THE TURKISH JOURNAL OF PEDIATRICS

VOLUME: 35 NUMBER: 2 APRIL - JUNE 1993

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

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The Turkish Journal of Pediatrics 35: 79-85, 1993

EVOKED POTENTIALS IN GUILLAIN – BARRÉ SYNDROME*

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SUMMARY: Topçu M, Ergin M, Nurlu G, Renda Y, Kanra G, Seçmeer G. (Neurology and Infectious Diseases Units, Department of Pediatrics, and the Department of Neurology, Hacettepe University Faculty of Medicine, Ankara, Turkey). Evoked potentials in Guillain-Barré syndrome. Turk J Pediatr 35: 79-85, 1993.

A prospective evaluation was made in a total of 19 patients with Guillain-Barré syndrome (GBS) by neurologic examination, visual evoked potentials (VEP), brainstem auditory evoked potentials (BAEP) and somatosensory evoked potentials (SEP) during the acute phase of the disease, three weeks later, and then again three months after the onset of symptoms. The results of electrophysiologic studies of the patients were compared with those of 19 healthy children. There were no statistically significant differences found in the mean VEP and BAEP values between the patient and control groups. However, the VEP and BAEP values were abnormal during the first and second stages of the disease in only a few patients. There was a statistically significant prolongation of the response in tibial and median SEP during the first and second stages of the disease when compared with the third stage and the control group. The Erb-Cervical 7 (C7) interwave latency was elevated in the median SEP. It was concluded that the prolongation of the response in SEP was diagnostically important in the acute phase of GBS. There was no correlation found between SEP and clinical progression. *Key words: evoked potentials, Guillain-Barré syndrome.*

Electrophysiologic studies have made significant contribution to the differential diagnosis and evaluation of Guillain-Barré syndrome (GBS). The findings obtained from electroneuromyographic and F-wave studies have demonstrated proximal conduction delays in some patients in the early phase of the disease[1,2]. The SEP technique, which can determine whether there is a block in sensory conduction, is almost as useful as the F-wave[3]. Consequently, it has been suggested that SEP and F-wave studies be used as complementary techniques[4,5]. The evoked potentials of patients with GBS have also been studied with the aim of ascertaining whether there is demyelination of the second and eighth nerves[3,4,6-8]. Although abnormalities in BAEP have been reported[8], some authors are skeptical about correlating abnormalities in BAEP with demyelination of the eighth nerve[3].

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The purpose of this study is to investigate the evoked potentials of the patients with GBS through the course of the disease and to correlate these values with the clinical findings for determining prognosis.

Material and Methods

Twenty-one patients with GBS were admitted to Hacettepe University Children's Hospital between November 1988-March 1990 for prospective evaluation. Evoked potential responses could not be obtained in two patients, who died shortly after a fulminating course of the disease. Those patients were excluded from the statistical evaluation. A study was made of the remaining 19 patients, sixteen of whom were re-evaluated three weeks after the acute phase of the illness and 11, three months after the acute phase by neurologic examination, VEP, BAEP and SEP. One patient was diagnosed as having Fisher syndrome. Eleven age and height-matched healthy children were chosen as the controls. Muscle weakness was assessed according to the grading criteria used by the GBS Study Group[9]. The motor disability grading criteria devised by this group is as follows;

Grade 0 Healthy.

Grade 1 Minor signs and symptoms.

Grade 2 Able to walk five meters without requiring a walker or equivalent support.

Grade 3 Able to walk five meters with a walker or support.

Grade 4 Bed or chairbound (unable to walk five meters with a walker or support).

Grade 5 Requires assisted ventilation (for at least part of the day).

Grade 6 Deceased.

VEP was performed by placing the electrodes according to 10-20 in the international EEG system (active at Oz, reference at Fz), and pattern stimulation was repeated 128 times. The mean on the waves with a frequency of 1 to 100 Hz was obtained. While evaluating VEP results, the P100 value was calculated as latency and the N1-P1 extreme points were calculated as the amplitude. Before BAEP was performed, the electrodes were placed according to 10-20 in the international EEG system (active at mastoid, reference at Cz) and the stimulation was repeated 1024 times. The amplitude of the sound in the stimulated ear was 75 decibels, and 45 decibels of masking sound was applied to the contralateral ear. The principal evaluation was based on I-V interpeak latency and first wave latency.

SEP was performed by stimulation of the median and the posterior tibial nerves. The electrodes were placed according to 10-20 in the international EEG system (active at Cc, scalp overlying the sensoriparietal cortex 2 cm behind the 10-20

system C3/C4 positions C7, erb and below, reference at Fz for median, active at Cz, reference at Fz for tibial). Vertex P1 peak latency was used in tibial SEP, while the latencies used in median SEP were C7 and Cc peak latencies and interpeak latencies between elbow-erb, erb-C7, and C7-Cc.

Values having a difference of more than 3SD from the controls were considered abnormal.

Results

The general features of the patients are presented in Table I. Prolongations of VEP values were detected in five patients (patients 4, 5, 6, 10, 17) during the acute phase, in three patients (patients 4, 12, 15) during the second examination, and in one patient (patient 4) during the third examination. Patient 4, diagnosed as having

Table I: General Features of Patients with GBS

Patient Number	Age (yrs)	Sex	Height (cm)	Onset of Symptoms (day)	CSF Protein (mg)	Motor Deficit 1.	2.	3.
1	13	F	144	11	240	3	1	1
2	11	M	142	7	240	4	1	0
3	8	F	118	6	144	5	3	0
4*	8	M	120	5	48	2	1	0
5	6	M	108	1	24/168	4	4	2
6	5	M	103	2	72	3	3	2
7	5	M	103	4	36/96	3	2	1
8	4	F	91	5	60/96	4	3	2
9	3	F	95	1	48/90	4	3	1
10	2	F	81	1	169	3	1	0
11	2.5	M	84	10	168	4	3	2
12	2	M	85	6	72	3	3	
13	14	M	162	4	48/108	3	3	
14	13	M	146	2	190	3	1	
15	9	F	121	7	48	4	2	
16	4	M	90	12	504	4	3	
17	4	F	89	6	208/120	4		
18	13	M	140	4	144	4		
19	9	M	122	7	121	3		
20	10	F	130	4	168	6		
21	10	M	135	3	72	6		

* Fisher syndrome.

Fisher syndrome, demonstrated prolongation of conduction time in all three measurements. There was no statistical significance in VEP P100 latency values between the patients and the controls.

An increase in the first wave peak latency was observed in only one patient (patient 10) during the acute phase. Elevations in interpeak latencies were detected in one patient (patient 10) during the acute phase, in one patient (patient 15) during the second examination, and in one patient (patient 10) during the third examination. When we compared the first wave BAEP values with the I-V interwave latency values of the two groups, we found that there were no statistically significant differences between the patients and the controls.

Tibial SEP Vtx peak latencies of five patients during the acute phase (patients 3, 10, 13, 15, 17), and in five patients during the second examination (patients 2, 3, 5, 10, 15) showed prolonged latencies. The differences between the patient and control groups during the first and second examinations were statistically significant ($p < 0.05$), but there was no statistically significant difference in the third measurement (Table II).

Table II: Statistical Comparison of Tibial SEP Vertex Peak Latency Values Between Patient and Control Groups

	Vtx PL (msec)	
Group	X	SE
Patient I	42.26	1.54
Patient II	42.70	1.88*
Patient III	38.24	0.82
Control I (19)	36.54	0.61
Control II (16)	36.34	0.64
Control III (11)	36.13	0.73*

* : $p < 0.05$ and significant; p values were calculated with respect to the difference between the means of the two groups.
SE : Standard error.
X : Mean.
Vtx : Vertex.
PL : Peak latency.

None of the values of median SEP Cc peak latencies in the patients was more than 3 SDs. The differences between the patient and control groups during the first and second examinations were statistically significant ($p < 0.05$) (Table III), but no abnormal values for mean C7 peak latencies were noted in the patients and there was also no significant difference between the patient and control groups

during the acute phase. The values of the patients progressively improved in consecutive examinations (Table III). Although no abnormal values of elbow-erb interpeak latencies were detected in the patients, there were significant differences between the patient and control groups during the first and second examinations (Table III). Mean Erb-C7 interpeak latencies in three patients during the acute phase (patients 3, 15, 19), and in one patient during the second examination (patient 3) revealed prolonged values. The difference between the acute phase and the other phases, and the difference between the patient and control groups in respect to first and second examinations were statistically significant (Table III).

Although there were no abnormal values for mean C7-Cc interpeak latencies in the patients, the values during the acute and other phases of the disease, and the values of the patient and control groups during the first and second examinations were significantly different (Table III).

Table III: Statistical Comparison of Median SEP Values in Patient and Control Groups

	Cc PL (msec)		C7 PL (msec)		Elbow-Erb IPL (msec)		Erb-C7 (msec)		IPL C7-Cc I (msec)	
	X	SE	X	SE	X	SE	X	SE	X	SE
Patient I	17.05	0.29*	10.95	0.36	3.68	0.13*	3.64	0.24*	6.05	0.1
Patient II	16.30	0.43*	10.35	0.40	3.65	0.14*	3.28	0.24*	5.90	0.1
Patient III	15.64	0.51	9.80	0.45	3.55	0.16	2.96	0.25	5.80	0.2
Control I (19)	15.20	0.39	9.80	0.33*	3.38	0.16	2.60	0.15*	5.41	0,
Control II (16)	15.01	0.45*	9.68	0.38*	3.33	0.17	2.56	0.17*	5.35	0,
Control III (11)	14.89	0.52*	9.75	0.42	3.31	0.19	2.56	0.19	5.16	0,

* : $p < 0.05$ and significant; p values were calculated with respect to the difference between the means of the two groups.
SE : Standard error.
X : Mean.
PL : Peak latency.
IPL : Inter peak latency.

Discussion

Although there are published reports about evoked potentials in GBS, all these studies have been conducted during the acute phase. To our knowledge no investigations have been made during the later phases of the disease.

In our VEP and BAEP studies, we found no statistically significant differences between the patient and control groups in all three stages of the disease. There

was a prolongation of P100 latency in all three measurements taken of the patient with Fisher syndrome. Rudolph et al[10] have detected abnormal BAEP values in Fisher syndrome, and Ropper and Chiappa[3] have found unilateral prolongation of I-V interpeak latency in one of three patients with Fisher syndrome. In our patient with Fisher syndrome, the BAEP and SEP values and central conduction time were within normal limits. The increase in VEP values in this patient may be due to a possible demyelination of the optic nerve. Abnormal BAEP implications were obtained in two of our patients. An increase in interpeak latencies was detected by Ropper and Chiappa[3] in three of 21 patients, and by Schiff et al[7] in five of six patients, two of whom were in the convalescent phase. It was observed that prolongation of latencies detected in our study had no relation to the duration of disease. With these results, it is difficult to say that GBS was limited to the peripheral nerves.

SEP has become a subject increasingly dwelt upon because it provides information about the conduction velocity of both the distal and proximal parts of the peripheral nerve and the central conduction velocity in GBS[3-6].

Median, tibial, peroneal SEP and F wave latencies have been investigated in the same studies[4,5]. SEP and the F wave provide valuable information in the diagnosis of GBS by detecting abnormalities in proximal nerve conduction [4,5]. Brown and Feasby[6] have reported that of 11 patients with GBS in the acute phase, ten had delays in proximal conduction and three had prolongation of cortical potential latencies detected by median SEP.

When we analyzed the SEP results obtained in our study, we found that five patients in the acute phase and seven patients during the third examination revealed abnormal tibial SEP results. The values obtained were over 2 SDs in a significant proportion of patients with nine patients in the acute phase. We believe that tibial SEPs yielded more meaningful results than did median SEPs.

In addition to the abnormal values obtained, the results of tibial and median SEP during the acute phase and three weeks later were significantly longer than in the control group and the values detected three months later in the patient group.

Abnormalities in median SEP C7-Cc interpeak latencies were detected in three patients, and statistically significant values of proximal sensory and cortical latencies compared to the control group and to values in the convalescent phase, which suggest that the disease is not limited to peripheral nerves and proximal parts, and that especially in the acute phase, the central nervous system can also be affected.

Although it was not possible to make a statistical correlation between SEP values and clinical staging because of technical reasons and an insufficient patient, number, it was observed that the prolongations detected by SEP persisted

throughout the acute and subacute phases, and that the latencies returned to normal after three months. It was also noted that muscle strength of the patients improved in three weeks, which was evident also during the last examination. However no correlation could be found between clinical improvement and normalization of SEP values.

We conclude that SEP is an important tool to diagnose GBS in the early phase, and that it should be used with other electrophysiologic methods of diagnosis.

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The Turkish Journal of Pediatrics 35: 87-91, 1993

COMPARATIVE THERAPEUTIC RESULTS OF PENICILLIN PLUS CHLORAMPHENICOL VERSUS AMPICILLIN PLUS SULBACTAM IN CHILDHOOD MENINGOCOCCEMIA*

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SUMMARY: Kanra G, Seçmeer G, Özen H, Ceyhan M, Ecevit Z. (Pediatric Infectious Diseases Unit, Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey). Comparative therapeutic results of penicillin plus chloramphenicol versus ampicillin plus sulbactam in childhood meningococcemia. Turk J Pediatr 35: 87-91, 1993.

Fifty-seven cases of meningococcemia were evaluated retrospectively. The age of the patients ranged between 2 and 17 years. Of the 57 patients investigated for the efficacy of antibiotic treatment, 31 (54.4%) were treated with benzylpenicillin plus chloramphenicol and 26 (45.6%) with ampicillin plus sulbactam. Patients with criteria for a poor prognosis (presence of disseminated intravascular coagulation, low arterial blood pressure, and altered consciousness) were divided equally into two treatment groups. There were no statistically significant differences between the two treatment groups except for the higher incidence of convulsion in the group given penicillin plus chloramphenicol. The mortality rate was 19.3 percent for patients treated with benzylpenicillin plus chloramphenicol and 7.6 percent for patients treated with ampicillin plus sulbactam ($p = 0.19$; overall mortality rate 14%).
Key words: meningococcemia, penicillin plus chloramphenicol, ampicillin plus sulbactam.

Acute fulminant meningococcemia is the most severe clinical form of meningococcal infection. It is characterized by an abrupt onset of purpura, shock, disseminated intravascular coagulation (DIC) and rapid progression to death[1]. The mortality rate remains at 19 percent with variations depending on the prevalence and clinical features of the disease, the host response and socioeconomic level of the population[2].

Current regimens employed in the treatment of meningococcemia include either benzylpenicillin-G alone or in combination with chloramphenicol, or ampicillin alone[3]. There are also reports of reduced penicillin sensitivity to meningococci[4,5]. Recently, sulbactam / ampicillin has been reported to be effective in treating childhood meningitis and other childhood infections[6,7]. Since a high mortality rate has been observed in patients with meningococcemia who were administered

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the penicillin plus chloramphenicol regimen and also because of the success achieved by the use of an ampicillin plus sulbactam regimen in treating other childhood infections[7], we decided to include ampicillin plus sulbactam as a regimen for treating meningococcemia.

In this study, 57 cases of acute meningococcemia treated at the Hacettepe University Children's Hospital were evaluated retrospectively and the results of treatment were analyzed. There is also a review of the current literature.

Material and Methods

From January 1984 to September 1990, a total of 57 patients diagnosed clinically as having meningococcemia and confirmed by laboratory findings were evaluated retrospectively. A diagnosis of meningococcemia was established if clinical manifestations of the disease and at least one of the following criteria were present:

1. Cultivation of the microorganism from the blood, cerebrospinal fluid or petechial lesions.
2. Demonstration of Gram-negative diplococci on the Gram-stained smear of CSF or petechial smear[2, 8].

Hypotension was defined as arterial systolic pressure values under 85 mmHg for patients over four years of age and a value of 75 mmHg for patients under four years of age[9].

Fisher's exact Chi-square, the Chi-square and Mann-Whitney U tests were used for statistical analyses. P values < 0.05 were considered significant.

Results

The age of the patients ranged from 2 to 17 years and the male / female ratio was 1.11.

The four prevailing complaints at presentation were fever (98.2%), vomiting (87.7%), purpuric lesions (70.1%) and headache (59.6%). Purpuric lesions were detected in 100 percent of cases, fever in 84.2 percent, signs of meningeal irritation in 80.7 percent, and alterations in consciousness (somnolence, stupor and coma) in 33.3 percent. Table I lists the features exhibited in the patients of both treatment groups. We were unable to discern any differences between the two treatment groups in respect to clinical features, except for the frequency of convulsion.

Laboratory findings on admission revealed leukocyte counts which varied from 2600 to 81000 / mm^3 and averaged between 14125 ± 9824 / mm^3 in the patients who died, and between 20193 ± 14324 / mm^3 in the patients who survived.

Table I: Clinical and Laboratory Features and Outcome of Patients in Both Treatment Groups

	Ampicillin/Sulbactam n = 26	Penicillin/Chloramphenicol n = 31
Clinical Features and Symptoms (%)		
Age (yrs)	6.48 ± 3.5 #	6.4 ± 4.0
Fever	26 (100)	30 (96.7)
Vomiting	25 (96)	25 (80.6)
Headache	15 (57.6)	19 (61.2)
Lethargy	16 (61.5)	18 (58.0)
Change in level of consciousness	9 (34.6)	10 (32.2)
Hypotension	8 (30.7)	7 (22.5)
Convulsion*	2 (7.6)	5 (16.1)
Other (abdominal pain, diarrhea, arthralgia, etc)	12 (46.1)	13 (41.9)
Laboratory Findings (%)		
WBC Count (/ mm^3) (range)	19577 ± 15820 (2600 - 81000)	20045 ± 12078 (5800 - 49000)
CSF leukocyte count > 10 / mm^3	19 (73.0)	25 (80.6)
Laboratory findings of DIC	5 (19.2)	4 (12.4)
Follow-up and Outcome		
Mean time period between onset of complaints and treatment (days)	1.5 ± 0.82	1.2 ± 0.66
Disappearance of symptoms and signs (days)	2.29 ± 1.51	2.52 ± 0.82
Duration of hospitalization (days)	9.12 ± 3.81	10.75 ± 4.82
Case fatality (%)**	2 (7.6)	6 (19.3)

* : $p < 0.05$
** : $p = 0.19$
\# : Plus - minus values are means ± SD

($p > 0.05$). There was also no difference in the average leukocyte counts between the two treatment groups: 20045 ± 12078 in penicillin + chloramphenicol group; and 19577 ± 15820 in ampicillin + sulbactam group ($p > 0.05$). DIC was confirmed by laboratory findings in nine (15.7%) patients.

