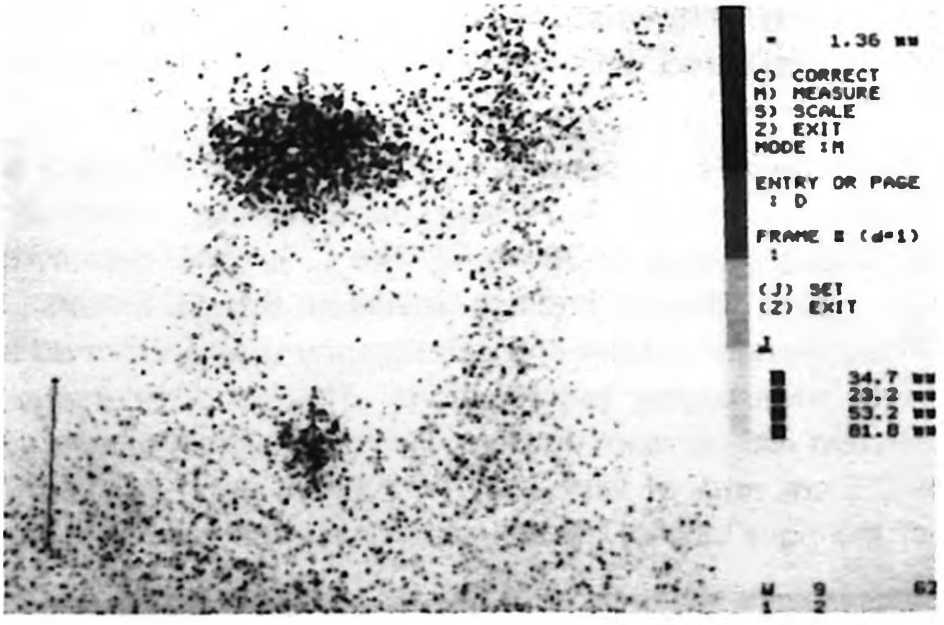

Fig. 2: ^{201}Tl-^{99m}Tc subtraction scan: A focal area of increased activity is present below the right lobe of the thyroid demonstrating the adenoma. There is an area of increased uptake in the bone on the right half of the corpus mandibulae.

Fig. 3: Thallium bone scan: Focal areas of increased uptake on both parietal bones and right corpus mandibulae (left, upper), on both distal femur and proximal tibiae (right, upper), on both distal tibia and fifth metatarsal bone (left, lower), on the left wrist (right, lower).

Discussion

The sensitivity of localizing parathyroid adenomas using the thallium-technetium subtraction technique was reported by Blake et al[5] to be 85 percent, and for hyperplasias 44 percent. Increased thallium uptake in the neck can also commonly be seen in thyroid carcinomas, thyroid adenomas, focal goitrous changes, Hashimoto's thyroiditis, rarely in neck metastasis, thyroid metastasis, lymphomas, sarcoidosis, and parathyroid carcinomas[6]. Correlation with ultrasonography and computerized tomography is necessary in order to eliminate false positive studies[4].

^{99m}Tecnetium-MDP bone scans are found to be abnormal in 58 percent of hyperparathyroid patients[7]. As far as we know, thallium bone scanning is not performed in hyperparathyroid patients. Thallium acts as a potassium analog, and is known to have a tumor affinity, but the exact mechanism is unknown[7]. It has been observed that in bone lesions diagnosed as Brown tumors, there is an accumulation of thallium, as in the case of adenomas. After a search of the literature we did not find any reports of focal thallium accumulation in Brown tumors associated with hyperparathyroidsm. Further investigation is necessary in order to elucidate this finding.

Summary

A case of parathyroid adenoma detected by ^{201}thallium-^{99m}technetium subtraction scintigraphy is presented. Focal areas of thallium uptake were observed in the bone. Bone biopsy findings revealed Brown tumors associated with hyperparathyroidism.

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The Turkish Journal of Pediatrics 31:155 - 158, 1989

URINARY TRACT TUBERCULOSIS IN A CHILD WITH HENOCH – SCHÖNLEIN PURPURA: A CASE REPORT*

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Key words: Henoch-Schönlein vasculitis, ureteral stricture, urogenital tuberculosis

Tuberculosis is still a major problem in developing countries where the risk of infection is about 2.6% annually, and 45% of the population is infected at the age of 20 years[1]. In adults 4-9% of cases develop urogenital tuberculosis[2] which is a secondary manifestation of pulmonary disease. However, in children this figure is estimated to be much lower[3].

We report an unusual case of urogenital tuberculosis in a child with strictures in the mid-portion of the ureter. As far as we know, such a stricture in childhood has not been reported in the English literature.

Case Report

A seven-year-old girl, the third child of healthy, unrelated parents, had a normal birth and early childhood. There was no known case of tuberculosis in the family. She was admitted to our hospital because of erythematous maculopapules on the lower extremities and buttocks, and abdominal pain. She was diagnosed as Henoch-Schönlein Purpura (HSP). Two weeks later, on her second admission, she was still complaining of severe abdominal pain and because hypertension was noted as well, she was hospitalized for further investigation.

