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Please note the following correction in the text of the Turkish Journal of Pediatrics 31 (2), Page 171. The last paragraph of the "Discussion part" should read:

"Increased vessel fragility is reported in genetic disorders of connective tissue; thus, the absence of increased vessel fragility observed in this particular family distinguishes it from these diseases".

The Turkish Journal of Pediatrics 31:263 - 269, 1989

THE TESTES AFTER UNILATERAL INCARCERATED INGUINAL HERNIA IN PREPUBERTAL RATS*

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Key words: incarcerated inguinal hernia, testicular torsion, contralateral testicular damage

Incarceration of an inguinal hernia is one of the most common reasons for emergency admission of young children[1]. Incarcerated inguinal hernia causes testicular venous obstruction which may result in hemorrhagic infarction[2]. Infarcted testes which are more common than infarcted bowels[1], are followed in frequency by ipsilateral testis atrophies in 10-15 % of children[3]. The other cause for hemorrhagic infarction of testis is testicular torsion[4]. In addition to ipsilateral testicular alterations, unilateral testicular torsion also results in contralateral testicular deterioration and diminished fertility[5,6].

A recent study we conducted also revealed that unilateral incarcerated inguinal hernias cause not only ipsilateral but also contralateral testicular deterioration in adult rats[7]. Although some experimental and clinical studies have falled to reveal the contralateral damage encountered in the prepubertal period[8,9], others have suggested it[4,10-12].

Therefore, we planned this experimental study to evaluate the effect of unilateral incarcerated inguinal hernias on ipsilateral and contralateral testes in prepubertal rats. Following unilateral incarcerated inguinal hernias, the testes are also compared to the contralateral testes of prepubertal rats subjected to unilateral testicular torsion.

Material and Methods

Thirty prepubertal (30-day old) male albino rats of the Hacettepe strain were used for the investigation. They were maintained in the animal facility, five animals to a cage, under controlled temperature and dark-light cycle. The rats had access to water and rat chow ad libitum.

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General anesthesia was administered to the animals by intraperitoneal instillation of pentobarbital. Surgery was performed through identically opened and closed left abdominoscrotal incisions employing the sterile technique. The animals were randomly divided into three groups, each consisting of ten rats. The experimental groups were as follows :

Group 1. Ten animals underwent a sham operation in which the left testis and caecum were exposed and repositioned in their original locations after placing a 4-0 silk suture on the tunica albuginea.

Group 2. Ten animals underwent clockwise 720° left testicular torsion. Torsion was maintained by a 4-0 silk suture passed through the tunica albuginea and the scrotal wall. Detortion of the testes was carried out through the same incisions at 24 hours.

Group 3. Left-sided incarcerated inguinal hernias were produced in ten animals. The caecum was grasped through the inguinal canal which remains open throughout the life of rats[13]. A caecal loop was advanced through the canal down to the scrotum, and a size 8 Nelaton catheter was placed in the canal near the caecal loop. The external inguinal ring was narrowed over the caecum and the catheter by using 4-0 atraumatic silk sutures. The catheter was then carefully removed and the incision closed (Fig. 1). The incarcerated hernias were surgically reduced through the same incisions after 24 hours of incarceration.

The animals were sacrificed after 15 days. Both testes were removed and placed in Bouin's solution. The specimens were embedded in paraffin blocks and the sections were cut and stained with hematoxylin and eosin. The ipsilateral testes, which were subjected to torsion were necrotic and were not evaluated

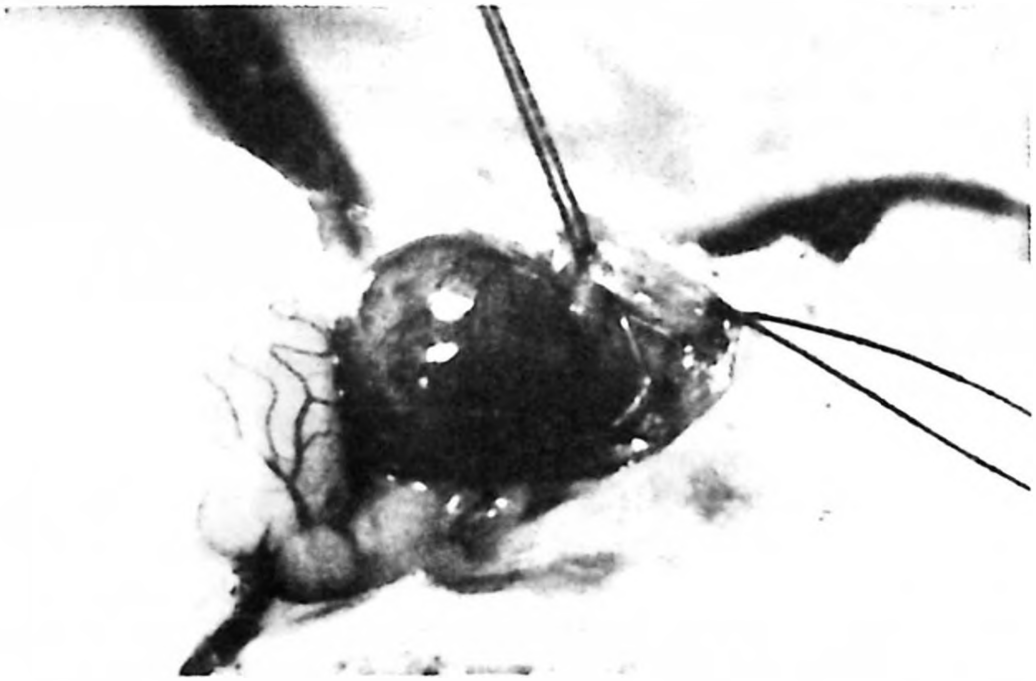

Fig.1- Prepubertal rat with an incarcerated caecal loop.

histologically. The other testicular biopsies were studied blindly and at random by the team's pathologist. Twenty-five of the most circular tubules were identified in each testicular biopsy section, and the diameters were measured with a 10x objective together with a micrometer ocular. The mean seminiferous tubular diameter (MSTD) of each testis was determined in microns. Germinal epithelium maturity was graded using a modified Johnsen testicular biopsy score[14]. By using a 40x objective, the 25 tubules were evaluated, and each tubule was given a score ranging from 1 to 10 according to the criteria shown in Table 1. The mean testicular biopsy score (MTBS) was calculated for each testis.

Statistical comparisons were made between the biopsies from the ipsilateral and contralateral testes of each group of rats using the Mann Whitney-*U*-test, and p values less than 0.05 were considered to be significantly different.

TABLE I: Testicular Biopsy Scores*

Score	Description
10	Complete spermatogenesis with many spermatozoa
9	only a few spermatozoa (5/tubule)
8	No mature spermatozoa, but late spermatids (differentiation to form spermatozoa)
7	Many spermatids without differentiation
6	Only a few spermatids (5/tubule)
5	Many spermatocytes
4	Only a few spermatocytes (5/tubule)
3	Only spermatogonia
2	Sertoli cells without germ cells
1	No cells

* If germinal epithelium is disorganized with sloughing or obliteration of the lumen, a lower score is given.

Results

Two animals in groups one and three died of unknown causes. Nine animals,each in groups 1 and 3, and ten animals in group 2 were available for evaluation at 15 days.

MSTD and MTBS are summarized in Table II. The difference between MSTD of the ipsilateral and contralateral testes was not significant in groups 1 and 3, but the ipsilateral and contralateral testes in group 3 differed significantly compared to the ipsilateral and contralateral testes in group 1.

TABLE II: Summary of Mean Seminiferous Tubular Diameters and Mean Testicular Biopsy Scores in Prepubertal Rats.