A CSF specimen which reveals a mere leukocyte count of 10 / mm^3 or greater points to a diagnosis of meningitis[10]. Forty-four of the total 57 patients had meningitis (77.2%).

When the patients were studied retrospectively, we found that out of 57 patients, 31 had initially been treated with benzylpenicillin G 300000 IU / kg / day given in six divided doses and combined with chloramphenicol 100 mg / kg / day in four divided doses intravenously, while the second group of 26 patients had received ampicillin 400 mg / kg / day plus sulbactam 100 mg / kg / day in four divided doses intravenously.

A total of eight patients (14%) died. While six patients (4, 4, 8, 9, 12, and 14 years of age; 19.3%) treated with penicillin and chloramphenicol died, only two patients (6 and 8 years of age; 7.6%) died in the ampicillin plus sulbactam group ($p = 0.19$, Fisher's exact test). DIC, low blood pressure, and an altered level of consciousness on admission were indications of a poor prognosis, while convulsions, the time petechiae appeared, the age of the patient and a leukocyte count below 10000 / mm^3 had no bearing on prognosis. The two treatment groups did not differ from each other in respect to frequency of poor prognostic factors.

Discussion

Despite recent advances in diagnosis and treatment of meningococcal infections, they are still regarded as dreaded diseases, meningococcemia in particular. The fatality rate is reported to be between 8.6 and 43 percent in different studies[1,11]. In our survey, the overall mortality rate was found to be 14.0 percent.

Another problem encountered in treating patients with meningococcal infections is that resistance develops to antibiotic agents including penicillin[2,4,5]. The mortality rate was 19.3 percent in the group we treated with penicillin.

Halstensen et al[3] reported that there was a significantly lower mortality rate associated with patients treated with penicillin or any other antibiotic in combination with chloramphenicol as compared with patients who were not given chloramphenicol.

They interpreted this finding as due to the effect of chloramphenicol in decreasing the destructive effect of beta-lactam antibiotic agents which prevents abrupt discharge of endotoxin. Rodriguez et al[4] compared the efficacy of the ampicillin plus chloramphenicol regimen with the ampicillin plus sulbactam regimen in treating pediatric patients with meningitis without considering the type of microorganism involved. They found mortality rates and neurologic sequelae to be lower when using the ampicillin plus sulbactam treatment regimen, which was at least as effective as the other combination.

Since high mortality accompanies meningococcemia, prompt and proper treatment should be initiated as rapidly as possible when this infection is suspected so that complications can be avoided. Even though there were no statistically significant differences between our two treatment groups in respect to therapy,

the lower mortality associated with the ampicillin plus sulbactam treatment group may be reason enough for choosing this regimen in treating childhood meningococcemia.

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The Turkish Journal of Pediatrics 35: 93-98, 1993

LONG-TERM RESULTS OF PATIENTS WITH CONGENITAL COMPLETE ATRIOVENTRICULAR BLOCK*

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SUMMARY: Çeliker A, Çiçek S, Özme Ş. (Pediatric Cardiology Unit, Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey). Long-term results of patients with congenital complete atrioventricular block. Turk J Pediatr 35: 93-98, 1993.

Congenital complete atrioventricular block is an uncommon disorder with a prognosis which is usually favorable. The disorder is sometimes associated with syncope, sudden death or cardiac pacing. It is difficult to determine the patients at risk of sudden death. In this retrospective study, hospital records of children who had been admitted to the Hacettepe University Children's Hospital between 1970-1990 for evaluation of complete heart block were examined. The study population, consisting of 39 children, 27 males and 12 females, had electrocardiograms consistent with complete heart block. These patients, diagnosed as having congenital complete A-V block, had an otherwise normally structured heart, and were followed up for a period of from one month to 15 years. Age at diagnosis ranged from 27 days to 17 years (mean: 86.9 ± 48 months). Of the 14 patients with symptoms (five with syncope, eight with exercise intolerance and one with presyncope), nine were paced electively and have done well. Clinical and laboratory features of the asymptomatic and symptomatic groups were compared to evaluate potential risk factors. *Key words: congenital complete heart block, isolated risk factors.*

Congenital complete heart block (CCHB) is a rare conduction disturbance. Clinical and laboratory features have been researched in order to determine patients at risk[1-7]. The disorder, originally thought to be benign, is sometimes associated with syncope, sudden death, or implantation of a pacemaker[1,3,8,9].

A persistently low ventricular rate[3,10], a prolonged QT interval[9], and a wide QRS complex have been correlated with an increase in risk among patients with CCHB. Past reviews have often combined subjects with and without structural heart defects, and some have even concentrated on unvariant analysis of the heart rate, without regard to other possible independent risk factors[6].

This study was designed to investigate potentially independent risk factors involved in the development of symptoms related to CCHB, and to report our

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experience in treating a large group of patients in our center afflicted with this disorder. All patients enrolled in this study had a normal cardiac anatomy.

Material and Methods

The hospital records of children who had been admitted to the Hacettepe University Children's Hospital between 1970 and 1990 were examined in retrospect. Patients were enrolled in the study if their electrocardiograms were consistent with complete heart block, and if there was confirmation of a normal cardiac anatomy. All 39 patients met the criteria of CCHB as defined by the International Study on Congenital Heart Block. The children had no previous history of acquired cardiac infection, myopathy or systemic disease.

Cardiac anatomy was evaluated by cardiac catheterization in four patients and by echocardiography in 15 patients. A normal cardiac anatomy was confirmed in the remaining subjects at the initial physical examination, X-ray and electrocardiogram.

Patients were divided into groups according to the presence or absence of one of the following symptoms: (1) sudden cardiac arrest (2) syncope (3) near syncope (4) congestive heart failure and (5) progressive exercise intolerance. Age at diagnosis and age at onset of symptoms were evaluated.

Electrocardiograms were available for 26 of 39 patients (63%). Thirteen patients did not have ECGs and, therefore, were not included in the statistical analysis of certain parameters. Current ECGs were examined for the atrial and ventricular rates, QRS duration and the corrected QT interval ($QT_c = QT / \sqrt{RR}$). A wide QRS was considered ≥ 0.10 sec, and a long $QT_c \geq 0.45$ sec. Heart rate response and exercise-induced ventricular ectopy were determined in some patients during stress tests. Electrophysiologic studies (EPS) were also performed in two subjects.

Risk factors were investigated by comparing the asymptomatic and symptomatic subgroups using the Student's *t* and Mann Whitney *U* tests.

Results

The study population comprised 39 children, 27 boys and 12 girls and the age at diagnosis ranged from 27 days to 17 years of age (mean: 86.54 ± 48.42 months). The follow-up period ranged from one month to 15 years (mean: 40.78 months). Age at last evaluation ranged from one month to 18 years. Nine children were paced. Of the 14 patients with symptoms (five with syncope, eight with progressive exercise intolerance and one with presyncope), one had a ventricular rate of 43 on the ECG and exercise intolerance. Pacing was advised, but her parents refused. The other patients with exercise intolerance had a ventricular

rate of more than 50 beats/min. Of these five patients with syncope, two refused pacer implantation, two were paced, and in one pacing is planned (Fig. 1). Holter monitoring data were available for two subjects, one of whom had a heart rate of less than 50 beats/min and was paced, while the other had a heart rate of more than 50 beats/min.

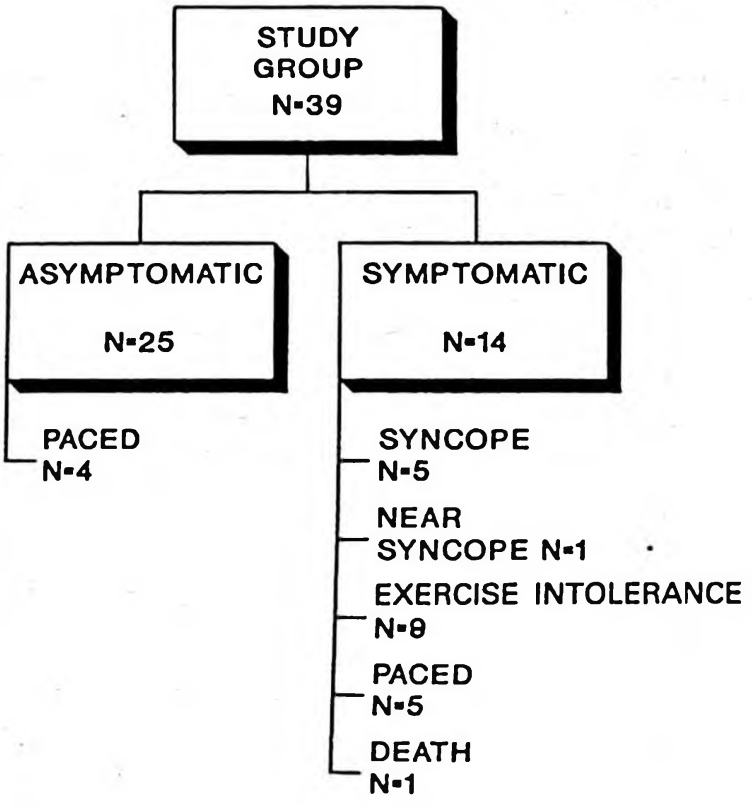

Fig. 1: Clinical outcome of study group.

An EPS was performed in two patients, in one an A-V nodal block was detected and in the other an infrahisian block. Only one patient died, a 27-day-old infant. The cause of death was attributed to noncardiac reasons.

When we compared the clinical features and the laboratory findings of the asymptomatic group with those of the symptomatic group, we found no statistically significant difference between the age at detection of symptoms in these groups (Table I). The development of symptoms did not seem to be related to the age of the patient (mean: 103.10 ± 63 mos.).

When we compared both groups, we were unable to discern any significant difference in respect to heart rate values. Data were also analyzed according to age (five-year) periods. The results remained the same. (Fig. 2).

A wide QRS was detected in two of 16 asymptomatic patients and in three of ten symptomatic patients (30%). A prolonged QT_c was found in five asymptomatic patients (31%) and in seven symptomatic patients (70%).

Table I: Comparison of Risk Factors for Development of Symptoms

	Asymptomatic	Symptomatic	P value
Clinical History	n = 26	n = 14	
• Age at diagnosis (mos)	85.76 ± 42	88.33 ± 55	$p > 0.05$
• Age at 1st symptom (mos)	–	103.10 ± 63	–
Electrocardiogram	n = 16	n = 10	
• Atrial rate (beat/min)	115.87 ± 34	99.20 ± 27	$p > 0.05$
• Ventricular rate (beat/min)	58.43 ± 12	49.40 ± 14	$p > 0.05$
• Wide QRS (≥ 0.10 sec)	11%	30%	–
• Prolonged QT_c (≥ 0.45 sec)	31%	70%	–

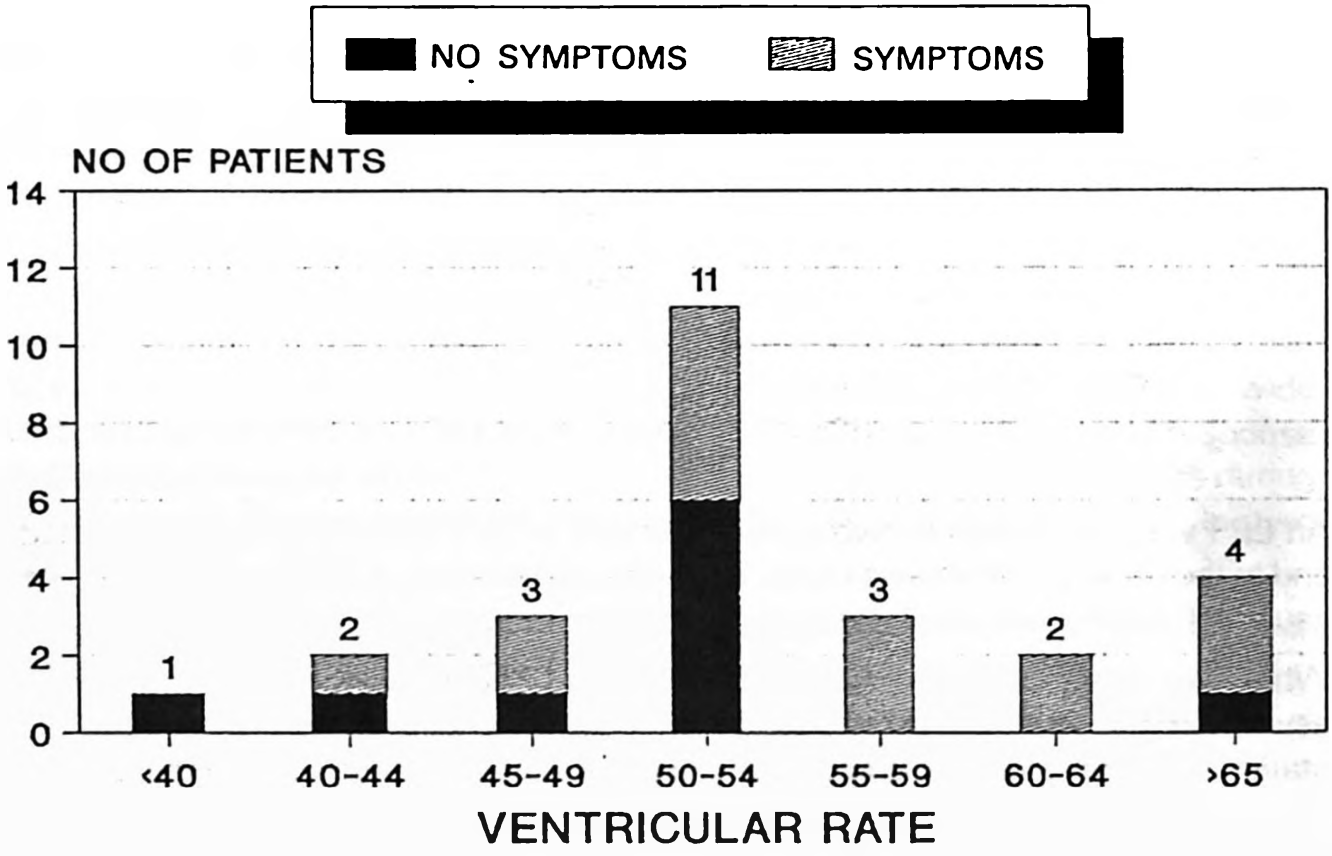

Fig. 2: Relationship between ventricular rate on ECG and clinical symptoms.

Discussion

Congenital complete A-V block is an uncommon disorder and the prognosis is usually regarded as favorable[11]. However, it is sometimes associated with such complications as deterioration, bradycardia, syncope or sudden death[3,8].

Complete heart block was well tolerated in most of the patients in this study. Our results are similar to those reported by Michaëlsson and Engle[12] of large multicenter series where approximately 86 percent of the subjects were alive at the time of the study.

A certain ventricular rate has been most frequently advocated as an indication for pacing in congenital heart block. A rate less than 55 beats/min for neonates and a rate between 40 and 50 beats/min for older individuals are correlated with disabling symptoms or death[13,1,6].

In the present study, the ventricular rate was less than 50 in only six of the 14 patients in the symptomatic group. Of the five patients with syncope, only three had a ventricular rate of 50 or less. On the other hand, the mean ventricular rate was 49.40 ± 14.2 in the symptomatic group and 58.43 ± 12.3 in the asymptomatic group. Thus there was no heart rate variable which distinguished the symptomatic patients. The atrial and ventricular rates were very similar in both groups. These results were obtained from surface ECGs, but if we had used Holter monitoring in all subjects, we could have gotten contrast results. In 1987 Dewey et al[6] reported a Holter monitoring study in CCHB patients with follow-ups for a mean of 8 ± 3 years which revealed that eight of the 13 patients with a mean heart rate of less than 50 beats/min developed cardiac complications of sudden death, syncope, presyncope or excessive fatique while awake. Based on this data, serious consideration should be given to recommending pacemaker implantation in asymptomatic patients with CCHB who have a mean awake heart rate of less than 50 beats/min.

In 1989 Sholler et al[14] reported a retrospective study of 43 patients and were unable to discern any significant difference in heart rate variation between the symptomatic and asymptomatic groups. They explained this discrepancy by the exclusion of patients with anatomic cardiac defects. However, these and our findings raise some doubt as to whether the ventricular rate is the single best index of a patient's compensatory response to CCHB.

With regard to the prevalence of a long QT interval, the first such study was conducted six years ago by Esscher and Michaëlsson[5] of Sweden. They found that 50 of 273 CCHB patients (22%) had a long QT_c interval. In the study of Sholler et al[14] done in 1989, prolonged QT_c was a rare finding, but all patients were symptomatic. In our present study group, 70 percent of symptomatic and 31 percent of asymptomatic patients had a long corrected QT interval. This result indicates a poor prognostic sign of the long corrected QT interval in patients with congenital complete atrioventricular block.

Some reports have focused attention on QRS duration as an alternate risk factor[9]. In 1982 Pinsky et al[1] reported a study conducted in a series of 65 patients with

CCHB. They found a QRS duration of 100 msec or greater for patients with block in or below the bundle of His, and noted that there was a trend toward frequent severe ectopy in children who had a prolonged QRS duration at rest. In this study we found a wide QRS duration in only one patient in the asymptomatic group and in three of the 16 symptomatic patients.