Physical examination on admission revealed an alert girl with a temperature of 36.5°C, respiration rate of 28/min, pulse rate of 100/min, and blood pressure of 140/100 mmHg. The rest of the examination was normal except for flank pain on the right side. Laboratory studies revealed that the hemoglobin level was 11.10 g/dl, peripheral white blood cell count 9200 per mm^3 with 72% neutrophils, 24% lymphocytes and 4% monocytes. The platelets were adequate and the red blood

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cell morphology was normal. The sedimentation rate was high (78 mm/hr). The PPD reaction was positive (13 × 13 mm). Urinalysis revealed no proteinuria, but microscopic pyuria. Urine cultures, a total of seven, were negative. Acid-fast bacilli were not recovered.

The patient's unexplained fevers, sterile pyuria and positive tuberculin conversion suggested the diagnosis of tuberculosis. The child was further evaluated for her hypertension. Chest X-ray was normal. Renal function tests were within normal limits. Serologic tests for rheumatoid factors, antinuclear antibodies, hepatitis B surface antigen and antibody, and an LE-cell test were negative. The C_3 level was 110 mg/dl, and C_4 level 44 mg/dl. The renin level was 18.5 ng/ml/hr (normal: 0.51-4.18 ng/ml/hr). Abdominal ultrasonography revealed a dilated bilateral renal pelvis and left proximal ureter. The IVP showed a segmentary stricture on the middle third part of the bilateral ureters, more pronounced on the left, causing acute obstruction on that side. The voiding cystouretrogram was normal. A left retrograde pyelography was performed and the stricture was verified.

Surgical intervention was decided because signs of obstruction were observed. During the operation, excision of the stricture and a uretero-ureterostomy was performed. A biopsy of the lesion revealed caseification and calcification, a specific chronic granulomatous inflammatory stenosing ureteritis.

The patient was given antituberculosis therapy comprising 20 mg/kg of isoniazid and 20 mg/kg of rifampicin. The hypertension and abdominal pain resolved after the operation.

Discussion

A primary diagnosis of HSP in our patient was based on the characteristic clinical features of a purpuric rash involving the lower extremities and buttocks and also abdominal pain. In spite of the patient's hypertension, repeated urinalysis only revealed 8-10 white blood cells per high-power field. Renal involvement accompanying the HSP seemed rather unlikely because of the absence of proteinuria and microscopic findings in the urine. In HSP one third of patients with renal involvement are expected to have hematuria, whereas, one fourth have proteinuria and/or the nephrotic syndrome[4].

Since 1980, ten cases of stenosing ureteritis in HSP have been reported[5]. All were over five years of age and presented with flank pain. Multiple segments of the ureter appear to be affected in a majority of these patients but the ureteropelvic junction seems to be the commonest site of obstruction. Histopathologic studies of the ureters of five of the patients showed necrotizing vasculitis and ureteritis in two, ureteritis, fibrosis and calcification in two, and a calcified ureter in one patient. The role of corticosteroid treatment in preventing ureteral strictures in HSP is uncertain[5].

In our patient, the biopsy diagnosis was characteristic of tuberculosis. Urogenital tuberculosis is caused by the blood-borne metastatic organism, *Mycobacterium tuberculosis*[6]. It has been reported that a time lag of 2-20 years occurs between the initial pulmonary tuberculosis infection and the manifestations of urogenital tuberculosis[3]. This lag probably accounts for the widely-held erroneous belief that urogenital tuberculosis does not occur in children. But specially in our country, tuberculosis should be sought in all cases of sterile pyuria or chronic urinary tract infections which do not respond to the usual antibacterial therapy. In a report from Babies' Hospital, New York, Ehrlich and Lattimer[3] noted that 17 of their 30 children were asymptomatic whereas the most common laboratory finding was microscopic pyuria. Another report from Mayo Clinic shows again, that half of the patients are asymptomatic and that frequency, and dysuria are the commonest symptoms[7] The tuberculin conversion is found to be positive in 5 percent of the cases and early morning urine specimens should be cultured and animal inoculations should be carried out, which again yield highly positive results.

Hypertension has been known to be associated with renal tuberculosis since 1940[6]. Hypertension may be due to the reduction in the blood supply to part or the whole of the kidney[6], or due to acute obstruction of the ureter as in our patient. A fall in blood pressure is expected after nephrectomy[6] or after the relief of the obstruction in such cases, respectively.

The relationship of Takayasu arteritis and tuberculosis has been suggested by several authors[8]. Although this subject is still controversial, a high incidence of tuberculin sensitivity is noted in children with Takayasu's arteritis and an adolescent has been reported to demonstrate complete symptomatic remission with antituberculosis therapy[8]. Such an association has not been reported with HSP. On the other hand immunological abnormalities in HSP have been reported in various studies. Thus, the HSP in our case, might have acted as an aggravating factor for the tuberculosis infection, which was previously asymptomatic. Still a possibility of coincidence cannot be discarded.