Groups	Mean Seminiferous Tubular Diameter (Micron)		Mean Testicular Biopsy Score	
	Right testes	Left testes	Right testes	Left testes
1	206.27±5.19	200.66±2.96	9.36±0.18	8.87±0.13
2	162.70±7.17		6.78±0.55	
3	176.55±5.59	168.22±6.04	7.96±0.44	6.33±0.45

*mean ± Standard deviation.

The differences between MTBS of the ispsilateral and contralateral testes were significant in groups 1 and 3. The MTBS of the ipsilateral and contralateral testes in group 3 also revealed significant differences compared to the ipsilateral and contralateral testes in group 1.

The MSTD and MTBS of the contralateral testes in group 2 differed significantly from the values of the contralateral testes in group 1, but they were not significantly different from the values of the ipsilateral and contralateral testes in group 3 (Figs. 2-4).

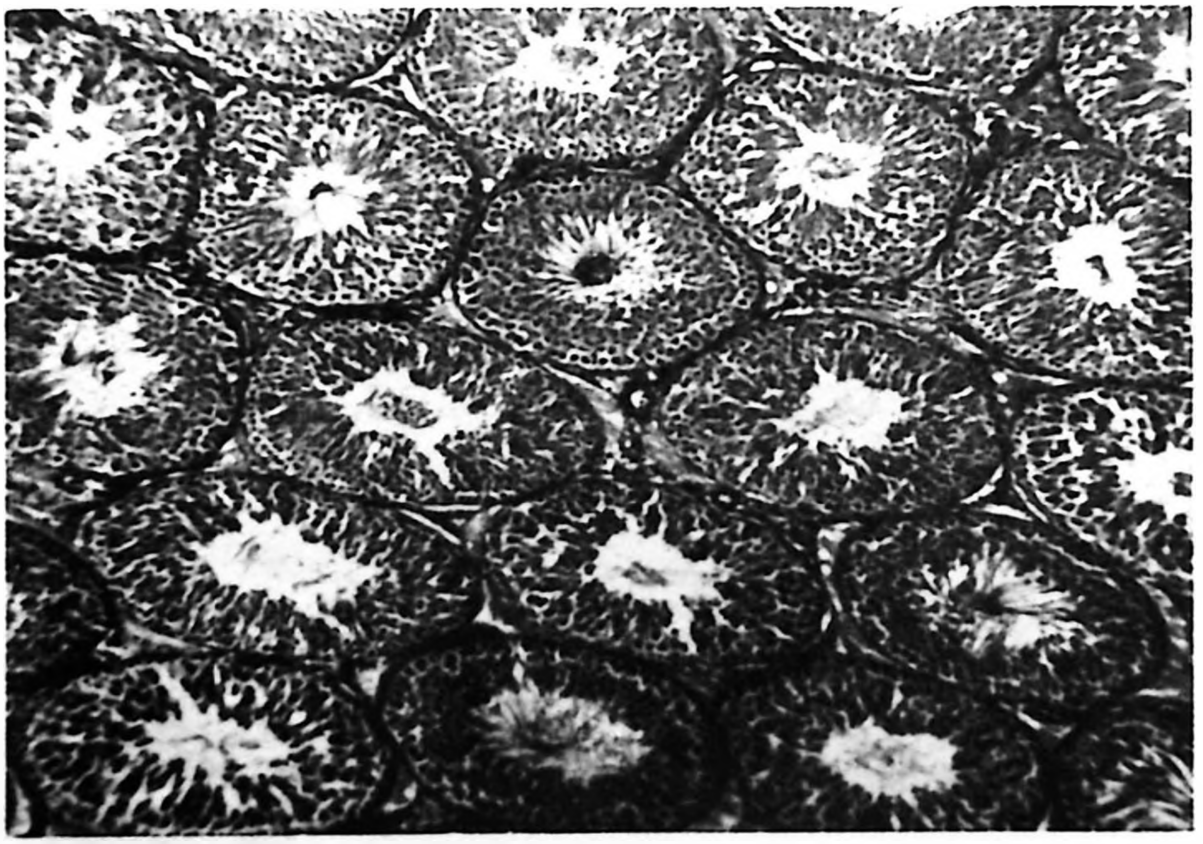

Fig.2- Contralateral testis from contol group demonstrating normal histology (H-E stain x95).

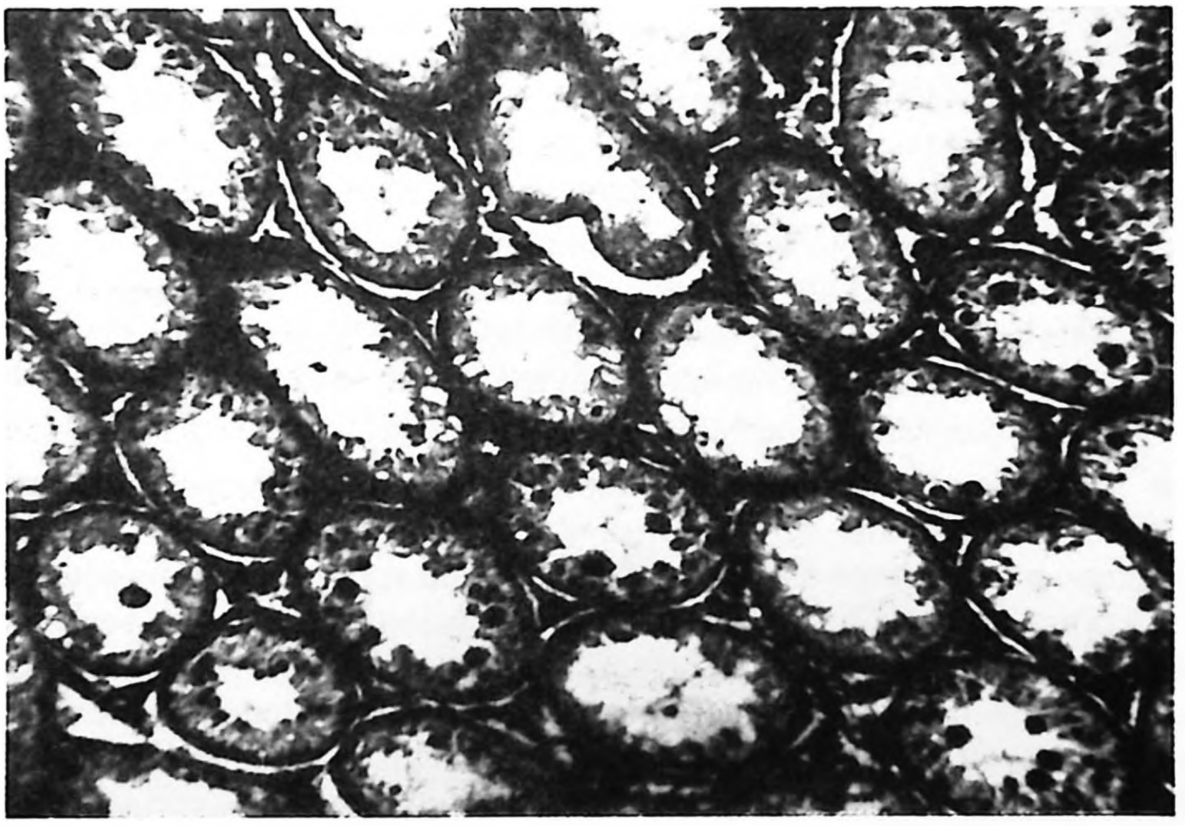

Fig.3- Microscopic appearance of a contralateral testis from torsion-detorsion group (H-E stain x95).

Fig.4- The contralateral testis of a rat from the incarcerated inguinal hernia group (H-E stain x95).