In conclusion, the consideration of a long QT_c as an alternate risk factor is supported by this study. This retrospective study does not invalidate the use of the heart rate as a criteria for prophylactic pacing in cases of isolated CCHB but suggests that other factors are strong independent predictors of symptoms.

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The Turkish Journal of Pediatrics 35: 99-103, 1993

ORAL REHYDRATION OF INFANTS WITH HYPERNATREMIC DEHYDRATION DUE TO ACUTE GASTROENTERITIS*

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SUMMARY: Altuntaş B, Teziç T, Kükner Ş, Ertan Ü. (Dr. Sami Ulus Children's Hospital, Ankara, Turkey). Oral rehydration of infants with hypernatremic dehydration due to acute gastroenteritis. Turk J Pediatr 35: 99-103, 1993.

Twenty-five infants with hypernatremic dehydration due to acute gastroenteritis were given oral rehydration therapy (ORT). The patients received a glucose-electrolyte solution (such as that recommended by the World Health Organization) over six hours (2:1 rotating method).

Twenty-three patients were successfully rehydrated within 48 hours after onset of therapy, while the two remaining patients attained normal serum Na^+ levels within 72 hours. Acidosis was noted in 10 patients which disappeared in 24 hours.
Key words: diarrhea, dehydration, hypernatremia, oral rehydration.

Many clinical studies have established the efficacy and advantages of using oral rehydration therapy (ORT) in treating infants with diarrheal dehydration[1].

The most widely used sugar-electrolyte oral rehydration solutions (such as those recommended by the World Health Organization) contain sodium in a concentration of 90 mEq/L. Although this type of solution has been used in treating mostly patients with isonatremic dehydration, it has been reported to be just as effective when given to patients with hypernatremic dehydration[2].

Despite its disadvantages, intravenous fluid therapy is still being used by pediatricians to treat even infants with mild or moderate dehydration due to gastroenteritis[3]. Electrolyte imbalance and metabolic acidosis are the main reasons why intravenous fluid therapy should be used in a hospital ward.

A Diarrheal Diseases Training and Treatment Center has been established in the Dr. Sami Ulus Children's Hospital in Ankara with the cooperation of the Turkish Ministry of Health and UNICEF with the aim of promoting ORT as treatment for diarrheal diseases, of acquainting mothers with this treatment and instructing them on how to care for infants with acute gastroenteritis, and also to train medical personnel in the methods of treating dehydrated infants with electrolyte imbalance and metabolic acidosis.

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This study was designed to report the results obtained with ORT in the treatment of patients with hypernatremia due to acute gastroenteritis and to also emphasize the superiority of this regimen to intravenous therapy.

Material and Methods

This study consisted of 25 patients with hypernatremic dehydration due to diarrhea who were admitted to Dr. Sami Ulus Children's Hospital Diarrheal Diseases Training and Treatment Center between July-September 1991. A brief medical history was obtained for each patient and a physical examination was performed. The infants were weighed without their clothing and a venous blood sample was drawn. Any value for serum Na^+ of 150 mEq/L or above constituted hypernatremia. The degree of dehydration was determined according to the WHO criteria[4].

Three patients were given fluids intravenously during the first hour of treatment because of peripheral collapse. They then received ORS (oral rehydration solution), a WHO formula which contains Na^+: 90 mEq/L, K^+: 30 mEq/L, Cl^-: 90 mEq/L, Citrate: 10 mEq/L, and glucose: 111 mmol/L and an osmolality of 331 mosmol/L. ORS was given in a rotating manner. This glucose/electrolyte solution was followed by plain water in a volume ratio of 2:1.

A nasogastric tube was inserted in those patients who had poor oral intake. After each infant received the estimated volume of fluid required for six hours, they were given another physical examination to determine if there had been any weight gain. Laboratory tests were also performed. The infants who still showed clinical signs of dehydration were given another course of treatment with ORS. After successful rehydration, they were either breast-fed or given a half strength formula (120 ml/kg/24 hr). The glucose-electrolyte solution was administered each time the infant passed a watery stool.

Results

Twenty-five infants with hypernatremic dehydration resulting from acute gastroenteritis were evaluated. There were 18 males and 7 females. Three patients had mild, 18 moderate and 4 severe dehydration (Table I).

The mean duration of diarrhea was 4.5 days. Most patients were brought to the hospital within the first three days of onset of diarrhea. Ninety-two percent of patients were receiving breast milk and supplements, while eight percent had never received breast milk. Forty-four percent of patients were malnourished. Ten had marasmus, and one was afflicted with marasmic-kwashiorkor.

The mean serum Na^+ value was 163 ± 10.9 mEq/L (min: 150 mEq/L, max: 187 mEq/L) and the mean serum potassium value was 4.4 ± 0.8 mEq/L. During

Table I: Characteristics of Infants with Hypernatremic Dehydration Treated with Oral Rehydration

Age (mos)	No. of Patients
3-6	14 (56%)
7-10	7 (28%)
11-14	2 (8%)
15-18	2 (8%)
Total	25
Degree of Dehydration	
Mild	3 (12%)
Moderate	18 (72%)
Severe	4 (16%)
Total	25

rehydration, the serum sodium level fell at a rate of 1.33 ± 0.8 mEq/L/hr. Normal serum Na^+ levels were attained in six hours (11 patients), twelve hours (4 patients), forty-eight hours (8 patients) and in 72 hours (2 patients). Acidosis was noted in ten patients and was corrected within 24 hours. All patients were successfully rehydrated; the mean rehydration time being 10.5 ± 1.2 hrs.

Discussion

Oral rehydration therapy has been quite successful in treating isonatremic, hypernatremic, and hyponatremic dehydration in addition to metabolic acidosis occurring during diarrhea.

Hypernatremic dehydration is particularly hazardous and is often accompanied by convulsion, intracranial hemorrhage and high mortality[5,6].

Convulsions are a notable complication in hypernatremic patients receiving intravenous therapy and oral rehydration alternating with plain water[7]. Slow intravenous replacement of fluid deficits is believed to lower the risk of convulsions. Convulsions in hypernatremic patients given intravenous fluids correlate with the rate of decrease in serum Na^+. Rates of decline $\leq$ 0.5 mEq/L/hr are reported to be safe, whereas faster rates are associated with convulsions[8].

Pizarro et al[2] have previously published their experience in treating 61 infants with hypernatremic diarrheal dehydration. They used a rapid method to replace the fluid deficits which consisted of a glucose-electrolyte solution alternating with plain water.

Five infants (8%) developed convulsions. The mean rate of fall of serum Na^+ levels in these five infants with convulsions was not significantly different from the rates noted in the remaining 56 infants without convulsions. Furthermore, the five infants with convulsions had serum Na^+ levels exceeding 160 mEq/L at admission. The authors investigated if the risk of convulsion during oral rehydration therapy could be diminished by slowing down the pace of oral rehydration parallel to the rate of fall of the serum Na^+ level. The volume of orally administered fluids required to replace fluid deficits was administered over a 12-hour period rather than over a 6-hour period, as had been previously done. According to this method, infants received a volume equivalent to twice the estimated fluid deficit over nearly 12-hours. None of the 35 infants administered the slow method developed convulsions[9].

There are several factors which play a role in the development of convulsions during treatment of hypernatremic patients in addition to the rapid fall of serum Na^+ levels such as improvement of acidosis and bicarbonate plasma levels, and a decrease in plasma osmolality due to a drop in the serum urea and glucose levels[10-11].

A rapid correction of acidosis causes brain hypoxia and an increase in plasma bicarbonate concentration causes an influx of K^+ from plasma to the cells[12,13]. Major induced seizures are accompained by an efflux of K^+ from the brain[14]. It may be hypothesized that inducing a major influx of K^+ to the brain by means of administering a sufficient amount of K^+ and bicarbonate to hypernatremic patients during rehydration can prevent convulsions.

Despite increased serum Na^+ levels ($Na^+ \geqslant 160$ mEq/L) and a rapid decline in the serum Na^+ level, no convulsions were observed in our patients during the administration of the ORS regimen. We therefore believe that an adequate intake of K^+ and bicarbonate, provided by ORS, can prevent convulsions, which strongly suggests that oral rehydration of hypernatremic and acidotic patients is extremely effective and safe. We are also of the opinion that pediatricians should practice in centers such as ours to gain the experience required to treat infants with diarrheal diseases.

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The Turkish Journal of Pediatrics 35: 105-109, 1993

PLASMA, ERYTHROCYTE AND URINARY SELENIUM LEVELS IN SICKLE CELL HOMOZYGOTES AND TRAITS*

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SUMMARY: Kılınç Y. (Pediatric Hematology Unit, Department of Pediatrics, Çukurova University Faculty of Medicine, Adana, Turkey). Plasma, erythrocyte and urinary selenium levels in sickle cell homozygotes and traits. Turk J Pediatr 35: 105-109, 1993.

Plasma, erythrocyte and urinary selenium levels were determined in 21 sickle cell homozygote patients, 20 siblings with sickle cell traits, 29 parents and in 21 healthy controls with an HbAA pattern. The mean levels of plasma and erythrocyte selenium and the daily urinary selenium depletion were found to be lower in the HbSS patients than in the controls ($p<0.02$; $p<0.001$; $p<0.001$, respectively). Urinary selenium depletion was found to be lower in the sickle cell trait siblings than in the controls ($p<0.001$), but the plasma and erythrocyte selenium levels were close to normal values ($p>0.05$). The mean erythrocyte selenium levels were found to be decreased in the parents as compared with the controls ($p<0.05$), which indicates that urinary selenium losses may be replenished primarily by sources in the plasma and in the erythrocytes before stores in the other parts of the body are used. *Key words: selenium, plasma, erythrocytes, urine.*

Selenium which exists mainly as compounds in nature is a trace element essential for man. It plays an important role in erythrocytic glutathione peroxidase (GSH-Px) activity. GSH-Px helps inactivate free radicals and peroxides, thereby, preventing tissue damage[1]. Selenium is found mainly in the liver, lens of the eyes, vascular endothelium, erythrocytes, heart, lungs, kidneys and in skeletal muscle. Fatty liver necrosis has been reported in guinea pigs[2] and smooth muscle disease in sheep[3] deficient in selenium. In addition, decreased microbicidal activity in neutrophils via deficient glucose utilization and reduced CO_2 synthesis[1] have been demonstrated in selenium deficient individuals. In China, Keshan disease has been reported in patients with low serum selenium concentrations[4], while in the United States, a diet deficient in selenium has been correlated with cardiomyopathy[5,6].

Sickle cell disease (SCD) is a chronic hemolytic disorder associated with recurrent vaso-occlusive events, organ dysfunction and anemia. Alterations in the selenium status and GSH-Px activity may affect vessel endothelium, and may give rise to insufficient tissue nutrition and perfusion.

This study was designed to determine the selenium status of patients with the hemoglobin S gene and of healthy age-matched controls. Comparisons were

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made between the selenium values of the homozygote HbSS patients, their siblings with the sickle cell trait and the parents.

Material and Methods

The study population consisted of twenty-one patients with homozygote sickle cell disease (HbSS) in the asymptomatic phase, 20 heterozygous (HbAS) siblings and 29 parents, who were selected from patient groups. The control group consisted of 21 healthy children with a HbAA pattern. Parental consent was obtained for all children who took part in the study.

The homozygote group consisted of 11 females and 10 males. The age range was from 3 to 17 years, with a mean age of 8 years. The sibling group consisted of 10 females and 10 males, with a mean age of 9 years 7 months. The parental group consisted of 17 females and 12 males. The age range was from 24 to 57 years, with a mean age of 35 years. The age range of the control group was from 3 to 22 years, with a mean age of 9 years 10 months.

Laboratory evaluation consisting of hemoglobin electrophoresis in which cellulose acetate strips with a pH of 8.6[7] were used was performed uniformly in all patients, siblings and parents. The fetal hemoglobin level was determined by the method of Betke et al[8]. The hemoglobin A_2 value was determined by scanning the electrophoretic strips and also by means of DEAE-Cellulose chromatography using Glycine-KCN developers[9]. Sickling tests were performed in all cases. Other routine hematological tests were carried out by conventional methods[10]. Blood samples were obtained by venipuncture and collected in demineralized and heparinized polystyrene tubes for plasma and erythrocyte selenium determinations. Daily urinary selenium excretions were also determined. Plasma, erythrocyte and urinary selenium levels were measured by a Turner Type III fluorometer using the method of Dye et al[11]. Statistical analyses were performed by using the Student's *t* test and correlation analysis.

Results

Plasma, erythrocyte and urinary selenium values of patients, siblings, parents and controls are presented in Table I. No statistical differences were found in the plasma selenium values between patients, siblings and parents. However, there was a significant difference in the plasma selenium levels between patients and controls ($p<0.02$).

There were significant differences in the erythrocyte selenium levels between patients and controls ($p<0.001$), and a slight difference between parents and controls ($p<0.05$). No other statistical difference was found comparing the other groups with each other ($p>0.05$).

Table I: Selenium Values in Plasma, Erythrocytes and Urine in Sickle Cell Homozygotes and Heterozygotes and in Healthy Controls

Hemoglobin Pattern	Plasma (μg/L) Mean ± SD (Low-High)	Erythrocyte (μg/ml) Mean ± SD (Low-High)	Urine (μg/day) Mean ± SD (Low-High)
HbSS (21) Patients	0.020 ± 0.004 (0.012 – 0.028)	0.085 ± 0.026 (0.050 – 0.140)	13.06 ± 9.33 (2.10 – 33.75)
HbAS (20) Siblings	0.025 ± 0.008 (0.014 – 0.047)	0.111 ± 0.036 (0.067 – 0.175)	10.05 ± 8.29 (1.35 – 32.00)
HbAS (29) Parents	0.023 ± 0.011 (0.010 – 0.044)	0.103 ± 0.032 (0.050 – 0.186)	21.76 ± 24.73 (4.00 – 70.10)
HbAA (21) Controls	0.031 ± 0.015 (0.017 – 0.062)	0.122 ± 0.046 (0.044 – 0.224)	38.62 ± 25.25 (10.70 – 95.92)

Daily urinary selenium excretions did not differ statistically between the patients and their siblings ($p>0.05$), but, there was a slight difference in mean selenium values between siblings and parents ($p<0.05$). However the most significant finding was that there was a highly significant difference in the daily urinary selenium excretions between patients, siblings and controls, respectively ($p<0.001$; $p<0.001$).

Discussion

In various types of hemolytic anemias, peroxide and free radical-induced hemolysis increases concomitantly with decreased Vitamin E and selenium levels[12]. Selenium plays an important role not only in protecting erythrocytes against oxidative damage, but is also effective in the maintenance and utilization of GSH.

Rotruck et al[13] reported that hemoglobin oxidation and hemolysis of erythrocytes may be prevented by selenium. Vitamin E also provides important protection against membrane oxidation, but cannot prevent hemoglobin oxidation. The high levels of GSH-Px observed in cases of selenium deficiency may be explained by the fact that selenium is required for the utilization, but not for the maintenance of GSH.

In our study there was a moderate difference in the plasma selenium levels between the HbSS patients and the controls ($p<0.02$). Natta et al[14] reported low plasma selenium and glutathione peroxidase levels in patients during a crisis and in those during the asymptomatic phase of the disease. Data supporting the

presence of oxidative stress in SCD indicate that it may affect the capillary bed endothelium leading to capillary tissue or organ dysfunction.

As shown in Table I, selenium concentrations in the plasma and in the erythrocytes of the homozygote patients were visibly low which may indicate that these patients are selenium deficient, the reason for which is unclear. It however may be related to the absorption, storage or mobilization of this trace element because the daily urinary excretion of selenium could not be an explanation for this loss. Although the selenium values in the siblings and in the parents were not as low as those found in the patients, they clearly demonstrate selenium deficiency when compared with the levels found in the healthy controls. This finding suggests that selenium is utilized in GSH-Px activity. In another study we conducted in 1984, we found low levels of selenium in erythrocytes, excessive urinary depletion of selenium and normal or high plasma selenium levels in patients with thalassemia major[15].

These findings suggest that the erythrocytes are one of the most important and sensitive, but not the sole-parameter of selenium storage. Thomson and Robinson[16] reported a positive correlation between erythrocyte GSH-Px activity and plasma selenium concentrations less than 150 μg/L. Rea et al[17] found that selenium storage may be restricted to the erythrocytes when erythrocyte selenium levels are below 0.15 μg/ml. Our results are consistent with the literature. In conclusion, we wish to note that low selenium stores in SCD patients may also affect the phenotypic expression in these patients.

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The Turkish Journal of Pediatrics 35: 111-114, 1993

PULMONARY DYSPLASIA WITH RENAL MALFORMATIONS: A COMMON CONNECTIVE TISSUE DISORDER?*

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*Haluk Topaloğlu MD**, Keriman Tınaztepe MD*****

SUMMARY: Yurdakök M, Hazıroğlu R, Topaloğlu H, Tınaztepe K. (Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey). Pulmonary dysplasia with renal malformations: a common connective tissue disorder? Turk J Pediatr 35: 111-114, 1993.

The effect of D-penicillamine (DPA) on the development of lung and kidney tissues was evaluated to determine whether the association of lung and kidney malformation results from a common generalized disorder of connective tissue in the fetal rat.

Ten animals received a daily dose of 300 mg DPA in their drinking water during the last six days of their gestation. Ten other pregnant rats were used as controls. At the end of the gestation period all the animals were delivered by cesarean section. We found that DPA treatment during gestation caused marked growth retardation in the offspring. Although the lung weight to body weight ratios did not differ between the study and control groups, the left-kidney weight to body weight ratios were found to be lower in the study group. Histologic sections showed pulmonary dysplasia with bronchomegaly, cystic alveoli, atelectasis, vascular aneurism, perivascular loose of connective tissue, small hemorrhagic foci in the lungs and caliechtasis. We hypothesize that a common connective tissue disorder induced by DPA during intrauterine life may cause lung and kidney malformations. *Key words: caliechtasis, cystic lung disease, D-penicillamine, pulmonary dysplasia, renal malformation.*

Since it has been recognized that there is an apparent association between spontaneous pneumothorax and congenital urinary tract abnormalities in newborn infants[1] and a predisposition to pneumothorax in patients with collagen synthesis defects such as Ehlers-Danlos disease and Marfan syndrome[2], we are of the opinion that a common generalized connective tissue disorder may affect both lung and kidney development. We performed an experimental study in rats to ascertain whether an induced collagen synthesis defect could lead to changes in lung and kidney development. D-penicillamine (DPA) was used in the study to induce a collagen synthesis defect because lysyl oxidase, which contains copper as an essential component, is important in the cross-linking of collagen and elastin and its activity is impaired by DPA[3].