Summary

A seven-year-old girl is presented, who was previously diagnosed as having Henoch-Schönlein vasculitis, and was further evaluated for hypertension. Urograms showed bilateral strictures of the ureter, causing obstruction on the left side. Tuberculosis, our preoperative diagnosis, evidenced by her sterile pyuria and PPD conversion was confirmed by the surgical specimen and treatment was begun.

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The Turkish Journal of Pediatrics 31:159 - 161, 1989

NIFEDIPINE IN THE TREATMENT OF ACRODYNIA*

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Key words: acrodynia, nifedipine treatment

Acrodynia is a very rare syndrome seen in infants and young children, and is attributed to repeated ingestion of or contact with mercury[1]. We observed a girl with this syndrome who seemed to immediately respond to the administration of nifedipine, and we report her findings.

Case Report

An eight-and-a-half-year-old girl was admitted to the Hacettepe University Children's Hospital on May 29, 1986, because of profuse perspiration, swelling, pain, itching, desquamation of the hands and feet, and a pink color of the nose and cheeks of forty days' duration. The last twenty days she started to complain of abdominal pain. The patient and her three siblings had been exposed to mercury at home (while at play) two months ago, but only she had these complaints which were getting worse.

Physical examination revealed a child who was listless, restless, irritable, and in a state of misery. With the exception of the findings on the extremities, the pink color of the cheeks and the tip of the nose, the other findings were not contributory. The extremities were cold and clammy. She was constantly complaining of a severe burning sensation and pain in the hands and feet. In addition to the fingers, the palms and soles also appeared edematous. The blood pressure was 170/130 mmHg.

Laboratory studies revealed that with the exception of proteinuria (622 mg/sqm/day) and mild hypoalbuminemia (3.2 g/dl), liver, and kidney functions, and electrolyte and hematologic findings were within normal limits. An excretion of 25 ng/ml of mercury was detected in the patient's urine. However, greater excretions of mercury were found in the urine of her three siblings (40-97 ng/ml; control: 4 ng/ml).

Due to hypertension, intravenous nifedipine therapy was initiated in a dose of 0.2 mg/kg four times a day. The next day the pinkish color of the nose, faded and the

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pain in the extremities decreased, though the blood pressure was not considerably affected. Therefore, nifedipine (0.2 mg/kg) was administered six times a day. The patient was discharged on the ninth day of treatment, when her symptoms started to regress, the proteinuria disappeared and her blood pressure was under control (130/90 mmHg). She continued to take oral nifedipine in a dose of 0.2 mg/kg six times a day. Her blood pressure remained under control and the skin lesions improved rapidly. Within two weeks her appetite improved and she did not have any complaints, though some of the discoloration on her fingertips remained. One-and-a-half months after the initiation of treatment with nifedipine the lesions on her hands and feet completely regressed, and therefore, the dose of nifedipine was gradually decreased. Four months later the excretion of mercury in the urine was found to be normal and the drug was discontinued.

Discussion

This patient had the typical findings of acrodynia including an elevated excretion of mercury in the urine. Since her two older and one younger sibling had greater excretions of mercury in the urine than our patient, and in addition they did not present with hypertension or any of the other complaints associated with acrodynia, we believe that this syndrome is the result of an unusual reaction to mercury. However, a more widely accepted hypothesis is that acrodynia is caused by mercury poisoning[1].

Since nifedipine has been recommended in the treatment of childhood hypertension[2] and Raynaud's phenomenon in adults[3], it was therefore administered to our patient to control hypertension and skin changes most likely related to vascular processes. Although her blood pressure became somewhat lower a half an hour after every intravenous infusion, it remained generally around 140/90 mmHg for a week, though her symptoms, especially the pain, restlessness and the pinkish color of her cheeks and nose had faded considerably. As soon as her blood pressure was under control nifedipine was given in oral doses which seemed to help improve all of her findings within 50 days. Since regression of the skin lesions was observed within a few days, and the blood pressure was controlled much earlier than the normalization of mercury excretion in the urine (55 ng/ml on the 13th day of treatment) the effect of nifedipine should be symptomatic on vascular lesions but not with a decreasing mercury level. None of the side effects of nifedipine such as flushing, headache, nausea, palpitation, dizziness or syncope were observed in our patient[4]. Although we have had very favorable results with the use of sodium nitropurisside in the treatment of erythromelalgia, it was not tried in this case, because it should only be used intravenously[5,6], which requires long hospitalization due to of the chronicity of the syndrome.

Since acrodynia is an extremely rare syndrome, a control study could not be carried out. But early response to treatment evidenced by full recovery in 50 days, strongly suggests that the therapy used was effective.

It has been shown that several metal cations such as lead and cadmium are capable of abolishing the cooperativity among the two nifedipine binding sites on calmodulin which increase the apparent affinity of calmodulin for nifedipine. Mercury can compete with these potentiating, metal cations on calmodulin and produce an inactivation of this active calmodulin conformer[7]. Therefore, the effect of nifedipine in this case may have occurred by displacing mercury with the binding of calmodulin to different cells.

Summary

A case of acrodynia in an eight-and-a-half-year-old girl is presented whose symptoms–profuse perspiration, swelling, desquamation, pain, itching of the extremities, pinkish color of the nose and cheeks and hypertension–responded sharply to nifedipine therapy.