Discussion

Since incarcerated inguinal hernias are commonly seen in prepubertal children[1], we performed the present experiment on sexually immature animals[13]. Although the representativeness of 30-day-old rats as a prepubertal model has been opposed[15], we believe that it resembles the situation of prepubertal children[4].

In experimental studies evaluating the contralateral testicular effects of unilateral testicular torsion, MSTD and the presence or absence of spermatozoa within a seminiferous tubule have been employed[15]. However, the testicular biopsy score has been suggested to be a more reliable method for evaluating the status of a testis[14]. Therefore, MSTD and MTBS have been used for testicular assessment.

Similar to previously reported alterations[16], our sham operation affected the maturity of the germinal epithelium of the ipsilateral testes compared to the contralateral ones, but the MSTD did not differ and spermatogenetic activity was still well preserved. We found that experimentally induced unilateral incarcerated inguinal hernias caused a decrease in MSTD and a depression in MTBS among the ipsilateral testes compared to controls. Although spermatogenetic activity was better in the contralateral testes compared to the ipsilateral testes, contralateral testicular histologic deterioration also accompanied ipsilateral testicular histologic alterations following unilateral incarcerated inguinal hernia. Contralateral testicular alterations, which were expressed in terms of decreased MSTD and depressed MTBS were observed after unilateral testicular torsion. The histologic alterations encountered in the ipsilateral and contralateral testes of the prepubertal rats subjected to unilateral incarcerated inguinal hernia and in the contralateral testes of the prepubertal rats subjected to unilateral testicular torsion were similar to the utilized parameters.

Experimentally induced unilateral incarcerated inguinal hernia results in histologically deteriorated ipsilateral and contralateral testes in prepubertal rats. The effect of unilateral inguinal hernia on subsequent fertility remains to be clarified.

Summary

The ipsilateral and contralateral testes after unilateral incarcerated inguinal hernia were evaluated, and compared to the contralateral testis after unilateral testicular torsion in 30 prepubertal rats. Control, torsion and detorsion at 24 hours, and incarcerated inguinal hernia and reduction in the 24 hour groups, each consisting of ten rats were established. The testes were harvested after 15 days. Mean seminiferous tubular diameters (MSTD) and mean testicular biopsy scores (MTBS) were determined and compared.

A decrease in MSTD and depression in MTBS, which was more prominent in the ipsilateral testes, were found in both ipsilateral and contralateral testes following

unilateral incarcerated inguinal hernia. The testicular damage encountered after unilateral incarcerated inguinal hernia was similar to the contralateral testicular damage following unilateral testicular torsion with the utilized parameters.

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DIGOXIN-LIKE FACTOR IN INFANTS OF DIABETIC MOTHERS NOT RECEIVING DIGOXIN THERAPY*

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Key words: cardiac glycoside, digoxin-like factor, infant of diabetic mother, newborn

Digoxin levels have been detected in the neonatal blood of cases in which neither mother nor baby had received digoxin. This activity has been termed the digoxin-like factor (DLF)[1-4]. It has been reported that DLF levels were found to be higher in the blood of infants born to preeclamptic mothers than in the blood of those born to healthy controls[5,6]. Thus, the clinical utility of DLF measurements in newborn infants might be important. In this report we present data from DLF determinations in infants of diabetic mothers.

Material and Methods

Fifty-nine full term newborns aged less than 48 hours who had been delivered at the Hacettepe University Children's Hospital were enrolled in this study. The gestational ages of the patients ranged between 38-41 weeks. All the babies were delivered normally except for 12 who were born by cesarean section. With the exception of those mothers who had been delivered via cesarean section in which general anesthesia was administered, the infants and mothers did not receive any medication including cardiac glycosides during pregnancy or delivery. There were no Apgar scores less than seven at one and five minutes. All the babies were in good health and there was no evidence of cardiac disease clinically, radiologically or electrocardiographically (ECG). The infants were evaluated and then separated into four groups: healthy-appropriate for gestational age (AGA)-controls (n:25), large-for-gestational age (LGA) babies (n:15), infants of diabetic mothers who were diet-controlled (n:13), and infants of insulin-dependent diabetic mothers (n:6). Four diet controlled mothers and three insulin-dependent mothers had pregestational diabetes for 8.2±2.4 years and

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5.7±2.1 years respectively. One milliliter of blood was taken from the infants to determine the digoxin levels in the first 48 hours of life and analyzed within the same day of collection using a commercial Fluorescence Polarization TDX System (Abbott Laboratories, Diagnostic Division North Chicago, IL 60064) having a sensitivity of 0.2 ng per milliliter.

The results were expressed as mean ± SD and statistical analyses were carried out using Student's *t* test.

Results

The results of this study are summarized in Table I. The serum DLF levels were similar in all the groups. The mean serum DLF levels were 0.33 ± 0.18 ng/m, 0.37±0.09 ng/ml, 0.45±0.32 ng/ml, and 0.43±0.23 ng/ml in the AGA-controls, LGA-controls, infants of diabetic mothers and infants of insulin-dependent diabetic mothers, respectively, ($p>0.05$) There was no correlation between birth weight and serum DLF levels.

TABLE I: Serum Digoxin-Like Factor Levels in Infants of Diabetic Mothers and Controls.

	Control AGA	Control LGA	Infants of diabetic mother	Infants of insulin-dependent diabetic mother
n	25	15	13	6
Male/Female	18/7	10/5	6/7	4/2
Body weight (g)	3233± 385	4217±243	3498±573	3684±806
Digoxin-like factor (ng/ml)	0.33±0.18	0.37±0.09	0.45±0.32	0.43±0.23

Discussion

The digoxin-like factor increases in umbilical vein blood and in the serum of newborn infants for 2-8 days when the DLF levels are inversely correlated to the gestational age[1-4]. Its correlation to birth weight is controversial[1,2]. We did not find a correlation between DLF levels and birth weight in our study.

The fetal adrenals, and probably the placenta, are the most likely sources of DLF. Endogenous DLG may be involved in regulating blood volume and pressure. Digoxin – like factor similar to the cardiac glycosides, increases cardiac contractility, constricts blood vessels and reduces the renal tubular reabsorption of

sodium. The increased blood pressure and reduced sodium absorption results in excretion of the excess volume.[1-4]

The incidence of hypertrophic cardiomyopathy in infants of diabetic mothers is known[7,8], and although it has not been documented this abnormality may affect the DLF of these infants. We excluded this possibility by clinical and laboratory studies. Our aim was to evaluate DLF in infants of diabetic mothers who had no cardiac abnormality prior to the structural changes. However, we did not find any difference in DLF levels of the infants of diabetic mothers and the controls. Our findings may add additional information to the literature regarding DLF in newborns.

Summary

Serum digoxin-like factor was detected in infants of diabetic mothers who were insulin-dependent or diet controlled. No statistical difference was found between the serum digoxin-like factor levels of the infants of diabetic mothers and the controls.

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NIPPLE DEVELOPMENT IN FEMALE PUBERTY*

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Key words: puberty, Tanner breast staging, Tanner pubic hair staging, nipple development

Sexual development scores are used in evaluating the sexual maturation of adolescents. The visual Tanner scoring system evaluates the development of genitalia and pubic hair in males, and breast development and pubic hair development in females[1]. Besides the visual system, an objective criteria, the orchidometer, is used to measure genital development in males[2]. However, at present, there are no objective devices available which can be used to determine breast maturation of girls[3]. To determine the sexual maturation of girls, the five stage classification of breast maturation and pubic hair development is used, but some ambiguity between breast stages 4 and 5 has been found[1-4]. The aim of this study is to determine the characteristics of nipple size in the different sexual stages of girls and to find measurable criteria between the five stages, especially stages 4 and 5.