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Material and Methods

Pregnant albino rats with a mean weight of 245 g were used in this study. Five animals received a daily dose of 300 mg DPA in their drinking water during the last six days of their gestation. Five other pregnant rats were used as controls and received no drug. At the end of gestation, all the animals were delivered by cesarean section. The serum copper levels were found to be lower in the animals that received DPA (range, 69-87 mg/dL), when compared with the control group (range, 95-98 mg/dL). All offspring (17 in the control group and 21 in the study group) were weighed and killed by decapitation. Their lungs and kidneys were removed, weighed and examined under light microscopy.

Results

We observed that DPA therapy during gestation caused marked growth retardation and a relatively decreased kidney weight in the offspring. The hematoxylin-eosin stained histologic sections showed pulmonary dysplasia with bronchomegaly, cystic alveoli, interstitial emphysema, atelectasis, perivascular loose of connective tissue and vascular aneurisms in the lung in addition to renal caliechtasis (Fig. 1) in the offspring of DPA-treated animals. Histological changes were not observed in any of the control offspring (Table I).

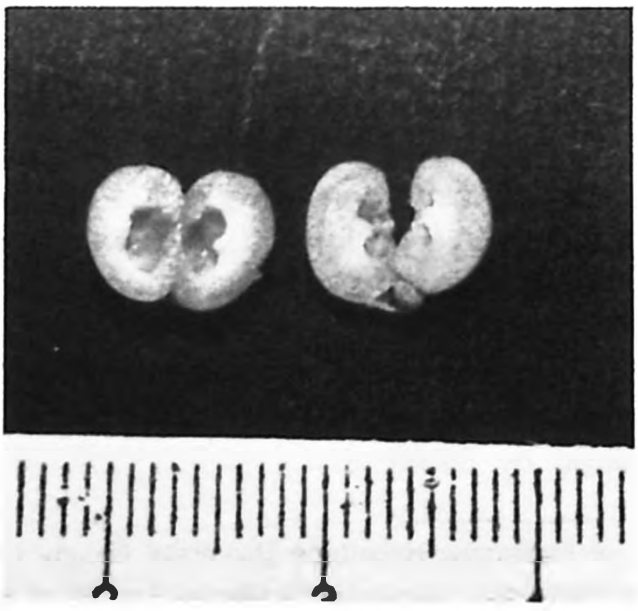

Fig. 1: Renal caliechtasis in an animal (on the left) whose mother had received D-penicillamine during pregnancy compared with the control (on the right).

Table I: The Findings of DPA Treatment During Gestation on the Fetal Kidney and Lung Tissues of Rats (mean ± SD)

	Control Group (n: 17)	Study Group (n: 21)
Body weight (mg)	9537 ± 390	8378 ± 483*
Left kidney weight (mg)	85.0 ± 9.6	60.5 ± 8.2*
LKW/BW (%)	0.89 ± 0.08	0.72 ± 0.09*
Caliechtasis		12 (57.1%)
Lung weight (mg)	258.3 ± 64.4	233.3 ± 55.6
LW/BW (%)	2.69 ± 0.57	2.78 ± 0.63
Cystic alveoli	–	17 (80.9%)

Abbr: LKW left kidney weight, LW: lung weight, BW: body weight.
* $p < 0.001$ compared with controls. Mann-Whitney *U* test.

Discussion

This study demonstrates that DPA therapy administered during gestation causes cystic alveolar lung disease and renal caliechtasis in rat offspring. Since it is known that bilateral pulmonary hypoplasia is almost always a finding in renal agenesis, and that it may also be present in diffuse and bilateral dysplastic kidneys functionally imitating bilateral renal agenesis, it has been postulated that pulmonary hypoplasia is most likely caused by increased external pressure secondary to oligohydramnios. However in cases of unilateral or bilateral renal cystic dysplasia (not the diffuse types), there have been no satisfactory explanations offered for the association of pulmonary hypoplasia with renal cystic dysplasia[1,4].

A common connective tissue disorder which involves both kidneys and lungs in an animal model is presented in this study. DPA is a powerful drug, especially since it is also a chelating agent, and therefore has wide-ranging effects. In addition to specifically inhibiting lysyl oxidase activity, it is difficult to attribute the results solely to an induced defect in collagen synthesis[5]. Therefore, additional studies are needed to support the hypothesis that a common connective tissue disorder may cause lung and kidney abnormalities.

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The Turkish Journal of Pediatrics 35: 115-119, 1993

GRISCELLI'S SYNDROME: CLINICAL FEATURES OF THREE SIBLINGS*

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SUMMARY: Sanal Ö, Küçükali T, Ersoy F, Tınaztepe K, Göğüş S. (Departments of Pediatrics and Pathology, Hacettepe University Faculty of Medicine, Ankara, Turkey). Griscelli's syndrome: clinical features of three siblings. Turk J Pediatr 35: 115-119, 1993.

Three siblings diagnosed as having Griscelli's syndrome (GS) are presented. The clinical features were partial albinism, silvery hair and absence of giant granules in the white blood cells. The diagnosis of GS was confirmed intra-vitam in the youngest sibling (propositis) at the age of nine months by the demonstration of irregular clumps of pigment in the hair shaft, and in particular melanocytes engorged with melanosomes in the skin biopsy, findings characteristic of this syndrome. A retrospective diagnosis of GS was made in the older two siblings.

The first sibling died at the age of two, having a clinical picture suggestive of bulbar poliomyelitis. However, no tissue was available for histopathologic examination. The second sibling developed fever, jaundice, seizure, hepatosplenomegaly and lymphadenopathy and died at the age of six. Postmortem examination of this sibling revealed lymphohistiocytosis in the liver and spleen. The propositus died at the age of five following development of central nervous system involvement.

Immunologic studies were not available in the first sibling. The IgG level was slightly low and the T-lymphocyte number was normal in the second sibling. The propositus had normal serum immunoglobulin levels and T-cell numbers and skin tests were positive with phytohemagglutinin and candida. *Key words: clinical features, Griscelli's syndrome.*

Griscelli's syndrome, first described in 1978, is characterized by partial albinism and immunodeficiency[1,2]. Patients may develop progressive neurological deterioration and lymphohistiocytosis and usually die of these complications[3-5].

We present a family in which three of five children of consanguineous parents were affected. Two of the children had partial albinism at birth and an absence of giant granules in the blood leukocytes. One sibling died at the age of two, and the other at the age of six. The third sibling, who also had partial albinism, was diagnosed as having Griscelli's syndrome after microscopic examination of the

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hair and electron microscopy of the skin revealed findings consistent with this syndrome. We report three siblings afflicted with Griscelli's syndrome because of the rarity of this disorder and also to stress the importance of differential diagnosis.

Case Reports

The propositus, a nine-month-old girl, who appeared in overall good health, was seen at the Hacettepe University Children's Hospital because of a history of sibling deaths in the family (Fig. 1). Physical examination was unremarkable except for the presence of partial albinism. The pathognomonic granules of Chédiak-Higashi syndrome (CH) were not observed in peripheral blood smears and bone marrow specimens. The peripheral white blood cell (WBC) count with the differential count and the platelets were within normal limits. Serum immunoglobulin (Ig) levels and the T-cell number were also within normal limits. Delayed type skin sensitivity tests were positive with phytohemagglutinin and candida and negative with streptokinase streptodornase.

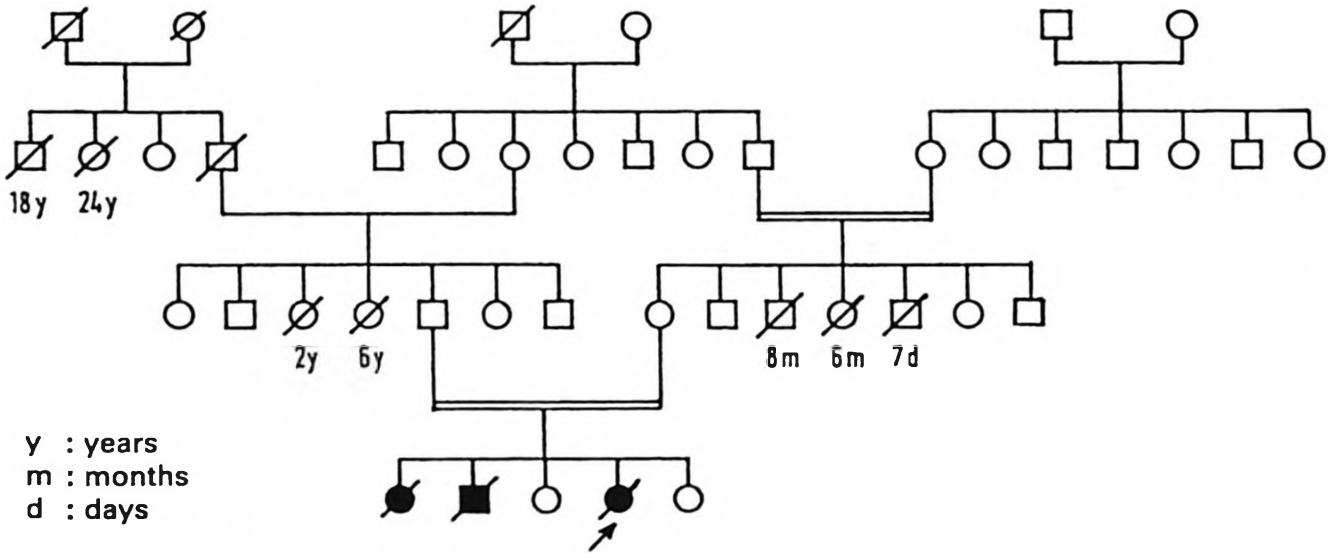

Fig. 1

Light microscopy of the hair revealed irregular clumps of pigment in the hair shaft and a random skin biopsy revealed rather large melanin granules in the deep portion of the epidermis, especially in the basal layer associated with a lesser degree in the dermis (Fig. 2a). Electron microscopy of the skin biopsy showed melanocytes engorged with melanosomes and very few melanosomes in the surrounding keratinocytes (Fig. 2b).

The patient was lost to follow-up. Recent contact with the family disclosed that at the age of five she developed progressive deterioration including ataxia,

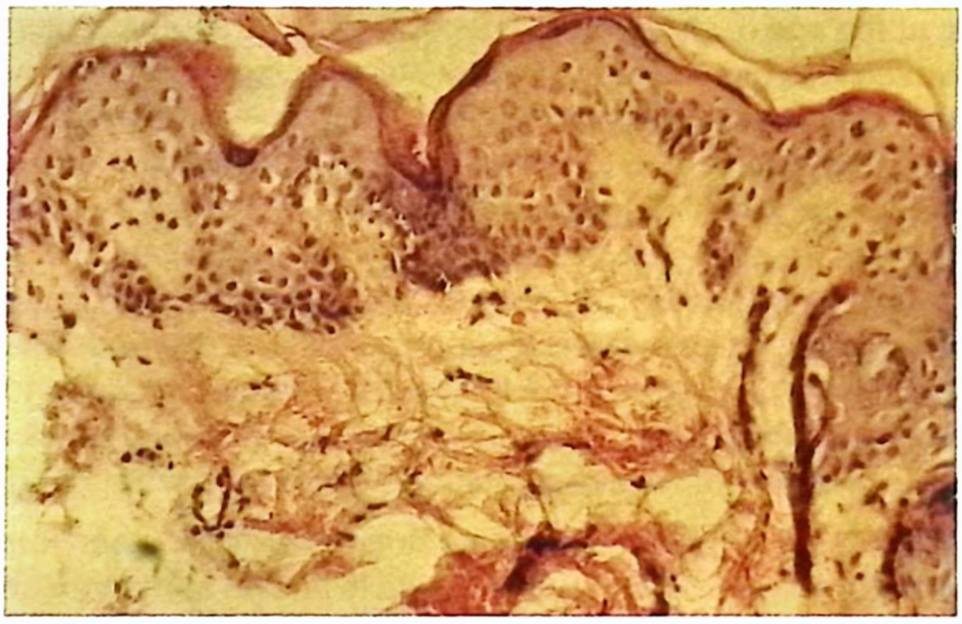

Fig. 2a

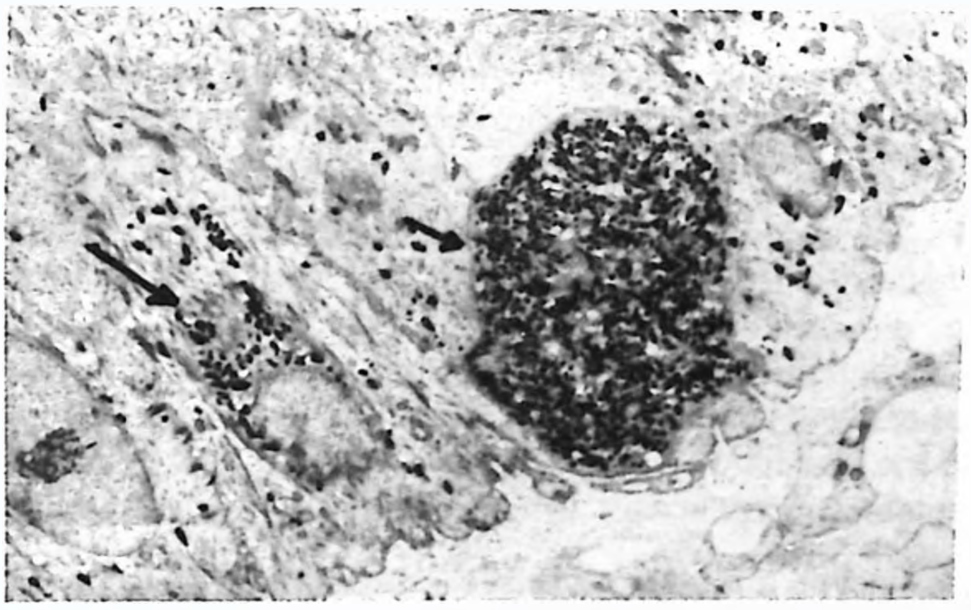

Fig. 2b

dysmetria, involuntary movements, pigmented lesions on the cheeks (which developed at the age of two), and thrombocytopenia. The patient died in another hospital within a period of two months. Her past history was unremarkable except for recurrent upper respiratory tract infections.

The first-born child of the family also had silvery hair and died at the age of two. The clinical picture was suggestive of viral paralytic disease, but no tissue was available for histopathological examination.

The older brother, who also had silvery hair, developed fever, jaundice, seizures, hepatosplenomegaly, lymphadenopathy, atypical lymphocytosis, and throm-

bocytopenia at the age of six. He had a peculiar dark red-purplish pigmentation on his cheeks which was described by his parents as being more prominent than that seen on the other two affected siblings. He died on the 22nd day of hospitalization. His white blood cell count varied between 2,000-14,000/mm^3, with a distribution of 20-66% lymphocytes, 39-75% neutrophils, a hemoglobin of 5.9-9.8 g/dl, and markedly decreased platelets on blood smears. No giant granules were noted in the blood leukocytes. Serum bilirubin and transaminase levels were elevated as were the uroporphyrin and coproporphyrin concentrations in the urine. The serum IgG level was slightly low (IgG subclasses were not determined) and the T-lymphocyte number was normal. Postmortem histopathological examination of the liver and spleen revealed infiltration of lymphocytes and histiocytes.

The parents were first cousins and they, along with two other female children who had dark hair, were healthy. A paternal uncle and an aunt, both of them blond, died of unknown causes at the age of 18 and 24, respectively.

Discussion

The diagnosis of Griscelli's syndrome is arrived at on the basis of the presence of a typical clinical phenotype (light skin color with silvery hair) and microscopic examination of the skin biopsy.

The clinical symptoms of patients with Griscelli's syndrome are similar to that seen in Chédiak-Higashi (CH) syndrome, but the granulocytes show giant cytoplasmic granules. In our patients, pigmentary abnormalities, clinical symptoms and the course of the disease suggested CH or Griscelli's syndrome. The absence of giant granules in the white blood cells, the microscopic findings of the hair and the electron microscopic changes seen in the skin of the propositus were consistent with Griscelli's syndrome.

Immunodeficiency is a feature of Griscelli's syndrome. Defects in T and B cell immunity having no consistent pattern have been described in these patients[3-6]. However, the stage at which immunologic studies performed may determine the results. By way of an example we cite the case described by Schneider et al[4] of a three-month-old girl with Griscelli's syndrome. She had normal T and B cell immunity before successful bone marrow transplantation, while her older brother, afflicted with the same disease, showed a decreased number of T cells, poor T cell mitogen stimulation with concavalin A and pokeweed mitogen. He died at the age of eight months.

Although detailed immunological studies were not performed, one of our patients had normal serum immunoglobulin levels, another had a slightly low IgG level, and both had normal T cell numbers.

Successful treatment of the syndrome with allogeneic bone marrow transplantation has been reported and seems to have a curative effect when performed early in the course of the disease[4].

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The Turkish Journal of Pediatrics 35: 121-125, 1993

IMINOGLYCINURIA: A BENIGN TYPE OF INHERITED AMINOACIDURIA*

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SUMMARY: Coşkun T, Özalp İ, Tokatlı A. (Pediatric Nutrition and Metabolism Unit, Department of Pediatrics, Hacettepe University Institute of Child Health, Ankara, Turkey). Iminoglycinuria: a benign type of inherited aminoaciduria. Turk J Pediatr 35: 121-125, 1993.