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The Turkish Journal of Pediatrics 31:163 - 166, 1989

A FOREIGN BODY IN A FOUR-DAY-OLD INFANT'S ESOPHAGUS: A CASE OF NEGLIGENCE*

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Key words: negligence, esophagus, foreign body

Most esophageal obstructions caused by the ingestion of foreign bodies occur in children under the age of four years[1]. The type of foreign body ingested is influenced by modes of living, customs, habits, environment and even nationality. Safety pins are found most frequently in infants seven to 15 months of age, while nuts and coins in children from one to two years and three to six years, respectively[2]. Although seen quite rarely, foreign bodies in the esophagus of neonates consist mostly of endotracheal tubes which had been swallowed; this situation often causes a delay in diagnosis[3-5]. Lisitsyn et al[6], who evaluated the incidence of foreign bodies lodged in the esophagus of neonates, found that out of 634 cases being reviewed, there were only three cases of neonates.

In this report we present a case of a four-day-old baby with a foreign body lodged in the esophagus who had been examined at other hospitals because of vomiting and respiratory distress.

Case Report

A healthy male infant was born after a normal delivery at 40 weeks gestation. He had no problems within the first three days, but on the fourth day a sudden respiratory problem occurred accompanied by a high temperature and peripheral cyanosis.

Within the following four days the patient had two admissions for pneumonia at other hospitals. At eight days of age he was finally admitted to Uludağ University Hospital suffering severe respiratory difficulty and vomiting.

Physical examination on admission revealed an infant with a temperature of 38.8°C, marked tachypnea, peripheral cyanosis and disseminated crepitant rales on lung fields. The chest x-ray showed no evidence of a foreign body (Fig. 1). Attempts at inserting a nasogastric tube failed because the tube coiled up. The

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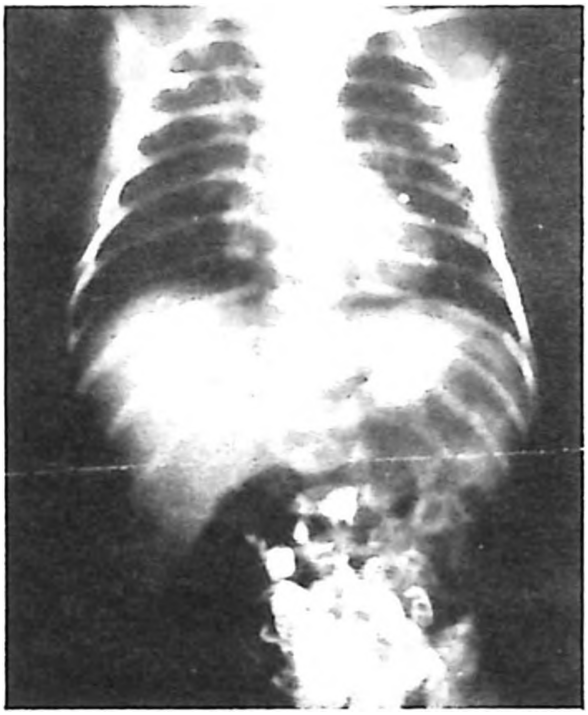

Fig. 1: Baby's chest x-ray: No signs of foreign body seen.

instillation of contrast material resulted in the visualization of an intra-esophageal obstruction (Fig. 2), the upper part of which was markedly dilated. Rigid esophagoscopy was performed under general anesthesia. Edema and inflammation were present. An esophageal foreign body, which turned out to be an ordinary

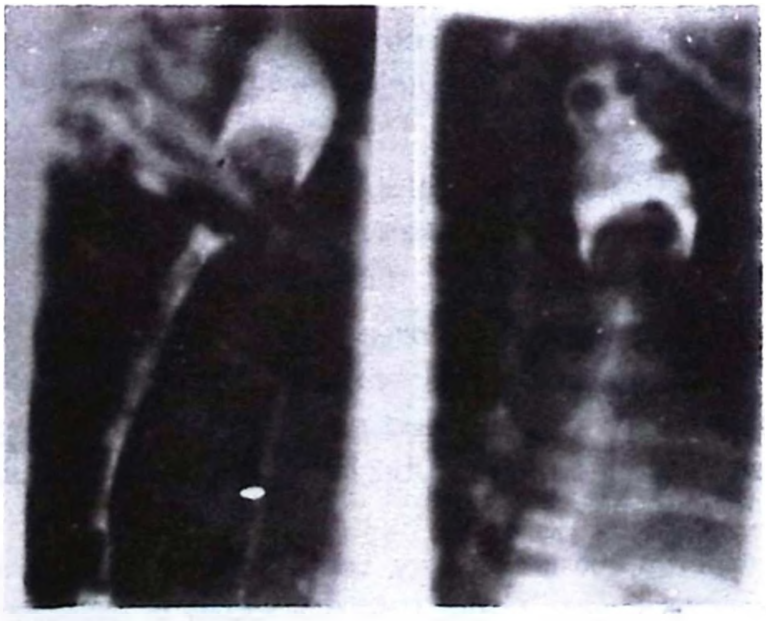

Fig. 2: Barium esophagram shows filling defect at the level of the aortic constriction.

bean, was removed from the level of aortic constriction (Fig. 3). The post endoscopic course was uneventful.