Material and Methods

Two hundred and thirty girls aged between 11 and 17 years, with no history of endocrinological or severe somatic problems who were seen at the Adolescence Unit of the Hacettepe University Children's Hospital were evaluated. Breast and pubic hair maturation was staged by Tanner's criteria. Masters and Johnson[5] mention that cold, tactile or psychic stimulation may lead to areolar engorgement which may mimic the areolar mound of breast stage 4, and that some changes in the diameter of the base of the nipple may also occur. To circumvent these problems, breast staging was assessed prior to breast palpation. The diameter of the areola and only the plateau portion of the erect nipple were measured by the same observer using a plastic ruler. Nipple diameter was compared to the breast and pubic hair stages and menstrual status. Menstrual status was calculated as the number of months subsequent to menarche by recall. For comparison, their results were categorized into four menstrual age groupings: premenstrural or length of time postmenarche. M(-): premenstrual period; M+1: postmenarche of one year or less; M+2: postmenarche of one-two years; M+3: postmenarche of more than two years.

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Results

Tables I, II and III show the nipple size of adolescent girls with respect to breast size (B), pubic hair (PH), and menstrual (M) status.

Table I: Nipple Diameter Versus Breast Development

Stage	Number of children	Nipple size (mm)±SD
B 1	18	1.80±0.87
B 2	45	4.24±2.18
B 3	59	5.93±2.07
B 4	59	7.10±2.28
B 5	49	8.67±2.70

B 1 vs B 2	$p<0.001$
B 2 vs B 3	$p<0.001$
B 3 vs B 4	$p<0.001$
B 4 vs B 5	$p<0.01$

Table II: Nipple Diameter Versus Pubic Hair Stages

Stage	Number of children	Nipple size (mm)±SD
PH 1	13	1.67±0.63
PH 2	47	4.36±2.03
PH 3	56	6.16±2.13
PH 4	58	6.95±2.20
PH 5	56	8.55±2.63

PH 1 vs PH 2	$P<0.001$
PH 2 vs PH 3	$p<0.001$
PH 3 vs PH 4	$p<0.05$
PH 4 vs PH 5	$p<0.001$

Table III: Nipple Diameter Versus Menstrual Status

Menstrual status	Number of children	Nipple size (mm)±SD
M(-)	79	4.22±2.16
M +1	62	6.57±2.26
M +2	40	7.23±2.39
M +3	49	8.48±2.60

M(-) vs M +1 $p<0.001$
M +1 vs M +2 $p>0.05$
M +2 vs M +3 $p<0.05$

Statistical analysis was performed using Student's *t* test in which the breast stage, pubic hair stage and menstrual status groups were compared with respect to their previous groups[6]. Significant increments in nipple diameter were noted between stages B1, B2, B3, B4 and B5 but the differences between stages B1, B2, B3, and B4 were more significant ($p<0.001$) than the difference between B4 and B5 ($p<0.01$). With respect to pubic hair stages, the differences between PH1, PH2, PH3, PH4 and PH5 from their previous stages were also statistically significant. The differences between PH1 and PH2, PH2 and PH3 and PH4 and PH5 were more significant ($p<0.001$) than the difference between the PH3 and PH4 stages ($p<4.05$). The nipple diameter was significantly greater in M+1 with respect to M(-) ($p<0.001$), and in M+3 with respect to M+2 ($p<0.05$). There was no statistically significant difference in the nipple diameters between groups M+1 and M+2 ($p>0.05$).

Discussion

The five stage classification of breast development as described by Tanner is widely used today. These stages are found by determining the breast bud and evaluating the shape of the areola and nipples[1]. In the studies carried out by Reynolds and Wines[7] and by Tanner[1], there is significant ambiguity between stages B4 and B5. In the former study, a secondary areola mound was absent in eight out of thirty-two girls. while seven others only had slight Tanner stage B4 development[7]. Tanner's experience was similar, and he also noted that in many girls the areola mound stage often persisted into adulthood[1].

In the semi-longitudinal study performed by Roche et al[3], areola development was compared to chronological age, pubic hair stage, age of peak height velocity, age of menarche and subcutaneous fat thickness. Although they found increasing areola size with pubertal progression, it was concluded that areola size was not

significantly related to any of the factors studied. This lack of correlation, they noted indicated that genetic factors were the primary determinants of areolar size. Rohn[4,8] performed two studies about nipple diameters in prepubertal and pubertal children. The results of these studies and our study are illustrated in Tables IV and V.

Table IV: Nipple Diameter Versus Breast Stage: Comparison of Other Studies

	Nipple size (mm) ± SD		
Stage	Rohn's cross-sectional Study[4]	Rohn's longitudinal Study[8]	Hacettepe study
B 1	2.89±0.81	3.00±0.77	1.80±0.87
B 2	3.28±0.89	3.37±0.96	4.24±2.18
B 3	4.07±1.32	4.72±1.40	5.93±2.07
B 4	7.74±1.64	7.25±1.46	7.10±2.28
B 5	9.94±1.38	9.41±1.45	8.67±2.70

Table V: Nipple Diameter Versus Public Hair Stage: Comparison of Other Studies

	Nipple size (mm) ± SD		
Stage	Rohn's cross-sectional study[4]	Rohn's longitudinal study[8]	Hacettepe study
PH 1	2.95±1.02	3.14±1.31	1.67±0.63
PH 2	3.32±0.91	3.69±1.34	4.36±2.03
PH 3	4.11±1.54	4.44±1.17	6.16±2.13
PH 4	7.15±1.81	6.54±1.47	6.95±2.20
PH 5	9.66±1.59	8.98±1.56	8.55±2.63

In our study there was a significant increment in nipple diameters in all breast and pubic hair stages with respect to the previous stages. In a cross-sectional study Rohn[4] found minimal development from Tanner stages PH 1 to PH 3 and B 1 to B 3, but found a significant increment from B 4 to B 5, and from PH 4 to PH 5. He discovered that the greatest growth in papilla diameter occurred after stages B 3 or PH 3. In his longitudinal study, he again found minimal nipple development from Stages B 1 to B 3, and from PH 1 to PH 3 and confirmed the results of his previous cross-sectional study[8]. With respect to menstrual status, Rohn[4-8] found the greatest growth in nipple diameter to be near menarche (from two years premenarche to one year post-menarche). In our study, the greatest growth in nipple diameter occurred between the M(-) and M(+1) periods (premenstrually and one year postmenarche). Rohn[4-8]significantly concluded that his data

demonstrate that nipple size increases the distinction between stages B 4 and B 5, and that B 4 is associated with a nipple diameter of 7 to 7.5 mm and that B 5 is associated with a nipple diameter of 9 mm or greater. In our study, the mean value of nipple diameter in B 4 was 7.10 mm and in B 5 it was 8.67 mm. We discovered that there was a greater increase in nipple diameter from B 1 to B 2 (2.44 mm) and from PH 1 to PH 2 (2.69 mm). This indicates the effect of increasing estrogen in B 2 and PH 2 which results in nipple growth. Increments in nipple size in each pubertal stage may also demonstrate the hormonal effect but it is our opinion that the role of race, nutrition and genetics in nipple size cannot be overlooked. We believe that more cross-sectional and longitudinal studies from different parts of the world may narrow the wide range of differences and help in assigning specific measurements for nipple size to the currently used Tanner breast stages.

Summary

Nipple diameters of 230 girls aged between 11-17 were calculated with the aim of finding measurable criteria for breast development during female puberty. There was a significant increment in nipple diameters in each breast and public hair stage with respect to the previous stages. The maximum increment was found to be from B 1 to B 2 (2.44 mm), and from PH 1 to PH 2 (2.69 mm). With respect to menstrual status, the greatest growth in nipple diameter occurred from the premenstrual period (M(-)) to one year postmenarche (M +1) (2.35 mm). These results are compared with other studies in the literature, and it was concluded that increments in nipple size in each pubertal stage is related to the hormonal status as well as to race, nutrition and genetics. More longitudinal and cross-sectional data are needed in order to find a measurable criteria for the Tanner breast stages.