The diagnosis of iminoglycinuria was established in two patients on the basis of increased urinary excretion of proline, hydroxyproline and glycine in the presence of normal plasma concentrations of these respective compounds. Routine metabolic screening was performed in these infants in order to find the cause for the developmental delay observed in one infant and the siblings deaths noted in the family of the other. These two patients gave further support to the previous suggestion that renal iminoglycinuria is a benign disorder with no recognizable clinical pattern. Its detection, therefore, requires screening programs or aminoacid studies. *Key words: glycinuria, iminoaciduria.*

Iminoglycinuria is a rare inborn error of metabolism associated with increased urinary excretion of glycine and the iminoacids, proline and hydroxyproline. It occurs because of a defect in the renal tubular transport mechanism shared by these three aminoacids[1,2].

Lack of a typical clinical picture peculiar to iminoglycinuria restricts the number of reported cases. The purpose of this paper is to describe the clinical and laboratory findings of the first two patients reported in Turkey afflicted with this disorder.

Case Reports

Case 1

A ten-day-old male infant was admitted to Hacettepe University Children's Hospital because of a family history of sibling deaths due to unknown causes. He was the seventh child born to parents who were first degree relatives. The pregnancy and delivery had been uneventful. Three other male children had died at around three months of age, and three females were alive.

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Physical examination revealed a normal, healthy infant with a body weight of 4200 g and length of 53 cm.

The results of urine analyses and blood examinations for hemoglobin, white blood cells, urea, electrolytes, alkaline phosphatase, proteins, glucose and pH were within normal limits. Paper chromatographic amino acid analysis of the urine sample demonstrated a marked increase in proline and glycine concentrations. A quantitative amino acid analysis of the serum and urine specimens was performed at the age of six (Table I).

Table I: Plasma Concentrations and Urinary Excretion of Glycine, Proline and Hydroxyproline in Two Patients

	Cases		
	1	2	Normal Values
Plasma (μmoles/L)			
Glycine	315	305	125 - 318
Proline	320	87	40 - 332
Hydroxyproline	Trace	23	-
Urinary excretion (μmoles/24 h)			
Glycine	8430	8802	165 - 1420
Proline	8960	19126	-
Hydroxyproline	1336	1820	-

The patient was doing well when seen for the last time at the age of six. His physical, mental and motor development was normal.

Case 2

A fourteen-month-old male infant was referred to the Hacettepe University Children's Hospital for evaluation of developmental delay. He was the product of consanguineous parents. Pregnancy and delivery had been uncomplicated. The parents had two older healthy children. The patient had experienced a seizure ten days prior to admission.

Physical examination revealed an infant with a weight of 11,700 g and a length of 79 cm. He had no contact with his surroundings and was unable to speak, stand unsupported or walk.

Routine metabolic screening was performed in order to ascertain the cause for the developmental delay observed in this patient. Results of paper chromatog-

raphy revealed that large quantities of proline and glycine were being excreted in the urine. At the age of two, a quantitative analysis of plasma and urine amino acids was performed, the results of which are presented in Table I. The EEG showed a bioelectric abnormality in the posterior part of the right hemisphere of the brain.

Material and Methods

Plasma and urine amino acid screening was performed by paper chromatography (butanol: acetic acid: water)[3]. Plasma and urine samples were then analyzed quantitatively by ion exchange chromatography on a LKB Alpha Plus Model 4151 amino acid analyzer using the standard method.

Results

In all the urine samples of the patients screened by paper chromatography, markedly increased concentrations of proline, hydroxyproline and glycine were detected. These findings were confirmed by quantitative amino acid analyses done using the amino acid analyzer. The plasma concentrations of the respective amino acids were within normal limits (Table I). The urinary excretion of iminoacids and glycine was normal in parents and sibs of patients.

Discussion

Iminoglycinuria is characterized by an abundant urinary excretion of glycine and the iminoacids, proline and hydroxyproline presumably due to a defect in the high capacity, low affinity group specific membrane transport system of the brush border membrane shared by these three amino acids while the plasma levels of these compounds are normal. Large amounts of iminoacids and glycine excretion have been described in premature and term newborn infants between 6 to 12 months of age and in patients with hyperprolinemia[1,2]. The latter two possibilities were unlikely in our patients because quantitative amino acid analyses were performed after age one and at the ages of six and two, respectively. The analyses we performed revealed increased urinary excretion of proline, hydroxyproline and glycine when the plasma levels of these three compounds were within normal limits (Table I).

There is no typical clinical picture attributed to iminoglycinuria[1,2]. While most patients with this disorder can live normal lives, others are observed to have mental retardation[4-8], convulsions[4,9], blindness[10], achromatopsia[11], deafness[10,12], failure-to-thrive[13] and transient hematuria with metopic suture[14].

It is not certain whether the iminoglycinuria caused the developmental delays in our patients, or if it was just a coincidental occurrence. Our patients were

diagnosed as having iminoglycinuria following routine screening which was carried out because of a family history of sibling deaths in the first case and developmental delay in the second. Since a developmental delay was only seen in Case 2, we drew the conclusion that the association of iminoaciduria with mental retardation and with some of the other clinical conditions mentioned above were only coincidental, and a consequence of the selection of subjects screened. Iminoglycinuria, therefore, appears to be a "harmless" inborn error of metabolism assuring a normal life span[1,2,10,14].

The occurrence of multiple cases with this defect in the same family, the presence of consanguinity in some of the reported families and hyperglycinuria without iminoaciduria in some of the parents indicate that iminoglycinuria is inherited as an autosomal recessive trait[1,2]. The parents of our two patients were first degree relatives, but we were unable to demonstrate an increase in glycine excretion in the urine samples of the parents or find any other affected siblings. Due to the possible genetic heterogeneity of the defect resulting from the existence of several allelic genes, there may be an associated impairment of intestinal amino acid transport in iminoglycinuria as seen in other inherited diseases such as cystinuria and Hartnup's disease, which involve renal tubular transport[1,2,7]. Fecal amino acid analysis was not available in our cases.

The present report is in accord with previous suggestions to the effect that iminoglycinuria of renal origin is a benign disorder with no clinical abnormality and that its detection depends on screening programs or amino acid studies. The link between iminoglycinuria and the accompanying clinical manifestations still remains controversial. There is need for additional case reports and studies in affected individuals at the cellular level in order to determine whether these are two separate defects, one leading to a benign condition, while the other to a symptomatic disease, as hypothesized[15].

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The Turkish Journal of Pediatrics 35: 127-130, 1993

ANESTHETIC MANAGEMENT OF A PATIENT WITH HEREDITARY FRUCTOSE INTOLERANCE AND PHENYLKETONURIA*

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SUMMARY: Çeliker V, Dural O, Erdem K. (Department of Anesthesiology and Reanimation, Hacettepe University Faculty of Medicine, Ankara, Turkey). Anesthetic management of a patient with hereditary fructose intolerance and phenylketonuria. Turk J Pediatr 35: 127-130, 1993.

This is a report of a five-year-old girl with phenylketonuria (PKU) and hereditary fructose intolerance (HFI) who underwent elective strabismus surgery. PKU and HFI are two inborn errors of metabolism which have an autosomal recessive mode of inheritance. This case report describes the anesthetic features of a patient with PKU and HFI, each defect requiring specific anesthetic management. *Key words: phenylketonuria, hereditary fructose intolerance, general anesthesia.*

Phenylketonuria (PKU) is an autosomal recessive disorder of amino acid metabolism characterized by a genetically determined absence of phenylalanine hydroxylase. If the disease is not diagnosed early and treated, it leads to mental retardation[1-3]. PKU occurs in 1 of 3954 newborn infants in Turkey[4]. In hereditary fructose intolerance (HFI), which is a genetic disorder of carbohydrate metabolism transmitted in an autosomal recessive pattern, there is a marked deficiency of fructose-1-phosphate aldolase B in the liver, renal cortex and in the small intestine[1,2].

According to reports from Switzerland, the incidence of HFI is presumed to be nearly 1 in 20,000 infants[4]. The statistical probability of both these defects occurring together is 1 in 75,080,000[4]. Both of these disorders were present in our patient, and each required specific anesthetic management.

Case Report

A five-year-old girl was previously diagnosed as having PKU and HFI because of an elevated blood phenylalanine level (>20 mg/dl) and sucrose and fructose intolerance. The patient has been receiving a low phenylalanine and sucrose/

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fructose free diet since she was one month-old[4]. The parents of the child are first cousins.

Since she had alternate exotrophia-hypertrophia, a right lateral rectus recession and a right medial rectus resection were planned under general anesthesia. There were no preoperative pathological findings except for molar hyperplasia. Liver and kidney function tests were within normal limits. There was no history of epileptogenic seizure.

After a six-hour period of no solid food, the patient was premedicated with atropine sulphate 0.015 mg/kg intramuscularly 45 minutes prior to surgery. She was given first priority on the elective surgery schedule and was infused with a 5% solution of dextrose in water. Anesthesia was induced by using intravenous thiopentone sodium 5 mg/kg and endotracheal intubation was facilitated with vecuronium bromide 0.1 mg/kg intravenously. Anesthesia was maintained with 0.5% halothane and 70% nitrous oxide in 30% oxygen. Towards the end of the operation, vecuronium bromide was reversed with neostigmine bromide 0.07 mg/kg and atropine 0.015 mg/kg intravenously. The operation lasted approximately 45 minutes. During the anesthesia the systolic blood pressure, heart rate, ECG, end tidal CO_2 (ET CO_2) and peripheral oxygen saturation (SaO_2) were monitored. Both hyper and hypocarbia were avoided. Approximately 24-hours postoperatively, nausea, drowsiness and weakness were observed because of the late feeding of the patient and she was transferred to the pediatric intensive care unit. She received a low phenylalanine and fructose/sucrose free diet. Since metabolic acidosis and hypoglycemia were present intravenous dextrose and bicarbonate therapy was initiated. She was discharged from the hospital on the third postoperative day.

Discussion

PKU may be associated with Charcot-Marie-Tooth disease, Down's syndrome, cystinuria, bilateral iris coloboma, cataract, and enamel hypoplasia. These patients may undergo elective surgery because of their primary pathology, as occurred in our case[1,4]. Untreated children may present clinically with eczema, decalcification of long bones, mental retardation, hyperreflexia, muscular hypertonicity, behavioral abnormalities, seizures and cataract[1-3,5]. There have been reports of increased incidences of congenital hyperthyroidism and pyloric stenosis in children with PKU who require specific anesthetic management[6-8].

In PKU patients, food should not be withheld for an extensive period preoperatively because it can result in a catabolic state characterized by the breakdown of tissue protein, and consequently, an elevated serum phenylalanine level. Therefore, these patients should be given first priority on elective surgery schedules. Minor surgery does not cause major long-lasting changes in the serum

phenylalanine level of PKU patients and, therefore, there is no need to alter the dietary regimen[2,9]. The effects of tranquilizers, narcotics and hypnotics used for preanesthetic sedation are quite unpredictable. A patient administered normal or abnormal doses of sedatives may develop severe respiratory depression which can persist into the postanesthetic period. A seizure-prone patient given preanesthetic agents, which induce respiratory depression, may develop seizures. Therefore, we suggest that anticholinergic drugs be used for preanesthetic sedation. Since glycopyrrolate does not easily cross the blood-brain barrier, as do atropine and scopolamine, it has less adverse effects than other drugs when administered to patients with abnormal brain metabolism and altered neurotransmitter activity[2,8]. If a patient has a history of eczema, care should be taken during the application of the face mask and the passage of the endotracheal tube because skin sensitivity may increase. After one year of age, if infants have not been treated for PKU, they may develop decalcification of the long bones. Therefore, a patient under general anesthesia should be carefully manipulated to avoid fracture of the extremities. In PKU patients with seizure disorders, bright lights and equipment such as electrocardiogram machines or other monitoring devices should be used with caution[2].

During anesthesia continuous measurement of body temperature, blood sugar determinations and, if available, continuous electroencephalographic monitoring should be carried out. Capnography and arterial blood gas analysis should be performed in seizure-prone patients for confirming continuous normothermia, normoglycemia and normocarbia[2]. In infants and children, halothane, oxygen and nitrous oxide may be employed in induction and maintenance of anesthesia. With inhalation agents, anesthesia is easily controlled and there is rapid recovery. The patient can receive an oral therapeutic regimen shortly after. In the patients who receive antiepileptic, or enzyme-inducing agents such as phenobarbital or carbamazepin, isoflurane may be used instead of halothane during anesthetic maintenance so as to assure not only a more rapid recovery, but perhaps more importantly a smaller degree of biotransformation of the inhalation agent to potentially toxic metabolites[2].

Hepatic intracellular concentration of fructose-1-phosphate becomes markedly elevated in HFI patients. The intracellular accumulation of fructose-1-phosphate causes renal tubular dysfunction and the inability to acidify urine which may result in generalized amino aciduria and albuminuria[1,2]. Patients who develop hypoglycemia, dehydration, or acid-base derangements due to both prolonged vomiting and renal alkaline losses should receive intravenous glucose and salt-containing solutions prior to surgery to achieve normoglycemia, normovolemia, a neutral blood pH and an adequate serum electrolyte concentration. In patients with hepatic dysfunction, anesthetic considerations are similar to those necessary in

any patient with a similar degree of hepatic dysfunction. An anesthetic agent which may be toxic to the liver should be avoided or used in minimal doses in HFI infants. These types of drugs may significantly impair drug conjugation functions and compounds that are biodegraded via this pathway which may have a prolonged effect on these patients. In patients with liver damage, the effect of succinylcholine is not prolonged if hypocholinesterasemia is not present. Except for vecuronium and pancuronium, the non-depolarizing muscle relaxants and decamethonium are unaffected by hepatocellular injury if there is no presence of renal dysfunction[2].

Systemic organ dysfunction did not occur in our patient who has been treated and followed up since the age of one. We complied with the principles of anesthesia, and therefore, our patient had a safe and effective anesthetic period. The development of hypoglycemia and acidosis because of late feeding postoperatively stresses that other than preoperative preparation and anesthetic management of the patient with metabolic disorders, postoperative care is equally as important.

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The Turkish Journal of Pediatrics 35: 131-134, 1993

BLUE RUBBER BLEB NEVUS SYNDROME: REPORT OF A CASE*

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SUMMARY: Tatar G, Özyılkan E, Telatar H. (Gastroenterology Unit, Department of Internal Medicine, Hacettepe University Faculty of Medicine, Ankara, Turkey). Blue rubber bleb nevus syndrome: report of a case. Turk J Pediatr 35: 131-134, 1993.

A case of blue rubber bleb nevus syndrome (BRBNS) in a 17-year old boy with multiple cutaneous and gastrointestinal hemangiomas is presented. The patient had iron deficiency anemia and pica. In addition, we describe, for the first time, left renal artery, right hepatic artery, and ureteral abnormalities in a patient with BRBNS. *Key words: blue rubber bleb nevus syndrome, gastrointestinal involvement, vascular abnormalities.*

The blue rubber bleb nevus syndrome (BRBNS) was first described by Bean[1] in 1958, and is named after the soft, bluish, rubber-like hemangiomas mainly of the skin and the gastrointestinal tract. These lesions may also be found in other locations such as in the peritoneal cavity, the heart, lungs, pleura, and central nervous system[2-4]. To date, over 40 cases have been reported.

Our patient, besides illustrating the characteristics of this syndrome, namely, the nature and distribution of the lesions and iron deficiency anemia, in addition presented with arterial and ureteral abnormalities.

Case Report

A 17-year-old boy was admitted to the Hacettepe University Hospital with the diagnosis of iron deficiency anemia. There was a 7-year history of geophagia. Flat, blue, non-tender lesions varying in size from 0.5 to 1.0 cm were seen on the hands, feet, tongue, and lip (Fig. 1). The hemoglobin was 7.6 g/dl and hematocrit 24%. Blood smear revealed microcytic, hypochromic red blood cells. The serum iron was 13 μm/L and total iron binding capacity 375 μm/L. Tests for occult blood in the stool were positive.

Esophagogastroduodenoscopy confirmed the presence of multiple 0.5-1.5 cm papillary bluish hemangiomas in the stomach and duodenum (Fig. 2). Colonosco-

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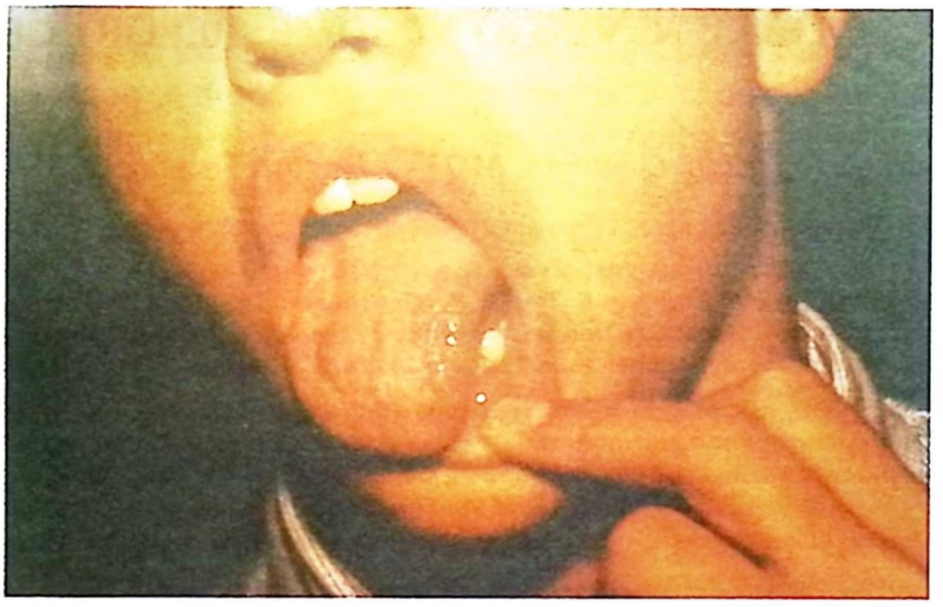

Fig. 1: Blue rubber bleb hemangiomas on the tongue.