Upon questioning his parents again, it was learned that since the infant's birth, his four-year-old sister had displayed an extraordinary affection for him, and as it apparently seems, his parents allowed them to play together alone using even small objects such as ordinary beans, as playthings.

Fig. 3: Removed foreign body (ordinary bean).

Discussion

The majority of swallowed foreign bodies, especially if round and smooth, reach the stomachs of young children without difficulty[7]. There are, however, several sites for the lodgment of foreign bodies in the esophagus at the levels of cricopharyngeal, aortic, and left main bronchus constrictions and the inferior esophageal sphincter[8]. Since the posterior tracheal wall is membranous in origin, it can easily be compressed by an esophageal foreign body, thus causing respiratory distress which becomes apparent when the child is placed in the supine position[9]. Respiratory symptoms can also occur as a result of infections of the surrounding tissues or from spillover of secretions into the trachea, resulting finally in tracheobronchitis or pneumonia..

Whenever an infant has unexplained dysphagia, dyspnea, cyanosis or wheezing, a complete x-ray, examination of the neck and chest, lateral neck x-ray, inspiratory and expiratory chest x-rays in both posterior-anterior and lateral positions, and the use of contrast medium, when indicated, has been recommended[1].

It has been stated that foreign bodies in the air and food pasages have been responsible for more accidental deaths at home of children under six years of age than any other single cause[7]. In cases of unexplained dysphagia, dyspnea, cyanosis or wheezing, tracheo-esophageal foreign bodies should be suspected, taking into account the fact that some of these objects are non-opaque.

In the two to three year-old age-group, children often put round objects such as beans into their mouths and easily swallow them without any difficulty. Some children even put objects in their nostrils which are extracted by parents on discovery. However, in the case presented, the self-introduction of the bean was impossible. Although there was no question that the parents had loved and cared for their children, it has to be conceded that their lower educational level provided the setting for the action of their daughter and the subsequent outcome.

Summary

A foreign body in the esophagus of a four-day-old male baby is presented. Since self-introduction of a foreign body is impossible at this age, the accident was considered to be the result of a form of neglect.

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The Turkish Journal of Pediatrics 31:167-171, 1989

MAY – HEGGLIN ANOMALY*
(A Presentation of a Family)

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Key words: May-Hegglin anomally, mild-bleeding disorder, Döhle body

The May-Hegglin anomaly is a rare autosomal dominant disorder characterized by the presence of single, large, bizarre, cigar-shaped platelets and Döhle bodies in the leukocytes. One third of the cases reported have associated thrombocytopenia. Most patients who have this disorder are asymptomatic or have a mild bleeding disorder[1-3].

May, who first described this disorder in 1909, noted the presence of blue inclusion bodies in the cytoplasm of white blood cells in association with large platelets that were in the peripheral blood smear of an asymptomatic girl. Similar observations were then reported by Hegglin in 1945. The hereditary nature of this anomaly was clearly defined in 1960, and less than 100 cases have been described to date[3-6].

Since this anomaly is rare, and because as far as we know, no cases have so far not been reported from Turkey, we thought this family worthy of presentation.

Case Report

The pedigree of the reported family is presented in Fig. 1. The subject, IK, age 9, was admitted to our clinic with a history of intermittent nose-bleeds and a two-year history of recurrent petechial rash on his extremities. He was the fifth child of parents who were not related. The subject had no remarkable prenatal, natal or postnatal histories. His brother, mother and uncle had similar complaints.

On admission the patient's general condition was good. He weighed 27 kg (70^{th} percentile) and his height was 132 cm (50^{th} percentile). Body temperature, heart and respiratory rate, and blood pressure were normal. He had a mild nose-bleed and a discrete petechial rash on his shoulders and extremities. The liver and spleen were not palpated. The other physical findings were all normal.