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AMYLOIDOSIS IN CHILDREN WITH FAMILIAL MEDITERRANEAN FEVER*

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Key words: amyloidosis, familial Mediterranean fever, colchicine.

Familial Mediterranean fever (FMF) is a heredofamilial disease that occurs predominantly in patients of Mediterranean, Eastern European, or Middle East origin, particularly Sephardic or non-Ashkenazic Jews, Armenians, Arabs, and Turks. This autosomal recessive disorder of unknown etiology is characterized by recurrent episodes of fever associated with serositis of the peritoneum and pleura, and arthritis.[1-3] An erythematous rash may also rarely occur. Familial Mediterranean fever is the cause of secondary amyloidosis. Since the disorder occurs frequently in Turkey, renal histopathological changes are looked for if nephrotic syndrome or proteinuria develops in a case with FMF and in all cases with nephrotic syndrome and proteinuria. [1-13]

The purpose of this report is to describe the clinical features and laboratory findings of 113 children with amyloidosis and to determine the benefical effects of colchicine as treatment for the disease.

Material and Methods

The survey included 113 subjects with amyloidosis secondary to FMF who had been admitted to the Departments of Pediatric Nephrology at Hacettepe University Hospital, and Ondokuz Mayıs University Hospital, from 1975 to 1986. There were 65 boys and 48 girls.

The diagnosis was established by the characteristic clinical findings of FMF such as fever, peritonitis and arthritis, and by the evaluation of renal biopsy specimens obtained from all patients. Those with either clinical or laboratory evidence of rheumatoid arthritis, chronic suppurative diseases or polyneuropathic familial amyloidosis were excluded from the study.

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The subjects were classified into two groups:

— Phenotype I: FMF episodes precede the development of amyloidosis.

— Phenotype II: Manifestations of amyloidosis precede FMF episodes or patients not living long enough for an attack to develop.

All patients were advised to follow a diet rich in protein. Salt intake was only restricted in edematous patients. All patients were treated with colchicine in a dose of 1.5-2 mg per day. The doses were determined according to the patient's tolerance.

Results

Sixty-five boys and 48 girls whose ages ranged between four to 17 years (mean 12.02 ± 3.12 years) were included in the study (Fig. 1). The male: female ratio was 4/3.

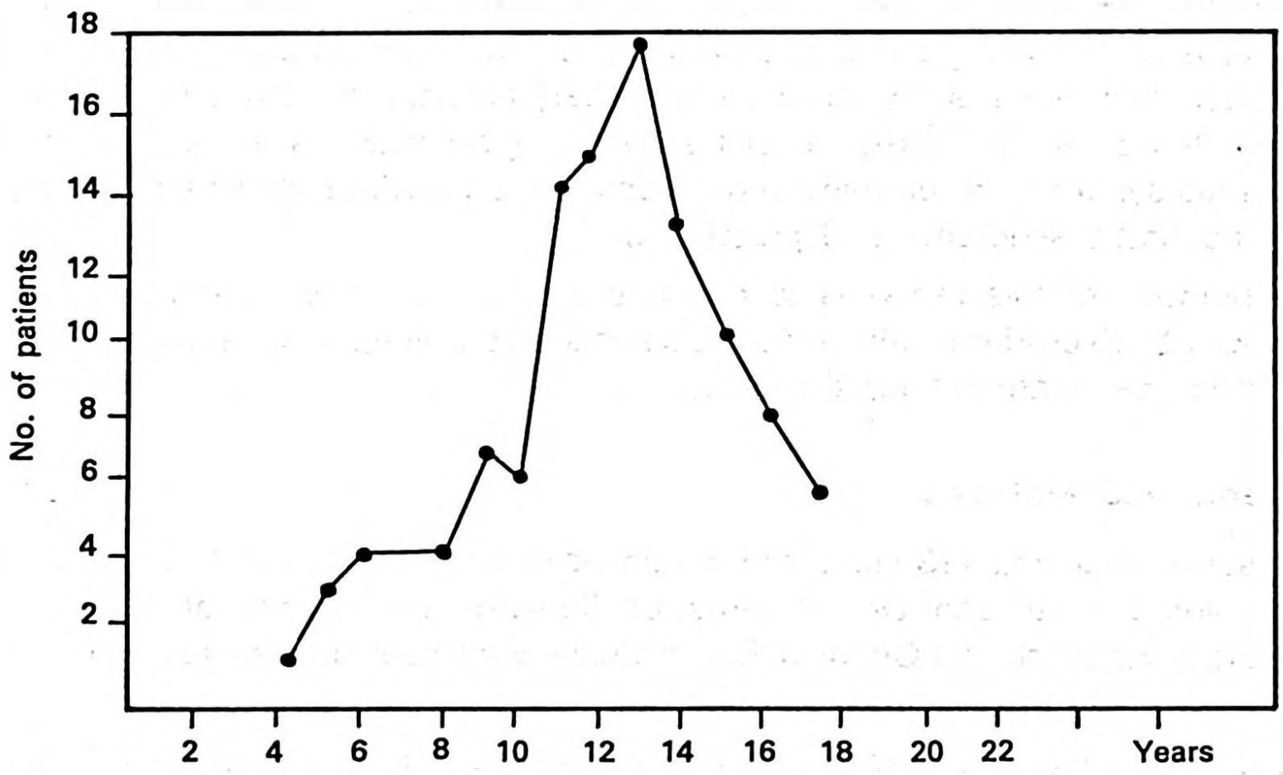

Fig. 1. Age distribution of patients (Yrs)

The patients were followed up for a mean period of 27 months (2-87 months). Most of our cases (84 patients, 74.33 %) demonstrated phenotype I characteristics while the others (29 patients, 25.67 %) phenotype II characteristics.

In phenotype I subjects, amyloidosis developed in a period of from two months to 14 years after the onset of periodic attacks.

As seen in Table I, fever is the most common feature of the disease. Episodes of abdominal pain and arthralgia were seen in one third of the patients. Only 24 patients had a positive family history for the disease.

The children were reexamined at least once, and we observed that all the symptoms occurring during the attacks were relieved by colchicine therapy. Eleven patients treated with colchicine (aged 11-13 years), who were followed up for 27-63 months, showed no signs of renal failure. Their growth rate was 4-6.5 cm per year.

The mean arterial systolic pressure was 107.71 ± 14.7 mmHg, and the diastolic pressure 69 ± 1.3 mmHg. During the follow-up period hypertension was noted in only five cases with renal failure.

Forty cases (35.39 %) had hepatomegaly (1-8 cm), and 14 cases (12.38 %) splenomegaly (1-9 cm).

Clinical and laboratory findings are shown in Tables I and II.

Table I: Clinical Features of Amyloidosis in 113 Children With Familial Mediterranean Fever.

	Number of Findings / Total Case (%) Number
Family history	24/113 (21 %)
Phenotype 1	84/113 (74 %)
Phenotype II	29/113 (26 %)
Fever (periodic)	68/84 (75 %)
Abdominal attacks	35/84 (41 %)
Arthritic attacks	34/84 (40 %)
Hepatomegaly	40/113 (35 %)
Splenomegaly	14/113 (12 %)
Hypertension	5/113 (4 %)
Renal failure	22/113 (19 %)

Table II : Laboratory Findings of Amyloidosis in 113 Children With Familial Mediterranean Fever.