Fig. 2: Endoscopic view of hemangiomas in the stomach.

pic examination revealed multiple 0.5-1.5 cm dark blue pedunculated polypoid lesions between the cecum and 20 cm from the anal orifice.

An aortagram showed the right hepatic artery originating from the superior mesenteric artery and two renal arteries originating from the aorta on the left side. There was an ectopic insertion of the left ureter into the bladder.

Abdominal ultrasonography revealed splenomegaly. Hepatitis B surface antigen was negative. Liver biopsy was normal. The splenomegaly was believed to have been caused by pica.

The patient was transfused with red blood cells and was placed on continuous oral iron supplementation.

At follow-ups his hemoglobin level remained at about 10 g/dl.

Discussion

The characteristic finding of BRBNS is a few to hundreds of skin lesions varying in size from 1 mm to 10 cm[3,5]. Three types of skin lesions have been described. Type I is a large disfiguring cavernous angioma that may increase in size and obstruct vital tissues. Type II is a "blue rubber nipple" covered with thin skin that is compressible, leaving an empty, wrinkled sac that rapidly refills. This is the commonest type and was presented in our patient. Type III is an irregular, blue-black macule or papule that may be punctate or merge with adjacent pigmented nevi and may blanch on pressure. The limbs, trunk, and face are the main sites of involvement. Lack of nail bed involvement distinguishes BRBNS from Osler-Weber-Rendu syndrome.

Intestinal hemangiomatous lesions are more frequently found in the rectum and distal colon than in the proximal colon[6]. Moreover, the number of lesions may increase with age[7]. In our patient, there were widespread lesions in the colon, stomach, and duodenum. The intestinal lesions were not biopsied because of the risk of severe bleeding.

Patients usually present with iron-deficiency anemia which is due to chronic blood loss from the gastrointestinal tract, as in our case. As in our patient, most cases of BRBNS do not have a positive family history[7]. Associated orthopedic abnormalities have been described in 14 patients[8]. Two patients with BRBNS presented with ophthalmologic manifestations[2,9]. Our patient is unique because he had vascular and ureteral abnormalities. Whether this is a coincidental association can only be made clear by performing angiographic studies more frequently in these patients.

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The Turkish Journal of Pediatrics 35: 135-140, 1993

UNUSUAL APPEARANCE OF THE LIVER ON ULTRASONOGRAPHY AND COMPUTED TOMOGRAPHY IN A PATIENT WITH CYSTIC FIBROSIS*

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SUMMARY: Men S, Yüce A, Özmen M, Akhan O, Kale G. (Departments of Radiology and Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey). Unusual appearance of the liver on ultrasonography and computed tomography in a patient with cystic fibrosis. Turk J Pediatr 35: 135-140, 1993.

A seven-year-old boy with cystic fibrosis (CS) who presented with abdominal pain is reported. Ultrasonographic and computed tomographic studies of the upper abdomen revealed unusual liver findings. An ultrasound scan showed a liver that was exceedingly heterogenous and a mixed echo pattern with dominant hyperechogenicity. Computed tomography showed large, multiple hypodense cyst-like lesions in the liver. Using the ultrasound scan as a guide, a needle biopsy was performed. The pathological findings were in accord with the findings obtained from ultrasonography and computed tomography, and were consistent with pathological findings seen in CS cases. *Key words: cystic fibrosis, ultrasound, computed tomography.*

Cystic fibrosis (CS) is a complex hereditary disorder, and the most common lethal autosomal recessive disease of the Caucasian population. Defective ionic transport across epithelial surfaces appears to be the major pathogenic mechanism and is responsible for a wide and variable group of clinical manifestations and complications. In addition to abnormalities of salivary and sweat gland secretion and bronchogenic and pancreatic dysfunction, CF frequently involves the liver. The exact incidence is difficult to determine since most studies have employed different methods to detect hepatic involvement and have investigated different age groups. More recently, ultrasonography (US) has been used to assess parenchymal abnormalities, the incidence of abnormal scans ranging from 23 to 60 percent, depending on the age of group studied. All these studies showed that the incidence of liver involvement increases with age[1,2]. The

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prevalence of frank biliary cirrhosis is probably five percent[3]. We present striking US and computed tomography (CT) findings in a CS patient with hepatic involvement.

Case Report

A seven-year-old boy with CF diagnosed at one year of age, was admitted to Hacettepe Children's Hospital for evaluation of abdominal pain. A diagnosis of CF had been established because the child had pulmonary infection, malabsorption and an elevated sweat chloride level (60, 80 mEq/L). He has been receiving pancreatic enzyme and fat-soluble vitamins. On this admission his height and weight measurements were below the 3rd percentile. Hepatomegaly was noted (three cm below the right costal margin and seven cm below the xiphoid).

Laboratory tests which included peripheral blood counts, liver function tests and prothrombin and partial thromboplastin times were within normal limits.

Abdominal ultrasound findings showed that the liver parenchyma was exceedingly heterogenous and had a nodular appearance. A mixed echo pattern with prominent hyperechogenicity, especially in the periportal areas, was observed. The liver was diffusely enlarged and the contours were irregular. The gall bladder was normal and the pancreas could not be visualized because of bowel gas which is a particular problem of patients with CF. The vertical length of the spleen was 107 mm and estimated to be at the upper limit (Figs. 1a,b). An abdominal CT scan showed hepatomegaly and multiple lobulated cyst-like lesions within the liver parenchyma which were several centimeters in size (Figs. 2a,b).

The attenuation values of −7, −8 and -14 Hounsfeld units (HU) were obtained after measuring the centers of the lesions and they were consistent with the HU values of fat. Relatively hyperdense thin septa separated the hypodense lesions from each other. Intra and extrahepatic bile ducts were normal on calibration. The pancreas was replaced by fat. The US scan and CT findings revealed cyst-like lesions which were considered to be fatty infiltration of the liver parenchyma surrounded by thin bands of fibrosis.

A needle biopsy of the liver was performed using a 17 gauge Menghini needle and guided by the ultrasound scans. A pathological examination of the specimen exhibited extensive fatty infiltration in the hepatocytes, periportal fibrosis, bile duct proliferation with mucinous bile plugging in the lumen and pericholangitis consistent with the liver pathology of CF.

Discussion

Exocrine gland dysfunction occurs in patients with CF which is characterized by abnormal secretions from the mucous glands. Although organ involvement in CF

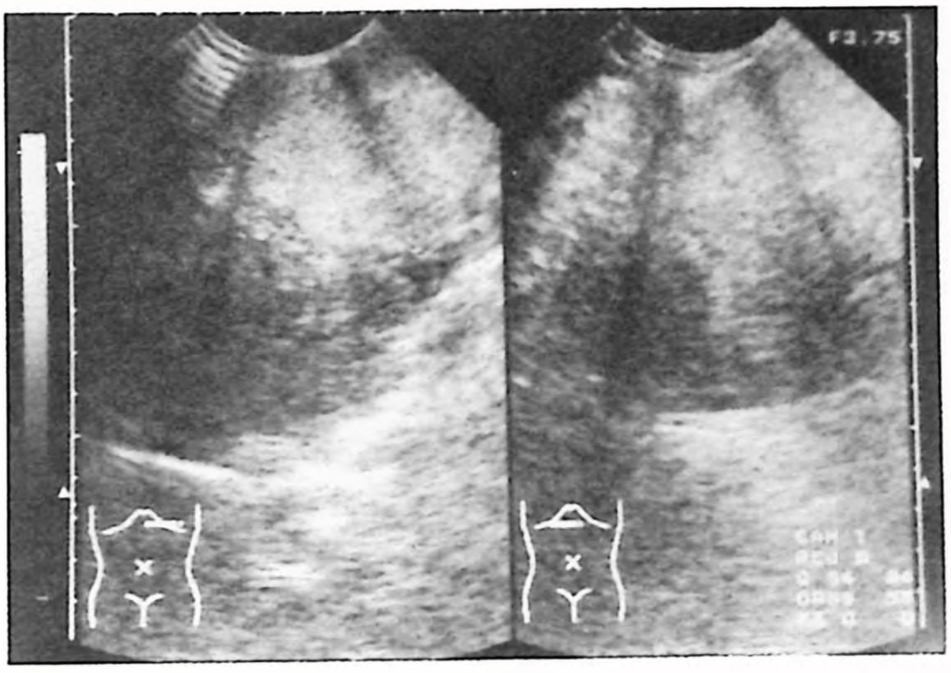

Fig. 1a

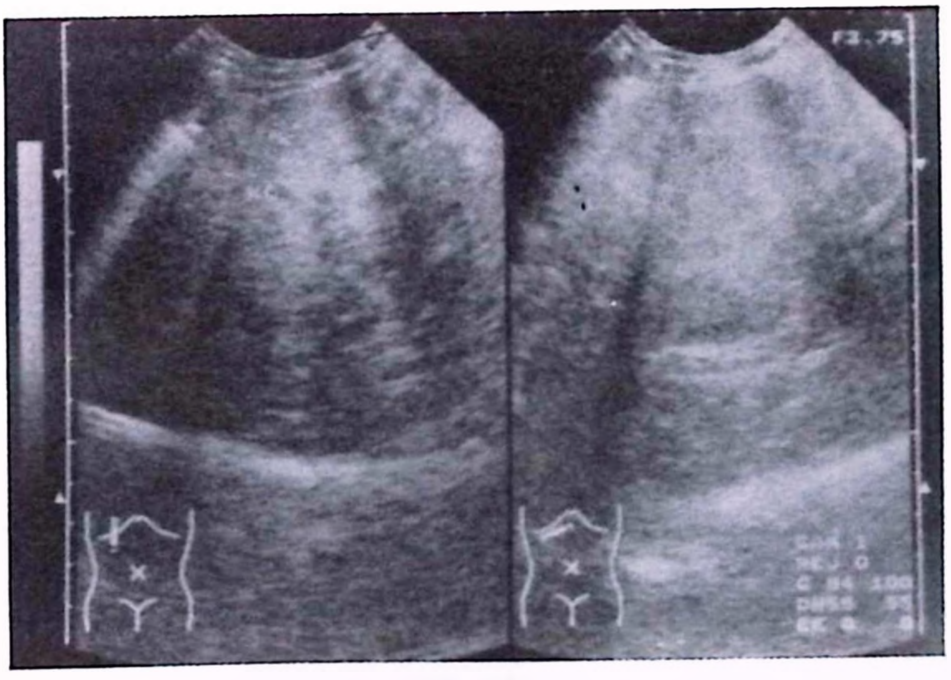

Fig. 1b

Figs. 1a, 1b: Subcostal axial and saggital sections show increased echogenicity throughout the liver parenchyma and a heterogenous echo pattern with nodularity.

varies, hepatic involvement tends to increase with age. The presence of CF-related liver disease has been ascribed to obstruction of bile ductules with inspissated mucus, and the development of progressive cholangitis, periportal fibrosis and biliary cirrhosis[2].

The clinical and pathological spectrum of hepatic disease is reflected in a wide range of sonographic findings. Some patients have normal hepatic sonograms,

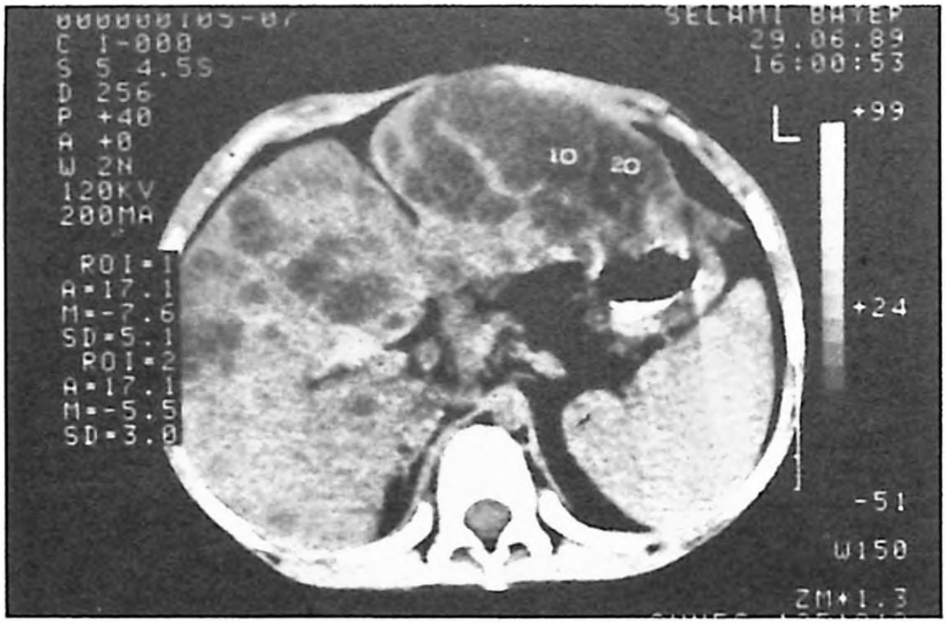

Fig. 2a

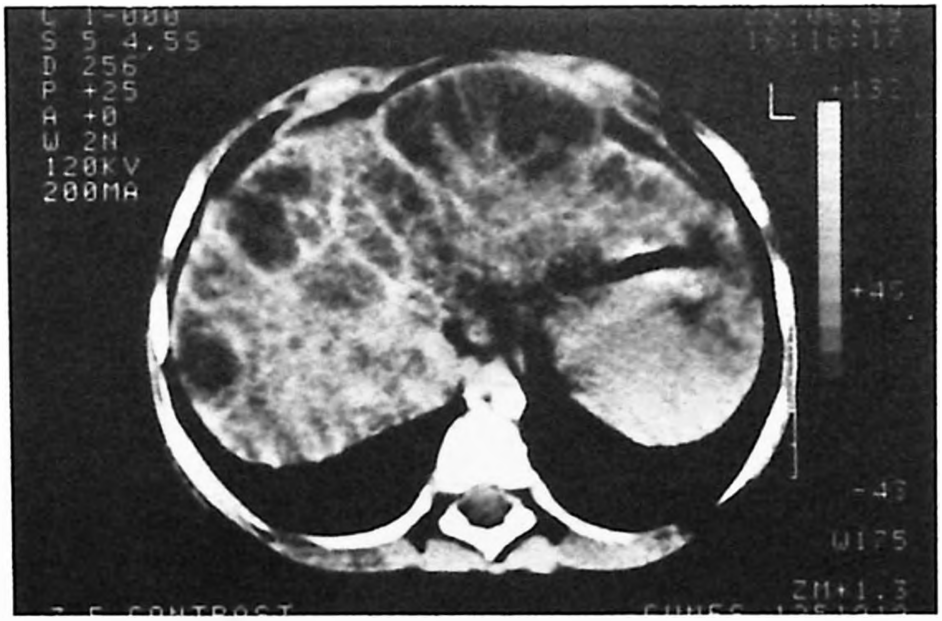

Fig. 2b

Figs. 2a, b: In the pre and post-contrast enhanced scans of the upper abdomen, multiple lobulated cyst-like lesions several centimeters in size and separated from each other by thin septa are seen. Note that there is no contrast enhancement within the lesions after administration of intravenous contrast material.

while others have irregular areas of increased echogenicity or alternating echogenicity and anechoicity and still others have rather prominent periportal echogenicity that corresponds to proliferation of bile ducts with or without biliary stasis, inflammatory changes, edema, fibrosis or a combination of these[1,4,5]. Fatty infiltration of the liver is clearly demonstrated on computed tomography. The entire liver may show decreased density with bright portal venous areas.

However patchy infiltration of the liver may also be detected. Cyst-like changes represent the areas of fatty infiltration surrounded by fibrosis[3,6].

The CT scans of our patient revealed large, hypodense cyst-like lesions several centimeters in size in the liver, which simulated space-occupying lesions, while the sonograms showed a liver with a heterogenous multinodulary appearance. To our knowledge, this is the first time such striking findings have been reported in a CF patient.

The lesions in our case mimic space-occupying lesions of the liver such as hepatocellular carcinoma, hepatoblastoma, multiple metastatic nodules, multiple abscesses, and polycystic disease of the liver.

The sonograms and CT scans did not demonstrate distortions or narrowing of the veins in the vicinity of the lesions in the liver as seen in hepatoblastoma, hepatocellular carcinoma or metastatic nodules[7]. In addition, the configuration of the cyst-like lesions observed in the liver of our patient was not consistent with the description of the cysts typical of polycystic disease[7,8].

Multiple liver abscesses may also mimic hepatic involvement of CF. On the CT scans of our patient there were thin linear bands surrounding the hypodense lesions which did not show the contrast enhancement expected in liver abscess[8], and, therefore, were considered to be thin bands of fibrosis rather than granulation tissue.

The US and CT findings of our patient were consistent with the findings obtained following the pathological examination of the biopsy specimen. Extensive fatty infiltration in the hepatocytes was considered to be responsible for the increased echogenicity in the nodular lesions seen on US scans. We believed that the periportal fibrosis, cholangiolar proliferation, mucoid material in the bile ducts and cholangitis demonstrated on the pathological examination accounted for the increased periportal echogenicity on the US scans, and we assumed that the thin hyperdense septa surrounding and infiltrating the hypodense lesions on the CT scans represented thin bands of fibrosis.

In conclusion, we hope that CT and US findings in this patient may aid the radiologist in becoming more familiar with the various radiological patterns of liver involvement in CF patients.

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The Turkish Journal of Pediatrics 35: 141-144, 1993

UNUSUAL NEUROLOGIC COMPLICATIONS OF TYPHOID FEVER (APHASIA, MONONEURITIS MULTIPLEX, AND GUILLAIN-BARRÉ SYNDROME): A REPORT OF TWO CASES*

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SUMMARY: Özen H, Cemeroğlu P, Ecevit Z, Seçmeer G, Kanra G. (Pediatric Infectious Diseases Unit, Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey). Unusual neurologic complications of typhoid fever (aphasia, mononeuritis multiplex, and Guillain- Barré syndrome): a report of two cases. Turk J Pediatr 35: 141-144, 1993.