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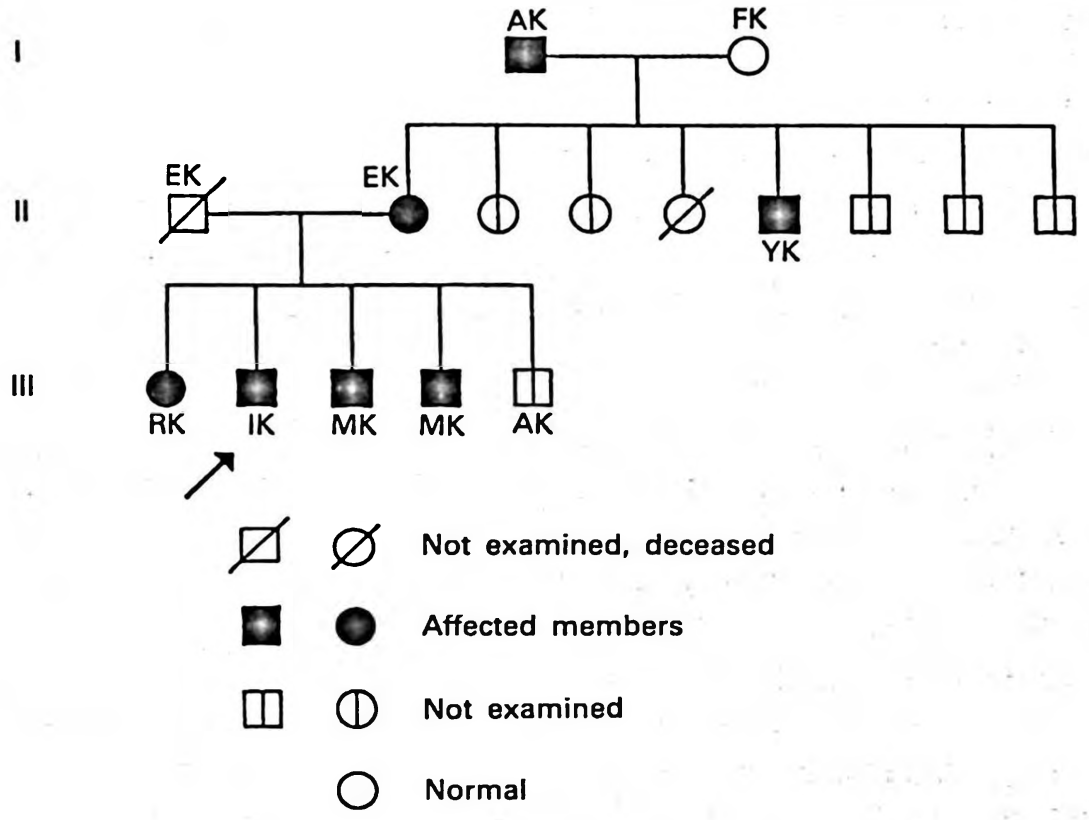

Fig. 1: Family pedigree.

Laboratory studies revealed that the hemoglobin was 12.8 g/dl, hematocrit value 37%, leukocyte count 7200/mm^3, and platelet count 38000/mm^3. Large, dense cigar-shaped or elliptical platelets and Döhle bodies in the granulocytes were observed in the peripheral blood smear. Bleeding time (Ivy) was 6 min (normal to 6 min), prothrombin time 14 sec (normal range: 11-14 sec), partial thromboplastin time 45 sec (normal range: 25-45 sec) and clot retraction was diminished (3 hours, Benmari incubation method). The tourniquet test and capillary fragility were normal. Platelet aggregation and ristocetin-induced agglutination were within the normal range. Erythrocyte sedimentation rate was 4 mm/h. Bone marrow examination, liver and kidney function tests, serum electrolytes, and chest-X-ray were also normal.

EK : mother, age 41, suffered from menorrhagia.
MK : brother, age 18, was asymptomatic, but affected.
MK : brother, age 15, had a life-long history of mild epistaxis and petechial rash.
RK : sister, age 12, was asymptomatic but affected.
YK : uncle, age 37, had a history of mild epistaxis and petechia.
AK : grandfather, age 67, was asymptomatic, but affected.

The family's data supporting a diagnosis of May-Hegglin anomaly are shown in Table I. Large, cigar-shaped platelets and Döhle bodies are illustrated in Fig. 2.

TABLE I: Family Data Supporting a Diagnosis of the May-Hegglin Anomaly

Patient age/yrs	Symptom	Giant, cigar-shaped platelets	Döhle bodies	Platelet count (mm^3)	Bleeding time (min) (Ivy)	Capillary fragility	Clot retraction	Platelet aggregation	Ristocetin-induced agglutination
İK (9)	+	+	+	38,000	6	Normal	Diminished	Normal	Normal
EK (41)	+	+	+	150,000	3	Normal	Normal	Normal	Normal
MK (18)	–	+	+	150,000	4	Normal	Diminished	Normal	Normal
MK (15)	+	+	+	74,000	6	Normal	Normal	Normal	Normal
RK (12)	–	+	+	74,000	6	Normal	Diminished	Normal	Normal
YK (37)	+	+	+	74,000	5	Normal	Normal	NP	NP
AK (67)	–	+	+	150,000	4	Normal	NP	NP	NP
Normal	–	–	–	150,000	1-6	Normal	Normal	Normal	Normal
				400,000					