	No. (%)
Anemia	34 (30 %)
Leukocytosis	55 (49 %)
Hypoalbuminemia	66 (58 %)
Hyperuricemia	30 (27 %)
Prolonged PT*	7 (7 %)
Prolonged PTT**	96 (85 %)
Hyperlipidemia	48 (42 %)
Hypercholesterinemia	84 (74 %)
Hematuria	29 (26 %)
Leukocyturia	42 (37 %)

PT* :prothrombin time; PTT** :partial thromboplastin time.

As seen in Table III, there was no significant statistical difference found between the hemoglobin, serum globulin, cholesterol, lipid and daily urinary protein excretion values before and after colchicine therapy. However, a significant difference was seen between the serum total protein and albumin values.

Table III- Some Laboratory Findings Before and After Colchicine Therapy.

	Before colchicine therapy (mean values)	After colchicine therapy (mean values)	P values
Hemoglobin (g/dl)	11.32±2.13	10.90±2	p>0.05
Total serum protein (g/dl)	4.73±0.99	5.01±1	p<0.01
Serum albumin (g/dl)	2.4±0.87	3.3±0.5	p<0.01
Serum globulin (g/dl)	2.29±0.60	2.3±0.7	p>0.05
Daily urinary protein (g/24hr)	2.65±2.12	2.69±1.9	p>0.05
Total serum lipid (mg/dl)	1098±381	1150±300	p>0.05
Serum cholesterol (mg/dl)	290±132	140±86	p>0.05

Discussion

FMF is characterized by recurrent attacks of fever accompanied by signs of peritonitis and/or pleuritis. Some patients may also have arthritis and skin lesions. The term "Familial Mediterranean fever" is suitable because many of those affected by the disease are of Mediterranean origin i.e., non-Ashkenazic Jews, Turks, Italians and Greeks.[1-3]

As is shown in Fig. 1, the number of patients with amyloidosis increased through out the adolescent period during which time the attacks of FMF were frequently encountered.

While there is no registry centre, as far as we know, the number of cases with amyloidosis secondary to FMF in our survey is the largest yet presented. In our group, 24 patients (21.23 %) had a familial history of FMF, which is a ratio lower than expected[3,9-13]. One of the most important characteristics of amyloidosis secondary to FMF is that it may be seen initially without showing any clinical signs of FMF, phenotype II. Even if there is preventive treatment in the future for secondary amyloidosis due to FMF, there will still be a problem for phenotype II cases. As seen in Table I, the incidence of phenotype II was high, even though it is mentioned as a rare variant.[3]

Although it is not possible to predict when amyloidosis formation occurs in FMF, it generally takes from four to ten years.[1,3,5,11-15]. Because FMF cases develop

according to the phenotype I or II classification there are really great differences between the appearance of amyloidosis and the onset of FMF attacks.[12-14] In fact, in our phenotype I cases there had been recurrent attacks for a period of from two months to fourteen years before amyloidosis developed or was diagnosed.

Symptoms of periodic attacks according to frequency in phenotype I patients were fever (25 %), abdominal pain (41 %), and arthritic attacks (40 %). As seen in our patients, fever in FMF has frequently been the presenting sign together with other findings (Table I). Abdominal and synovial attacks reported in the literature, as 95 and 75 percent, respectively were seen less frequently in our study.[3,9,10]

All our cases with FMF attacks were examined at least once, and it was observed that periodic attacks could be relieved by colchicine. Our results also support the argument that colchicine may be used as a drug to diagnose FMF.[4,16-27]

Out of 113 patients, only five presented with hypertension. These hypertensive cases were those who had been followed up for one–three years. The general opinion is that these subjects may have had hypertension during the period of end stage kidney disease because of kidney shrinkage. Reports in the literature state that the proportion of hypertensive cases at the end-stage period may reach 20-30 percent[3,12,13]. It is commonly considered that amyloidosis generally results in hypotension because of adrenal involvement.

Our patients had hepatomegaly (8 cm) and splenomegaly as well; only two cases with splenomegaly did not evidence hepatomegaly.

In the cases without renal failure, obvious anemia was not seen. Only 34 cases (30 %) had mild anemia (Table II). While it has been suggested that anemia is not a common finding in amyloidosis, it generally appears in the uremic stage of the disease[1,3,11,13]. In the cases with slight anemia, this finding was not due to the colchicine administered. Leukocytosis was not an important finding; it was present in only fifty-five subjects, the others were normal.

Sixty-six patients had severe hypoalbuminemia. This condition was encountered in a patient who manifested a serum albumin value as low as 0.7 g/dl. We noticed that there were increasing serum total protein and serum albumin values in the cases treated with colchicine but that there were no changes in the serum globulin values.

We concluded that the increase in the values of serum total protein and albumin of the patients on colchicine could depend partly on good patient care, i.e, a good diet, amino acid tablets and also partly on the beneficial effect colchicine has on amyloidosis. There was only one case in which proteinuria had disappeared over a period of two years while the patient was receiving colchicine. However, with the

cessation of the drug by the patient, FMF findings and proteinuria reappeared. Some observations have suggested that amyloidosis associated with FMF could be put into full remission with colchicine[25].

Another important finding in 96 (84.95 %) of the cases that we followed was that the PTT had increased (Table II) which is an important observation for secondary amyloidosis. Despite the significant amount of amyloid deposition in the liver, alterations in hepatic function were generally considered to be minimal. An increase in the level of PTT is an early and important indication of liver dysfunction assisting a clinical evaluation of amyloidosis[1,3,7]. The serum uric acid level was high in nearly 25 percent of the cases, while the serum cholesterol and lipid concentrations were high in 75 percent of the patients. There was a correlation between hypercholesterinemia and hyperlipidemia. But we were not able to find any changes in the serum lipid and cholesterol levels in the cases treated with colchicine.

Summary

In this survey 113 children with secondary amyloidosis due to familial Mediterranean fever are reviewed in regard to their respective histories, and physical and laboratory findings. The benefical effects of colchicine in the treatment of this condition are evaluated. The number of children presented with amyloidosis secondary to familial Mediterranean fever was considerable. The male-female ratio was 4/3. It was observed that the number of patients with amyloidosis increased through the adolescent period, and that most of the cases demonstrated phenotype I (74.33 %). Another important finding was the increase of partial thromboplastin time in 96 out of 113 cases (84.95 %). All the symptoms of the periodic attacks were relieved by colchicine. A significant difference was found between the serum total protein and albumin values before and after colchicine therapy.

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CARDIAC EXTENSION OF WILMS' TUMOR*

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Key words: Wilms' tumor, intracardiac tumors, childhood solid tumors

Wilms' tumor comprises about 20 percent of solid tumors in childhood[1], and it ranks second among extracranial solid tumors[2]. The tumor exhibits a marked tendency to invade vascular structures such as the renal vein and inferior vena cava[2]. Cephalad progression of inferior vena caval involvement and direct cardiac extension of Wilms' tumor can occur. This complication has been documented by some authors preoperatively, intraoperatively, postoperatively or by postmortem observations[2-9]. With the new developments in noninvasive diagnostic methods the number of cases diagnosed preoperatively are increasing. Cases in which intracardiac tumors are diagnosed preoperatively present a technical challenge to the surgeon, and removal of the tumor requires cardiopulmonary bypass. If the tumor extending into the heart is removed intact, and without embolization, and if the patient is otherwise free of nodal or distant metastases, the disease can be considered to be in Stage II[3].

The clinical features of two patients with direct extension of Wilms' tumor into the renal vein and inferior vena cava and to the right atrium are presented in this paper.

Case Reports

Case 1

A four and a half year-old boy was brought to the Istanbul University Children's Hospital with complaints of body swelling and palpitation.