Although typhoid fever can frequently lead to such neurological manifestations as confusion, delirium, and encephalopathy, Guillain-Barré syndrome, aphasia and mononeuritis multiplex occur very rarely. In this report, we describe two patients with typhoid fever who developed these unusual complications. *Key words: typhoid fever, aphasia, Guillain-Barré syndrome, mononeuritis multiplex.*

Neurological complications are seen in 5-35 percent of patients with typhoid fever[1]. Frequent signs and symptoms include confusion, delirium, convulsions, and meningism, which mostly result from encephalitis and/or encephalopathy. However, aphasia, peripheral neuropathy and Guillain-Barré syndrome are rarely seen, especially as complications of typhoid fever[1-7] in children. We present two patients with typhoid fever, one who developed aphasia and mononeuritis multiplex and the other, ataxia and Guillain-Barré syndrome.

Case Reports

Case 1

A thirteen-year-old boy was admitted to the Hacettepe University Children's Hospital because he had difficulty in walking and talking. He had a 15-day history of malaise, fever, headache, and somnolence and a seven-day history of progressive speech impairment resulting in aphasia. He also had progressive weakness of the extremites and was unable to walk unaided for the last three days prior to admission.

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Physical examination revealed a well developed child with normal vital signs. Neurological examination disclosed a conscious well-oriented child. Deep tendon reflexes were reduced in all extremities. The patient suffered a 60 percent loss of muscle strength in the lower extremities and a 20 percent loss in the upper extremities. He developed motor aphasia. All other physical findings were within normal limits.

Laboratory studies revealed a hemoglobin of 11.65 g/dl, white blood cell count 5000/mm^3, with a differential count of 2% band forms, 56% polymorphonuclear leukocytes (PMNL), and 42% lymphocytes. Erythrocyte sedimentation rate was 85 mm/hr. SGOT was 80 IU/L, SGPT 61 IU/L, alkaline phosphatase 132 IU/L, ammonia 248 μg/dl (normal = 20-120 μg/dl), HBsAg (−), anti-HBs antibody (−), LE cell (−), C3 170 mg/dl (normal = 60-120 mg/dl), C4 36 mg/dl (normal = 20-40 mg/dl), and ANA (−). The lumbar puncture revealed 7 PMNL/mm^3. Protein content was 48 mg/dl, glucose 80 mg/dl and viral and bacterial cultures were negative.

Cranial CT, visual and auditory evoked potentials were normal. An EEG disclosed moderately severe irregularity in bioelectrical activity, especially in the left hemisphere. Electromyographic examination was consistent with mononeuritis multiplex.

Salmonella group D "O" antigen was positive in 1/320 titer, and Salmonella group B, H and O antigens in 1/320 titer.

A rapid recovery of the patient was noted after the administration of oral trimethoprim sulfamethoxasole. On the tenth day of therapy, the patient was able to walk unaided and spoke clearly. He was discharged on the 13th day of hospitalization.

Case 2

A nine-year-old boy was admitted to the Hacettepe University Children's Hospital because he had difficulty in walking. He had a 40-day history of fever, headache, arthralgia, nausea, vomiting, and anorexia and an 18-day history of diplopia and weakness of the legs which spread to the arms. Deep tendon reflexes in the lower extremities could not be elicited. Ten days later, the weakness of the extremities and the diplopia diminished, but the patient still had difficulty in walking.

Physical examination revealed an axillary temperature of 36.5 °C, pulse rate 96/min. and respiratory rate 22/min. His general condition was satisfactory. Neurological examination disclosed a child who was conscious and who had no sensory or motor dysfunction. The cranial nerves were intact, deep tendon reflexes were normoactive and cerebellar tests revealed normal results except for an ataxic gate. The results of the funduscopic examination were within normal limits.

Laboratory studies revealed hemoglobin 12 g/dl and white blood cell count 6800/mm^3. Examination of the peripheral blood smear revealed 66 percent neutrophils, 2% eosinophils, and 32% lymphocytes. The urine analysis, and liver and kidney function tests were all within normal limits. Lumbar puncture revealed no white blood cells, protein was 120 mg/dl, glucose 63 mg/dl, and simultaneous blood glucose 106 mg/dl. Group D salmonella was isolated from the stool culture. Results of serologic tests showed Salmonella group D "H" and "O" antigens positive at 1/160 titer.

Electromyography revealed impeded nerve conduction velocity consistent with Guillain-Barré syndrome. The cranial CT was normal.

Ampicillin was administered intravenously. The patient recovered completely and was discharged.

Discussion

From five to thirty-five percent of typhoid fever cases present with neuropsychiatric manifestations such as peripheral neuritis, facial palsy, aphasia, intracerebral bleeding, encephalopathy, meningitis, meningismus, delirium, coma, hemiplegia, convulsions, parkinsonism, schizophrenia, ataxia or Guillain-Barré syndrome[1-4]. Among the neurological findings, meningismus, convulsions, confusion and delirium are quite frequent, while mononeuritis multiplex, aphasia and Guillain-Barré syndrome are rarely seen[1-7].

An evaluation of 959 patients with typhoid fever in Nigeria in 1972[2] revealed that 57% developed delirium, 5% meningism, 0.2% meningitis, 1% parkinsonism, 0.7% sensorimotor neuropathy without albuminocytologic dissociation, 1.7% convulsions, 0.3% mononeuritis multiplex, 2.6% were in a semicoma, and 1% were in a coma.

In 1968, Scragg and associates[3] showed that out of 316 patients with typhoid fever, nine (2.8%) had aphasia and that only one also had hemiplegia. All patients recovered completely within eight weeks. The etiopathogenesis of aphasia in typhoid fever is still unclear, but it is thought to be caused by Salmonella encephalitis.

Although it was not possible to isolate salmonella in the cultures obtained from Case 1, clinical presentation, history and the serologic tests were consistent with typhoid fever[8]. The fact that the patient recovered shortly after the initiation of antibiotic therapy supports the hypothesis that aphasia and mononeuritis multiplex most likely resulted from typhoid fever.

Peripheral neuritis in typhoid fever may be manifested as sensory motor peripheral neuritis, mononeuritis multiplex or Guillain-Barré syndrome[1].
Isolated cerebellar ataxia in typhoid fever is the second most common

neurological symptom after delirium. In 1985, Wadia and associates[4] demonstrated that in 718 patients with typhoid fever, the incidence of neurologic disturbance was 5 percent and that about 50 percent of them (2.3% of the total) had cerebellar ataxia. The cerebellar ataxia was mostly an isolated entity which abated within a mean of 9.4 days and a maximum of six weeks.

In Case 2, in addition to the albuminocytologic dissociation in CSF, the history, physical findings and electromyographic findings were also consistent with Guillain-Barré syndrome. The patient developed ataxia, but had no other finding of cerebellar dysfunction. Group D Salmonella was isolated in the stool culture, and antibody titers were found to be high in the serum. This patient also made a complete recovery in a short time following intravenous ampicillin treatment.

It should be emphasized that the classical findings of typhoid fever encountered in adults may not be observed in children. The child with typhoid fever may be afebrile and present only with aphasia, ataxia, Guillan-Barré syndrome, mononeuritis multiplex, schizophrenia, or parkinsonism. Thus, if a patient has unexplained neurological findings, salmonellosis should definitely be suspected.

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The Turkish Journal of Pediatrics 35: 145-150, 1993

SUBEPENDYMAL GIANT CELL ASTROCYTOMAS IN TUBEROUS SCLEROSIS*

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*A. Fahir Özer MD******, *Canan Erzen MD*******

SUMMARY: Özek MM, Özek E, Pamir MN, Özer AF, Erzen C. (Departments of Neurosurgery and Pediatrics, Marmara University Faculty of Medicine, Istanbul, Turkey). Subependymal giant cell astrocytomas in tuberous sclerosis. Turk J Pediatr 35: 145-150, 1993.

Two cases of tuberous sclerosis with subependymal giant cell astrocytoma are presented. This rare autosomal dominant disorder was also detected in family members of the patients who had never had any symptoms of cerebral involvement. Both patients underwent surgery because of signs of increased intracranial pressure.
Key words: tuberous sclerosis, subependymal giant cell astrocytoma.

Tuberous sclerosis (TS) is a neurocutaneous disorder inherited as an autosomal dominant trait which affects various organ systems with different clinical manifestations. The estimated incidence figure is 1 in 30,000[1].

It is well known that subependymal tumors in the periventricular region, termed subependymal giant cell astrocytomas, may occur in TS. These tumors have a definite appearance, with predominantly elongated astrocytes and giant cells[2]. Although they are histopathologically benign lesions, they can appear after the acute onset of hydrocephalus and increased intracranial pressure. Therefore, early detection of a subependymal giant cell astrocytoma (SGCA) is of clinical importance in a TS patient and computed tomography (CT) screening of first degree relatives of these patients is advised.

Case Reports

Case 1

A 12-year-old boy, who was right-handed and had normal mental development, first experienced generalized seizures at the age of eight. A diagnosis of TS was

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then established. The patient, the product of a normal delivery, had a normal gestational and perinatal history. His parents were not related, but his 35-year-old father, who was mentally retarded, had intractable seizures. The neurological examination was unremarkable except for ash-leaf spots, adenoma sebaceum and bilateral papilledema. A CT scan revealed an intraventricular mass, with mild enhancement, arising from septum pellucidum which obstructed both foramen of Monro. Both lateral ventricles were dilated and severe periventricular edema was present (Fig. 1a).

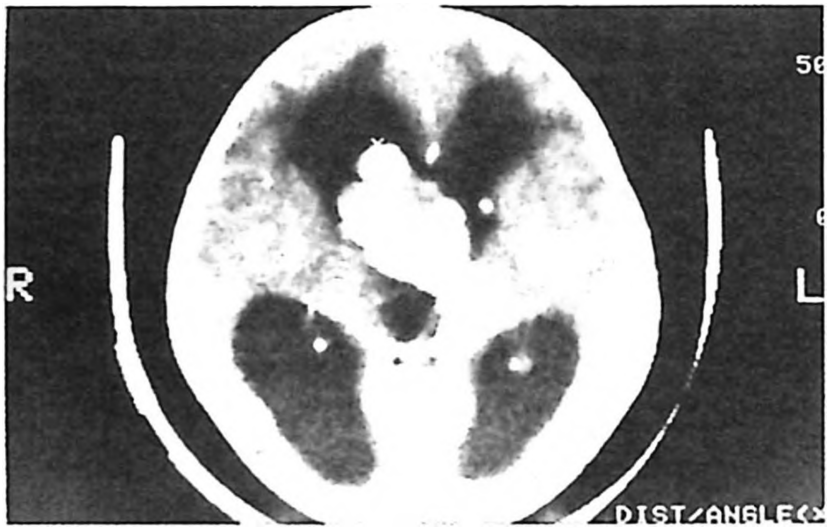


Fig. 1a: Intraventricular mass obstructing both foramen of Monro resulting in hydrocephalus.

The tumor, with the exception of a small part infiltrating the mesencephalon, was removed using the transcortical, transventricular approach. Histopathological examination revealed giant astrocytes as the predominant cell type and pyramid-shaped cells with short, stubby processes. There were no mitotic figures

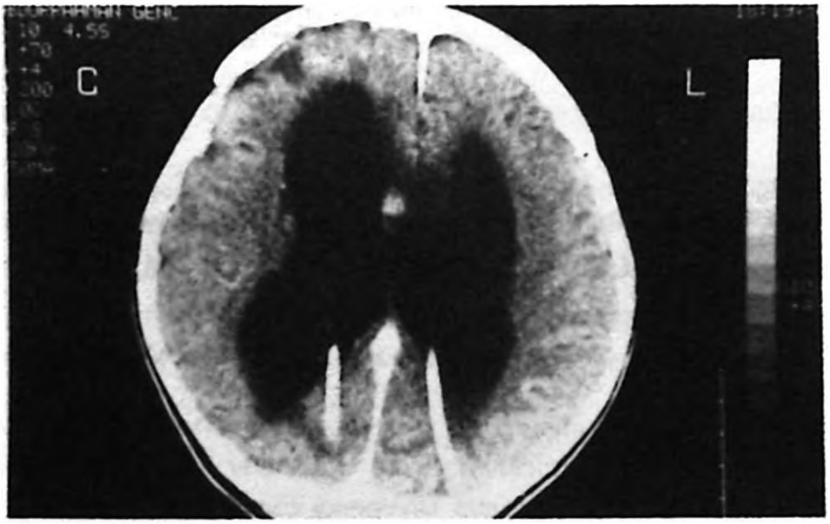


Fig. 1b: Postoperative CT scan demonstrating a residual intraventricular mass and the inserted shunt system into both lateral ventricles.

or anaplastic changes. The tumor was diagnosed as a subependymal giant cell astrocytoma. The postoperative course was uneventful, and the patient's seizures were completely controlled with medical therapy. Because of the subtotal excision of the tumor and the presence of hydrocephalus, a biventriculoperitoneal shunt was inserted two months after the first operation. A CT revealed a small residual tumor which had decreased in ventricular size (Fig. 1b). The 35-year-old father of this patient was also examined by CT scanning which showed multiple areas of periventricular calcification (Fig. 2). The patient's 3-year-old sibling also had areas of periventricular calcification, though he had never experienced any symptoms of cerebral involvement associated with TS (Figs. 3,4).

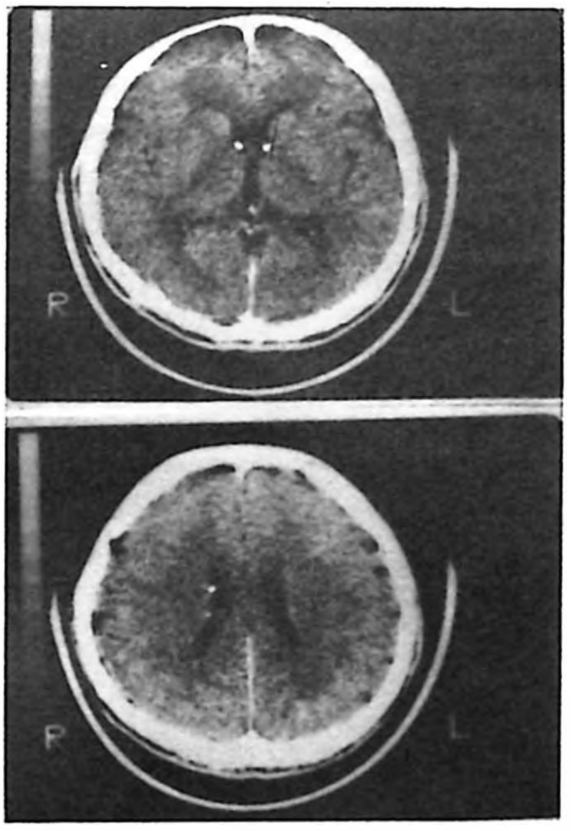


Fig. 2: Multiple areas of periventricular calcification in the 35-year-old father.

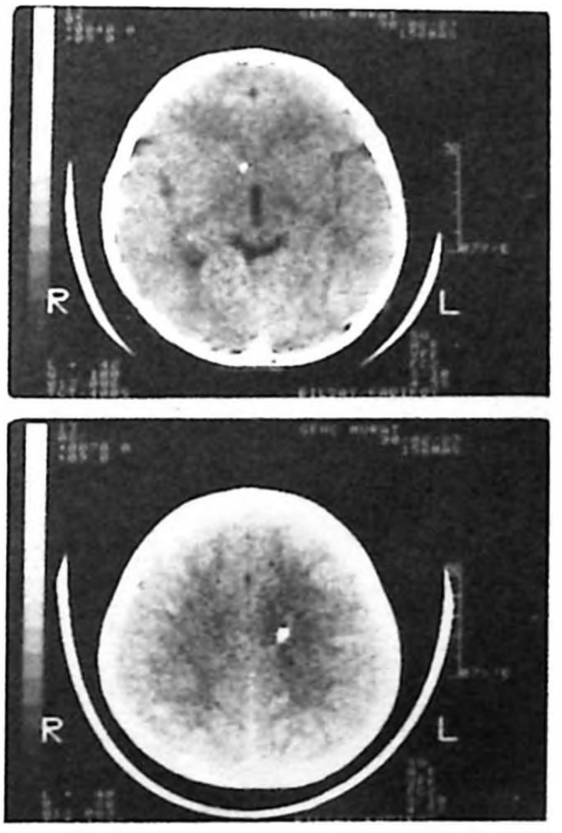


Fig. 3: Two areas of periventricular calcification in the 3-year-old brother.