NP: Not performed

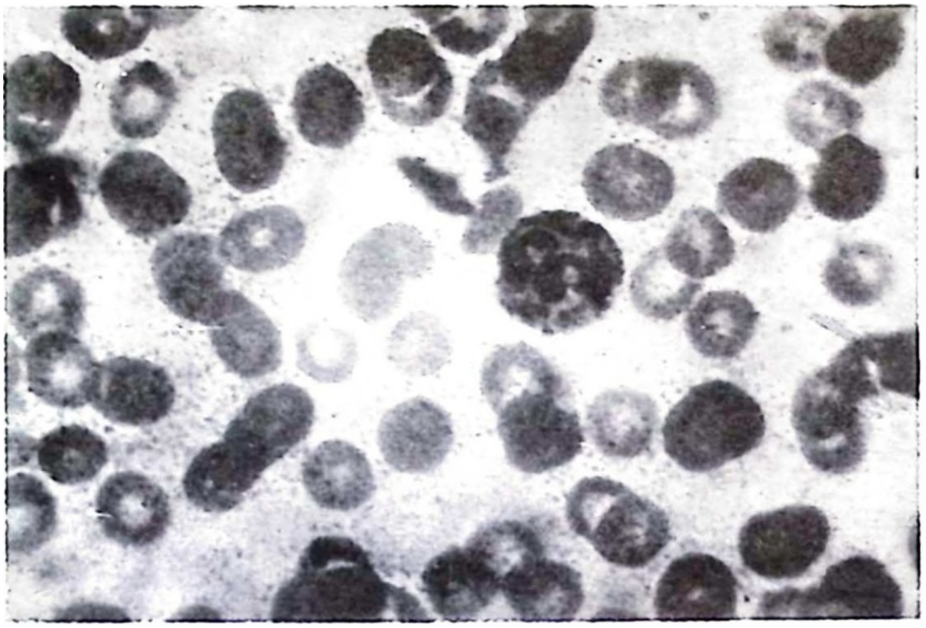

Fig. 2: Large, elliptic and bizarre platelets and Döhle bodies are seen in blood smear of propositus (Peroxidase).

Discussion

The majority of patients with May-Hegglin anomaly do not have bleeding manifestations. In this group, the disease entity may be discovered incidentally. In some cases, mild hemorrhagic manifestations have been the only specific clinical problem. Even though thrombocytopenia is a consistent abnormality, most patients reported do not have significant bleeding[4,6].

Platelet survival is usually normal in May-Hegglin anomaly, however a decrease in platelets has been reported in some cases[1,2,6,7]. The presence of a normal megakaryocyte number in the marrow evaluation indicates normal platelet production. It is postulated that impaired and abnormal megakaryocyte fragmentation leads to both number and size alterations of the platelets[2]. Since larger and younger platelets are thought to be hemostatically superactive than the smaller and older ones, patients with May-Hegglin anomaly do not have severe bleeding episodes[4].

In this anomaly, pale-blue staining inclusions are found in the cytoplasm of the neutrophils, eosinophils, basophils and monocytes; these RNA patches are named Döhle bodies. Döhle bodies were first described as an acquired phenomenon in scarlet fever and may be found in acute infectious and toxic processes and burns. It was demonstrated that they disappear after recovery[5,8].

In this family the subject and his three siblings had mild bleeding symptoms. All investigated members of the kindred had Döhle bodies and large, bizarre, cigar-shaped platelets. Except for the subject, all of them also had normal and

abnormal platelets on the blood smears. Four members of the family had thrombocytopenia. Among them, only RK was asymptomatic, though she had diminished clot retraction. The association of thrombocytopenia, diminished clot retraction and an asymptomatic state may be seen in May-Hegglin anomaly.

Large platelets are also seen in the Bernard-Soulier syndrome, the Gray platelet syndrome and genetic connective tissue diseases[9]. Bleeding time, ristocetin-induced agglutination and platelet aggregation were found to be within normal ranges in this family, thereby allowing us to distinguish this anomaly from the Bernard Soulier and Gray Platelet syndromes. Thus, the presence of increased vessel fragility observed in this particular family may have been due to a different form of genetic connective tissue disease.

Acknowledgement

We wish to thank Professor Çiğdem Altay for her helpful advice and Associate Professor Türkiz Gürsel for her assistance in studying the platelet functions.

Summary

The May-Hegglin anomaly is a rare autosomal dominant disorder characterized by the presence of large, bizarre, cigar-shaped platelets and Döhle bodies in the leukocytes. This rare anomaly was detected in seven members of a family. It is emphasized that in making a differential diagnosis this disorder must be distinguished from the other mild bleeding disorders.

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The Turkish Journal of Pediatrics 31:173 - 175, 1989

HYPERNATREMIA IN TWO COLLODION BABIES*

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Key words: hypernatremia, collodion baby

In 1978, Jeanneau et al[1] described a case of hypernatremic dehydration occurring with seborrheic dermatitis. Hypernatremia associated with congenital lamellar ichthyosis was reported by Garty et al[2]. Recently, two siblings with Netherton syndrome complicated by neonatal hypernatremia were reported[3].

We present two cases of collodion babies with recurrent hypernatremia hoping that they might be of interest since hypernatremia is a rare laboratory finding for a dermatologic disorder and a preventable cause of neonatal morbidity.

Case Reports

Case 1

A four-day-old female infant having a typical collodion-baby appearance was referred to our University Hospital. She was born at term following a normal pregnancy. The parents were first-degree relatives. A male sibling with a normal appearance died during the first week of life of unknown causes.

Physical examination revealed an infant weighing 2300 g whose entire body was covered with a peeling collodion-like membrane (Fig. 1). Ectropion and eclabium along with flexion contractures of the extremities were present. The patient's temperature was 36.8°C, pulse rate 132/min, and respiratory rate 40/min.