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Physical examination revealed a child with periorbital and pretibial edema. His liver was palpable three cm below the right costal margin. The cervical veins were distended. Maximal cardiac motion was detected in the xiphoid area. A II/VI systolic-diastolic murmur was audible around the same area. His blood pressure was 105/80 mm Hg and pulse rate 135/min. The hemoglobin and leukocyte counts were normal with a sedimentation rate of 22.40, and 60 mm at 30 minutes, one hour, and two hours, respectively. Urinalysis revealed 1+ albuminuria. Microscopic examination of the urine showed six or seven erythrocytes per field; the ECG was normal. The chest x-ray demonstrated cardiomegaly. M-mode and two-dimensional echocardiography revealed a large mass in the right atrium which moved from the right atrium into the tricuspid valve and the right ventricle and back into the right atrium in rhythm with the cardiac systole and diastole. As a result of these findings a tentative clinical diagnosis of a right atrial myxoma was made and surgery was decided. During open heart surgery a mass measuring 6 x 6 x 3 cm with an attached pedicle was discovered which almost completely filled the right atrium. The mass which extended into the inferior vena cava was removed and was diagnosed histopathologically as a mixed type of Wilms' tumor. Following surgery, intravenous pyelography and renal ultrasonography were performed which revealed a small mass in the left kidney (Fig. I). Ultrasonographic examination of the inferior vena cava showed fine linear

Fig. 1: Intravenous pyelography following cardiac surgery demonstrating deformation of the pelvis-caliceal system due to intrarenal tumor.

echogenic structures. Ultrasonography and scintigraphy revealed a normal spleen and liver. Bone marrow examination and bone x-rays demonstrated no metastases. Chemotherapy was initiated which was followed by a left nephrectomy, performed two weeks later. The extracted kidney was larger than normal, and a mass was noted at its upper pole. The renal capsule was intact. The area in and around the inferior vena cava was free of tumoral metastases. Histopathologically, the tumor was visualized in the branch of the renal vein as a thrombus-like mass (Fig. 2). A vena caval venogram using the percutaneous technique was taken postoperatively and revealed a minimal filling defect above the level of the renal vein. Radiotherapy was added to the treatment. After three and a half years, the patient is symptom-free, growing and developing normally.

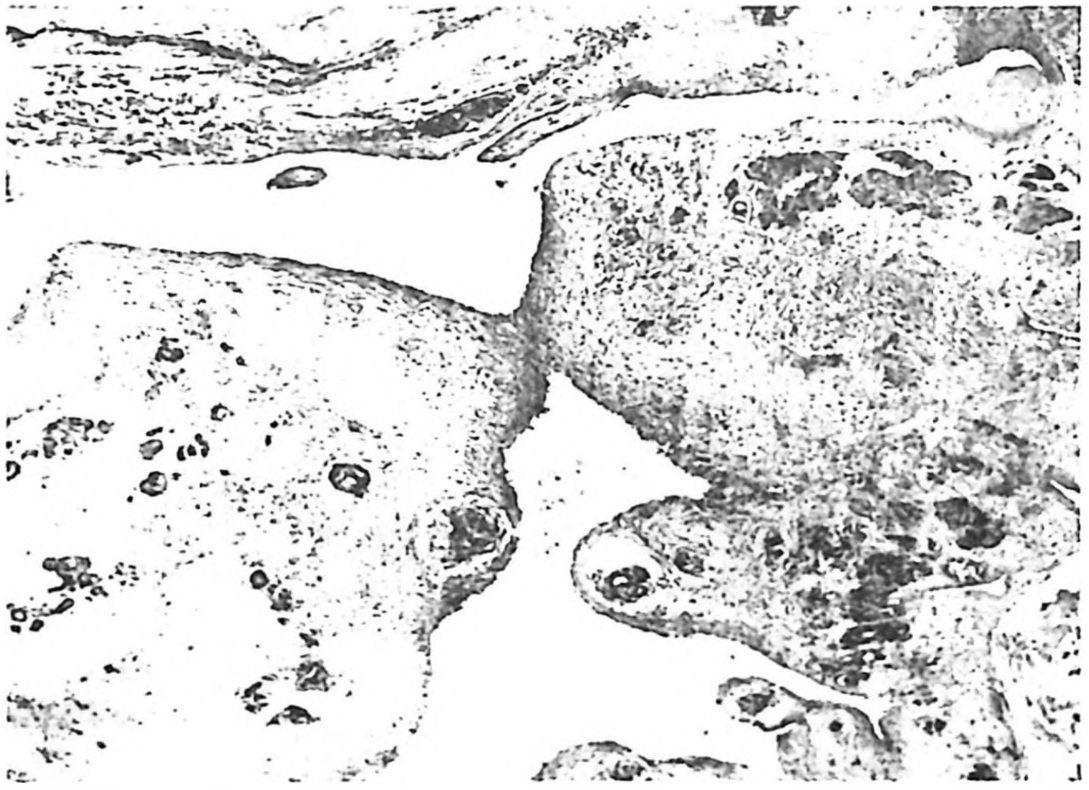

Fig. 2: Formation of the polypoid-shaped thrombus of the tumor in the renal vein branch.

Case 2

A seven-year-old boy was admitted to the Istanbul University Children's Hospital presenting with complaints of tiredness, periorbital edema, jaundice,and a reddish color to the urine. Six months prior to this admission the diagnosis of Wilms' tumor was established and the patient underwent a nephrectomy. He was also given chemotherapy.

Physical examination revealed dyspnea, diffuse edema and obvious jaundice, A pericardial friction rub, and I/VI pansystolic murmur in the xiphoid area were present. The cervical veins were engorged. The liver exceeded the costal margin by four cm. Laboratory examinations revealed a normal blood count and

sedimentation rate. SGOT was 918 U, SGPT 948 U. A chest x-ray demonstrated cardiomegaly and ECG low voltages over the left precordial leads. Two dimensional echocardiography revealed a mass in the right atrium with an attached pedicule. A fairly large amount of pericardial fluid was also present (Fig. 3). The patient's condition was poor. A preoperative diagnosis of extension of Wilms' tumor was established and surgery was planned. During open-heart surgery a 9x5x4 cm yellowish-white mass was removed. Similar to the first case, a pedicule extended into the inferior vena cava. Pathological examination of the mass revealed a Wilms' tumor rich in mesenchymal components (Fig. 4).