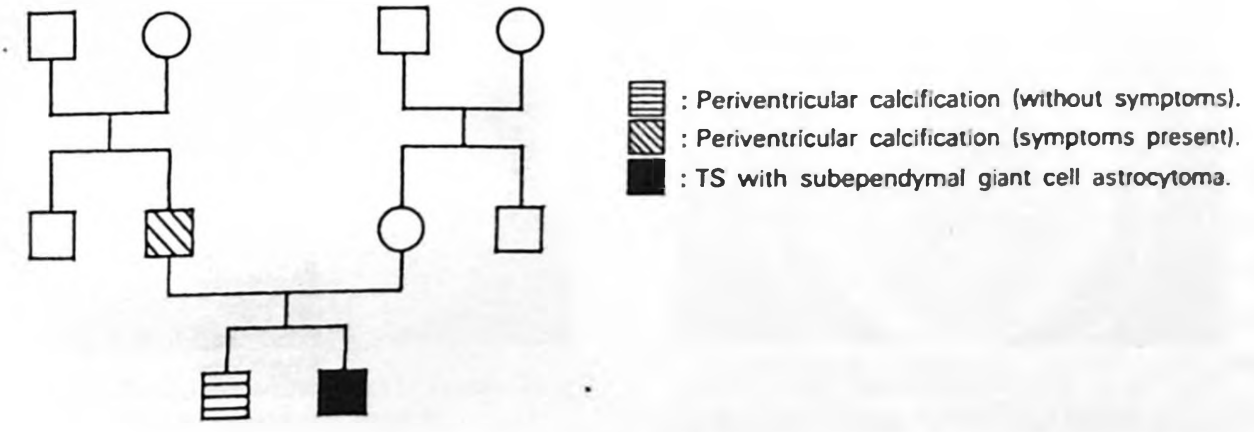
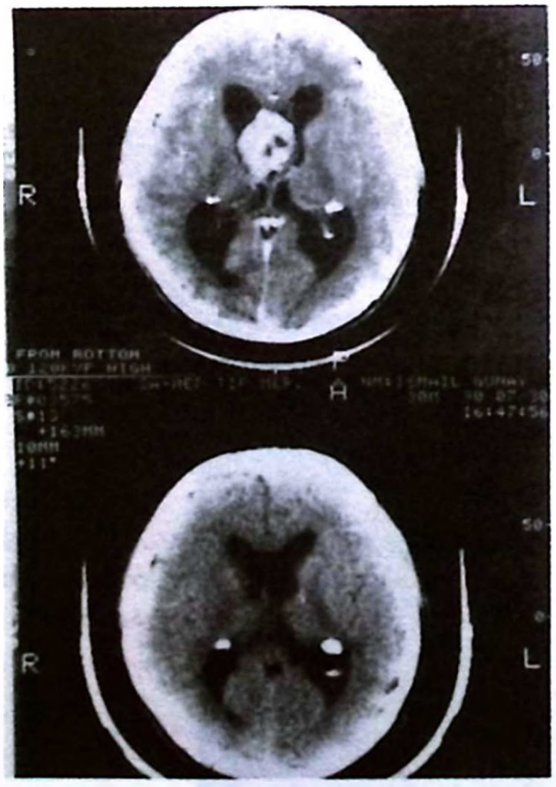


Fig. 4: Pedigree of first case.

Case 2

A 30-year-old right-handed male was admitted to our clinic for evaluation of a two-month history of severe headache. A physical examination revealed ash-leaf spots on the skin, while a neurological examination demonstrated bilateral papilledema and visual-field defects. A CT scan showed areas of multiple periventricular calcification and a mass located in the region of the right foramen of Monro (Fig. 5a).

The patient underwent surgery in which the interhemispheric transcallosal approach was used. After reaching the right lateral ventricle, the tumor was totally extirpated and the CSF pathways were reopened. Histopathological examination revealed astrocytes, with extensive homogenous, eosinophilic cytoplasm. The nuclei were eccentrically located, vesiculated and occupied by large nucleoli. There were irregular vascular spaces and calcification. The postoperative course was uneventful. A CT scan taken four months after showed no evidence of the primary tumor. The areas of periventricular calcification remained the same in size (Fig. 5b). The CT scan of the patient's father, who has experienced generalized seizures, disclosed periventricular areas of calcification. An examination of the patient's one-year-old son, who was symptom-free, also revealed multiple areas of periventricular calcification (Fig. 6).



Figs. 5a,b: An intraventricular mass arising from the right side of the septum pellucidum. Appearance after total removal of tumor.

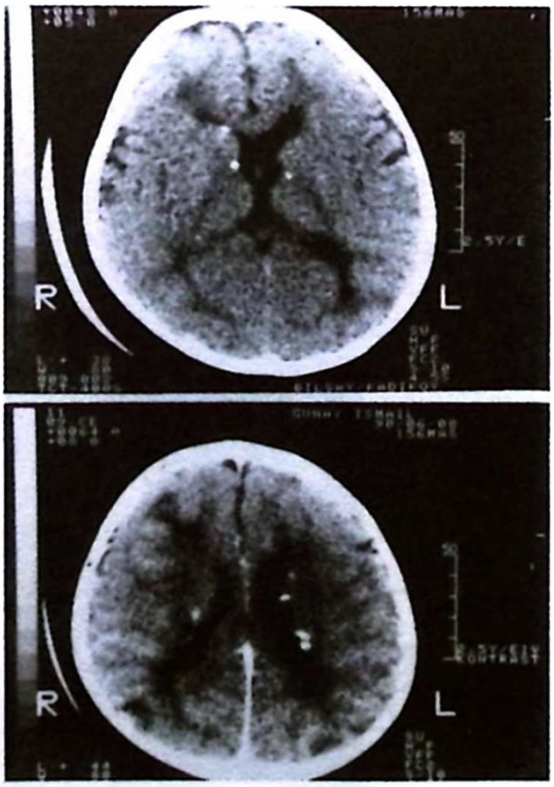


Fig. 6: Areas of periventricular calcification in the child of the second case.

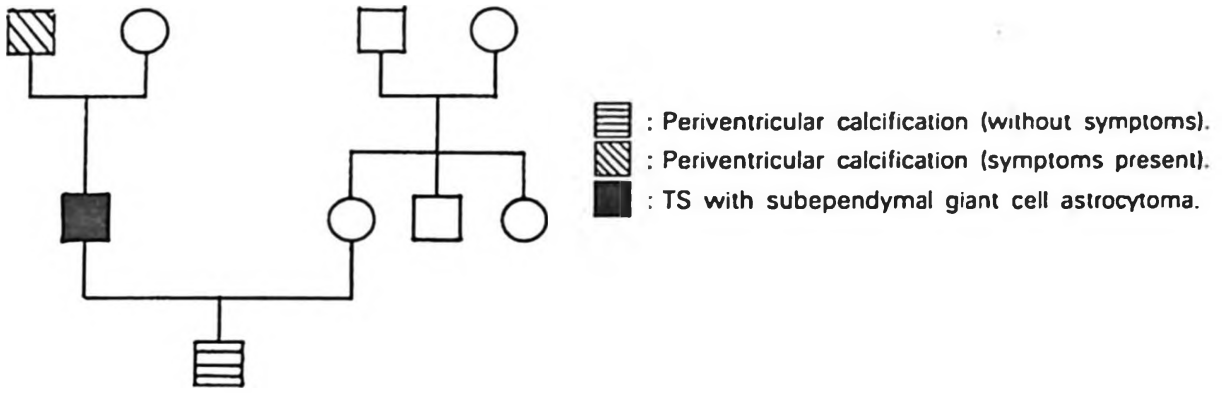


Fig. 7: Pedigree of second case.

Discussion

TS, which was first reported by Von Recklinghausen in 1862, commonly presents with features of Vogt's triad such as seizures, mental retardation and facial adenoma sebaceum[1]. Later it was discovered that the inherited gene in TS is located on chromosome 9. Two different loci for TS genes have been described, but no phenotypic distinction has been recognized in subjects studied[3,4]. Seizures are the most common symptom and may appear anytime after birth. Infantile spasms are particularly common in affected infants[1]. More than 25 percent of patients with infantile spasms will later develop signs of TS[5]. In our report, Case 1 and the father of Case 2 had generalized seizures, but not in the form of infantile spasms.

Mental function varies greatly among TS patients. Although mental retardation is a characteristic feature of the disease, about 33 percent of patients diagnosed by other clinical signs have normal intelligence[4]. Our patients had a normal intelligence quotient.

Some reported cases are close relatives of TS patients who have never experienced symptoms of cerebral involvement, although they have at least one of the pathognomonic hamartomas[3]. This finding is consistent with the relatives of our cases. Therefore, in order to ascertain whether an individual has TS, it is necessary to screen first-degree relatives, as we did. Until recently, a majority of TS cases were diagnosed by skin lesions.

Nowadays, more emphasis is placed on findings, elicited by organ imaging[2,4]. The presence of subependymal nodules in the lateral ventricles, cortical tubers and areas of calcification in the periventricular region, indicate cranial involvement[6]. Computed tomography has become an indispensable method for identifying intracranial pathology in TS, but magnetic resonance imaging, which has only recently been used to study TS patients, demonstrates subependymal nodules with greater clarity than does CT scanning[3,7,8].

Although the incidence of intracranial calcification increases with age, SGCA's are relatively rare. In a 60-patient series, diagnosed as having TS clinically and by CT scans, Maki et al[7] found only one patient with neoplastic changes. Since this entity has been interpreted as being between a neoplasm and a heterotopia, there is some disagreement regarding therapy[9,10]. SGCA's do not appear to be highly sensitive to radiation therapy, and have not been reported as highly invasive tumors in any of the published series[3]. Walker et al[11] considered that the only indication for surgery were signs and symptoms caused by the mass, such as increased intracranial pressure or hydrocephalus. We are also of the opinion that if these conditions are present, then surgical intervention is indicated.

It is well known, that SGCA's grow into the ventricular cavity, and often reach enormous sizes contributing to the high operative morbidity and mortality[3]. Since the total removal of a SGCA indicates a total cure, the importance of early detection of these tumors by screening techniques should be emphasized.

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The Turkish Journal of Pediatrics 35: 151-153, 1993

MEGALOURETHRA ASSOCIATED WITH PRUNE-BELLY SYNDROME*

*Ali Gökalp MD***, *E. Yener Gültekin MD****

SUMMARY: Gökalp A, Gültekin EY. (Department of Urology, Cumhuriyet University Faculty of Medicine, Sivas, Turkey). Megalourethra associated with prune-belly syndrome. Turk J Pediatr 35: 151-153, 1993.

A 14-day-old male infant with megalourethra is presented because of the rarity of the anomaly and its association with prune-belly syndrome. The lax, wrinkled appearance of the abdomen, bilateral cryptorchidism and severe dilatation of the urinary system are features included in the classic triad of the prune-belly syndrome. Our patient had the scaphoid variety of megalourethra since the penis appeared elongated and floppy in the fusiform form. *Key words: megalourethra, prune-belly syndrome, congenital anomaly.*

Megalourethra is a very rare congenital anomaly characterized by dilatation of the penile urethra. It is secondary to absent corpus spongiosum. In this report, we describe a case of megalourethra associated with prune-belly syndrome[1-5].

Case Report

A 14-day-old male infant was referred to our clinic for evaluation of an abnormally large phallus. A marked ventral bulging of the penis was noted, which increased with voiding. The abdomen was lax and there were several wrinkles on the abdominal wall (Fig. 1). Both kidneys were palpable, the right measuring 10×10 cm in size. The testes were nonpalpable. There was no neurological deficit and examination of the fundus was within normal limits. *E.coli* was isolated from the urine and appropriate antibiotic therapy was initiated. A huge urethra was seen on the urethrogram (Fig. 2). An antegrade cystography was performed by means of a percutaneous tube which demonstrated bilateral vesicoureteral reflux and hydroureteronephrosis with massive ureteral dilatations (Fig. 3). The finding of a lax and wrinkled abdominal wall, bilateral cryptorchidism and dilatation of the urinary collecting system were considered to be the classic triad of the prune belly syndrome. Cutaneous vesicostomy was performed to facilitate emptying of the bladder. Reconstruction of the urethra was scheduled to be performed at the end

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Presented as a poster at the 19th International Congress of Pediatrics, Paris, France, July 23-28, 1989.

of the first year, but the baby was never brought in for a follow-up, and we learned that he had died six months after discharge.

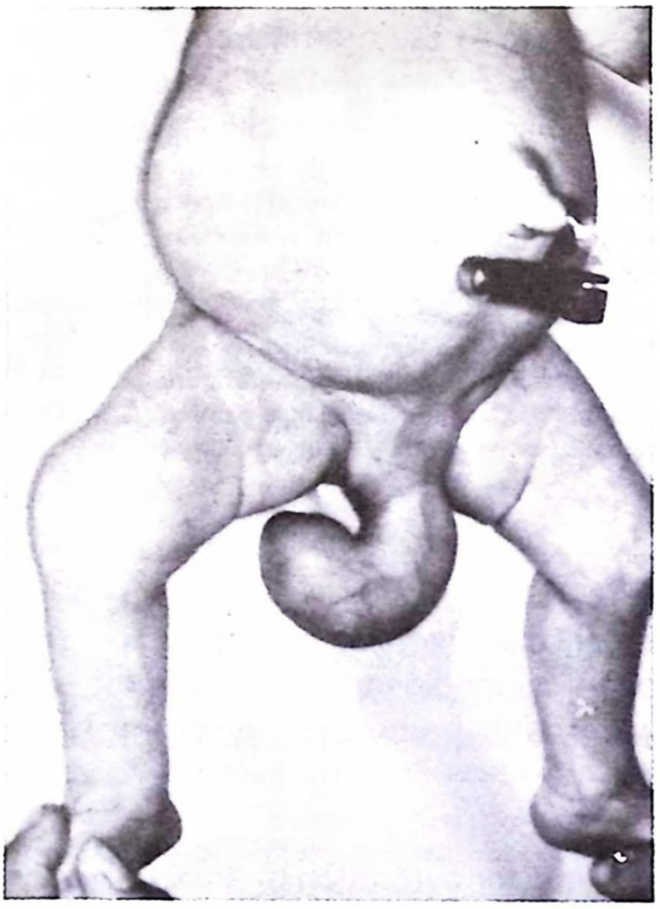

Fig. 1: An abnormally large phallus.

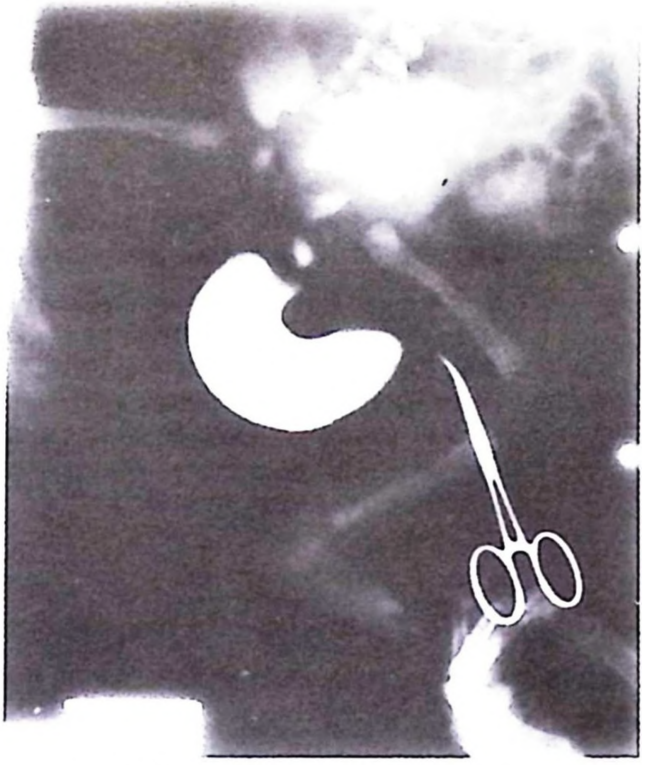

Fig. 2: Retrograde urethrogram.

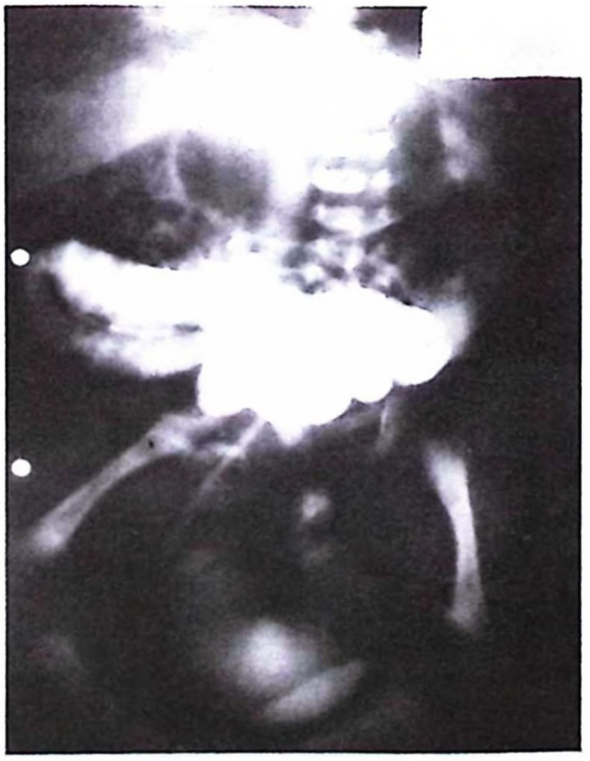

Fig. 3: Antegrade cystography.
Bilateral vesicoureteral reflux, hydroureteronephrosis and antegrade filling of the urethra are seen.

Discussion

Megalourethra is a very rare congenital malformation characterized by dilatation of the penile urethra. Forty-one cases have been reported so far in the literature[1,2,4,5]. The term megalourethra to describe this anomaly was originally suggested by Nesbitt. The etiology of megalourethra is unknown, but it is presumed to result from an arrest in the embryogenesis of the corpus spongiosum at an early stage. In some cases, the corpora cavernosa are affected as well, resulting in their absence or atresia. Therefore, megalourethra has been subdivided into scaphoid and fusiform types. The fusiform variety represents the severest form of this anomaly in which there is a complete absence of the corpora cavernosa and corpus spongiosum. A more commonly encountered form of megalourethra is the scaphoid variety. In this type, there is a loss of the corpus spongiosum over the distal part of the urethra, but the corpora cavernosa are normally developed. It is generally accepted that the scaphoid and fusiform types of megalourethra represent varying degrees of a single disorder rather than two separate entities. Congenital urethral diverticula are not part of this anomaly since they are usually located in the bulbar urethra and cause obstruction. There is no obstruction in megalourethra.

Megalourethra may be associated with prune-belly syndrome since mesenchymal development is defective in both these disorders. The association of megalourethra with upper urinary tract anomalies (such as hydroureteronephrosis, azotemia, cystic displasia) has been reported[3]. This point must be stressed because the status of the upper urinary tract determines the ultimate outcome. This anomaly has also been reported in association with posterior urethral valves, hypospadias and imperforate anus.

Treatment consists of urethroplasty with resection of the excess urethral tissue and reconstruction of the urethra. Prognosis depends mostly on the upper urinary tract status and the severity of the associated anomalies.

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