Laboratory findings included hemoglobin 11.9 g/dl, white blood cell count 12,000/mm^3, serum vitamin A level 12 gamma/dl (normal: 15-60 gamma/dl), Na^+ 171 mEq/lt (normal: 140 mEq/lt), K^+ 4.8 mEq/lt, and Cl^- 120 mEq/lt. The chest roentgenogram was normal. Blood and urine cultures yielded no growth.

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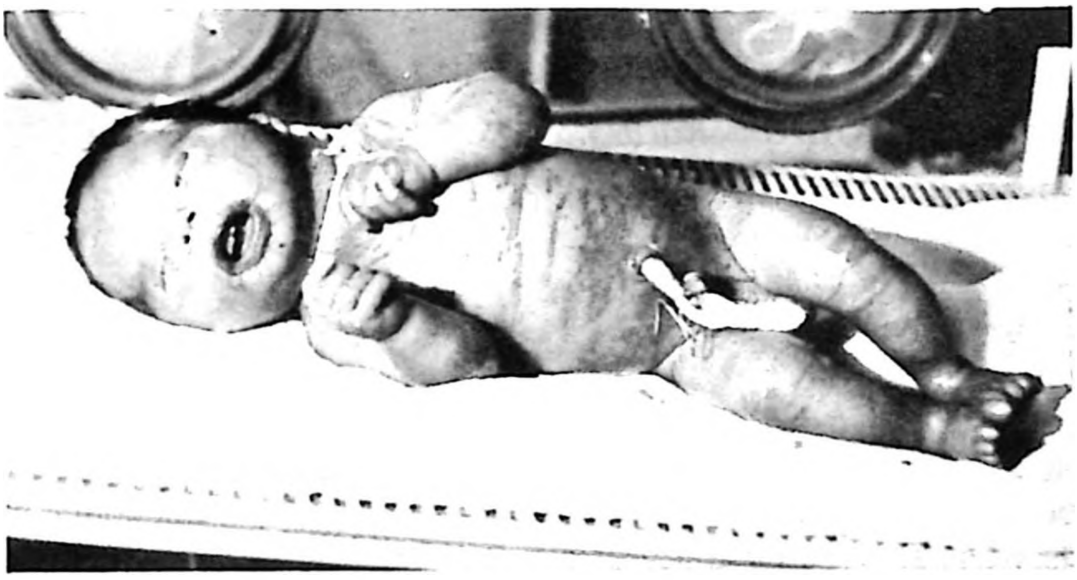

Fig. 1: General appearance of the patient.

The patient was given ampicillin and tobramycin for five days in order to prevent infection along with 5000 I.U. vitamin A. Intravenous fluids for rehydration were administered. Vasoline containing five percent lactic acid was applied topically. The patient responded well to the therapy and the serum sodium concentration returned to normal on the third day of treatment.

Case 2

A five-hour-old male infant was transferred to our University Hospital because of a generalized skin disorder. As in the first case, his parents were first-degree relatives.

Physical examination revealed an infant weighing 2290 g, who was icteric. He presented with a collodion-like membrane, eclabium and ectropion. Laboratory findings were within normal limits except for hyperbilirubinemia (total bilirubin 11.9 mg/dl and a negative direct Coombs test).

Phototherapy and topical vaseline-lanolin were applied. Hypernatremia developed on the third day of phototherapy. The serum sodium concentration was 165 mEq/lt. There was no diarrhea, vomiting, fever or other cause of hypernatremia except for the skin disorder and phototherapy. After rehydration the serum sodium level was found to be normal. Since the subsequent course was normal, the patient was discharged in a week.

After ten days, the patient was readmitted to the hospital suffering from dehydration and hyperirritability. The serum sodium level was 170 mEq/lt. The hypernatremia which had recurred was treated by the administration of intravenous fluids, and the condition improved. He was discharged and given a skin care regimen.

In the treatment of collodion babies application of topical keratolytic agents have been used and measures have been taken to prevent other complications. Erdem[4] has reported five cases treated successfully with a topical vasoline preparation which contained five percent lactic acid. Lactic acid is an alpha-hydroxy acid compound, the effect of which is anti-keratinogenic. In one of our cases vasoline containing five percent lactic acid was applied.

Complications seen in collodion babies are skin irritation, water loss via the epidermis, pyodermia and pulmonary infection[4]. We wish to emphasize that there is an elevation of serum sodium levels in collodium babies. It is known that hypernatremia may occur when there is a considerable increase in the area of thin erythematous skin or increased skin loss (burn, phototherapy, preterm or generalized dermatoses)[1-3,5]. In the cases presented, no other cause of hypernatremic dehydration such as diarrhea, vomiting, tachypnea, polyuria, fever or ambient temperature was found. In Case 1, the only cause of hypernatremia was the peeling of the skin. However, Case 2 experienced two episodes of this disorder. Phototherapy may have aggravated the water loss via the lungs and the skin, and the second episode may have only been related to the skin disease.

We are of the opinion that early recognition of hypernatremia and the replacement of water loss is extremely important, especially in neonates. Therefore, serum sodium concentrations should be routinely examined when dealing with generalized skin disorders of the newborn.

Summary

Two cases of collodion babies with hypernatremia are presented, and the importance of this electrolyte abnormality in skin disorders is also stressed.

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