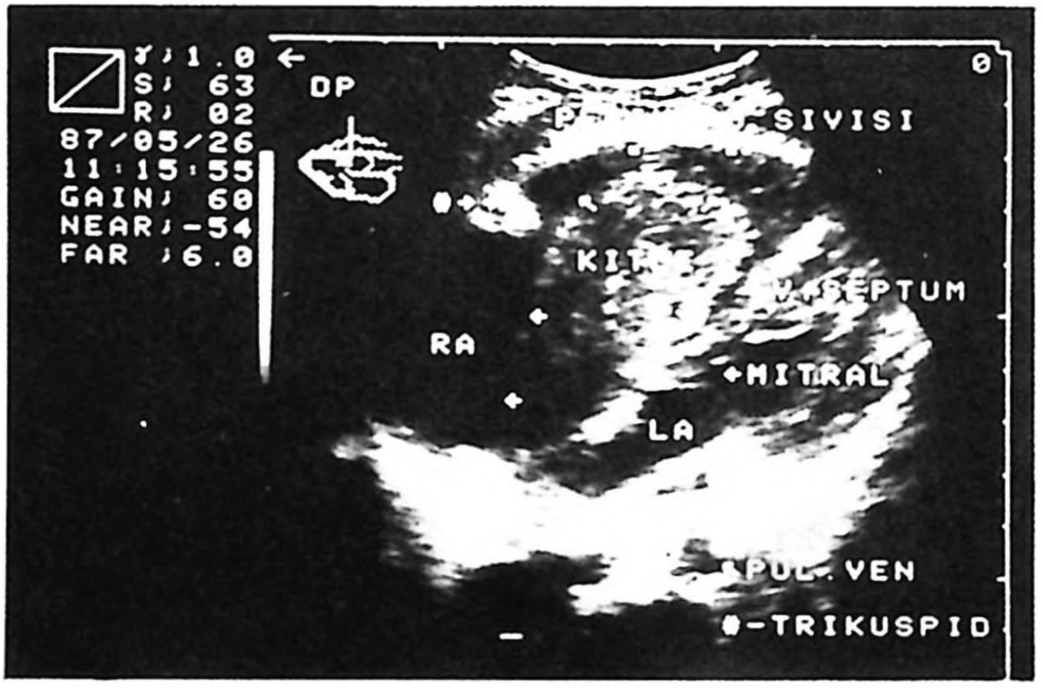

Fig. 3: Echocardiogram showing tumoral mass in the right atrium

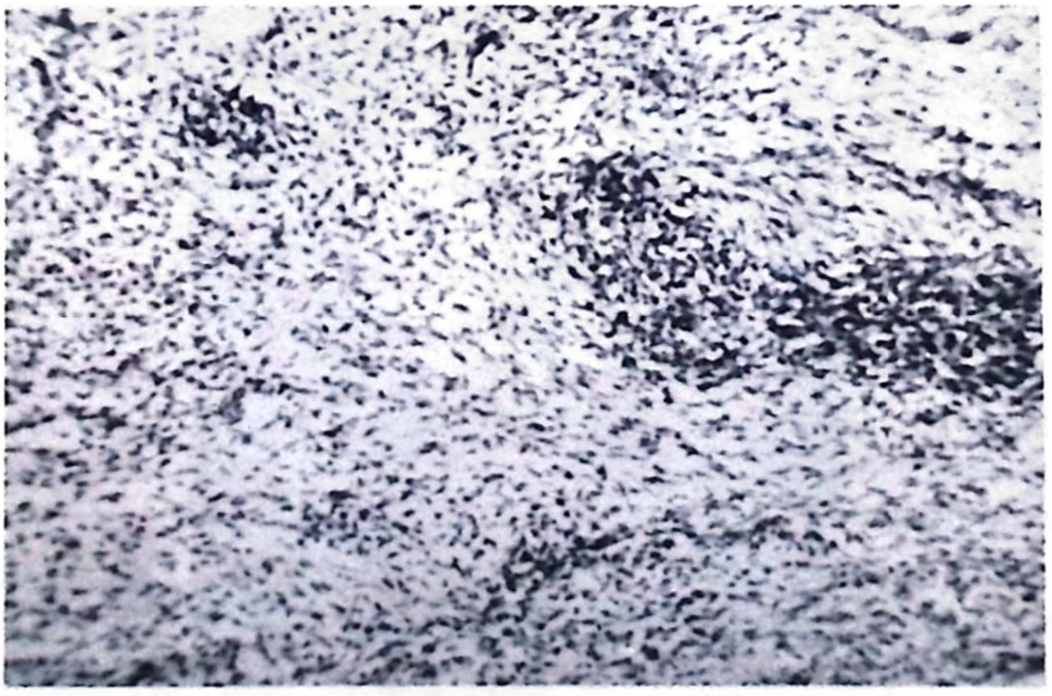

Fig. 4: Mesenchymal appearance and anaplastic cells

Postoperatively, the patient made a very rapid recovery. Work-up and treatment was similar to the first case. Two years postoperatively, the patient is still alive, well and symptom-free.

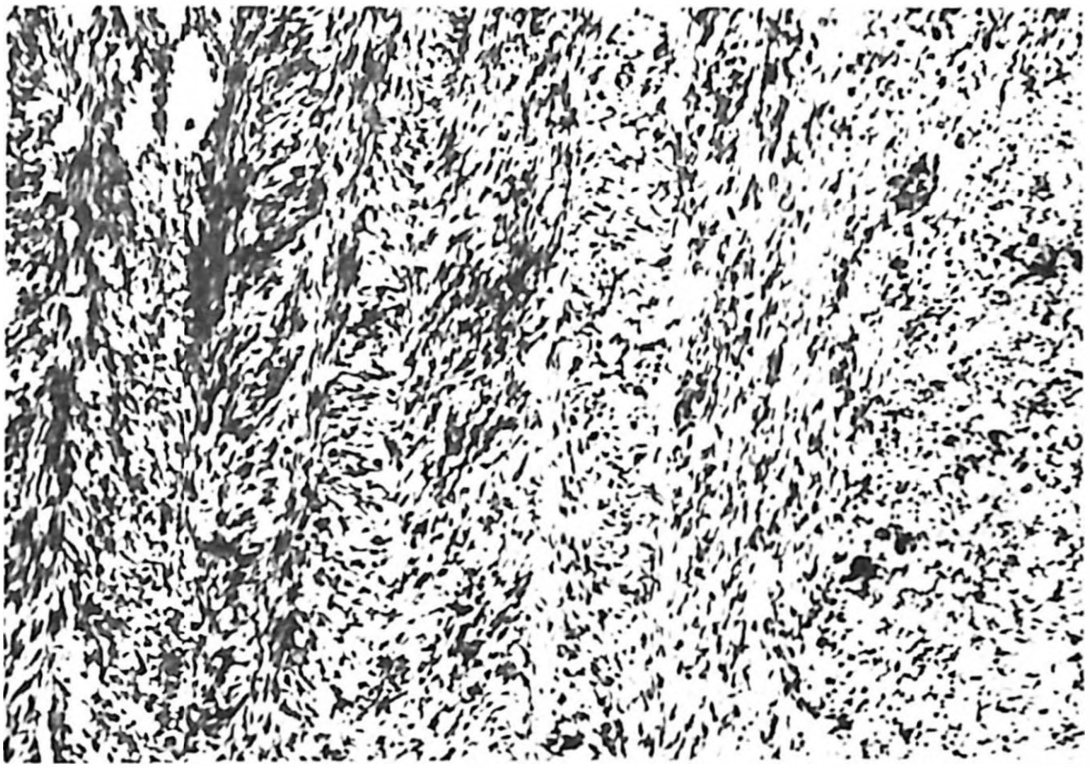

Fig. 4: Sections of the tumoral mass showing embryonic and mesenchymal characteristics in two different representative sections.

Discussion

Neoplastic diseases of the heart, pericardium and great veins, whether primary or secondary are unusual in children[4,5,10,11] Extension of Wilms' tumor into the inferior vena cava and the right atrium also rarely occurs. The National Wilms' Tumor Studies (NWTS) have reported the incidence of this tumor as 15:2280 (0.7 %)[3]. Only six of these 15 cases were diagnosed preoperatively. Of the remaining cases, five were diagnosed during surgery and four postoperatively. Chan et al[4], reported 293 Wilms' tumor cases in a series of 3641 solid tumor cases. Of these, nine had intracardiac metastases and three were diagnosed at postmortem examination. In this study the incidence of intracardiac metastases of Wilms' tumor was about three percent which is four times more than that reported by NWTS.

In our Children's Hospital thirty-two cases of Wilms' tumor have been diagnosed in the past 15 years. The two cases presented in this report are the first in which intracardiac metastases have been diagnosed. To date, there have been approximately forty reported cases of Wilms' tumor with intracardiac metastases[2-9], ten of which were reported prior to 1981. All had right kidney involvement, however, later reports mention both right and left kidney involve-

ment. In our cases, primary renal involvement was on the left side in the first case, and on the right side in the second case.

Cardiac metastases usually present with congestive heart failure and primarily symptoms of right-sided heart failure. Both our cases had findings of right-sided heart failure. In the first case, the mass was diagnosed by echocardiography, but initally the tumor was thought to be a myxoma and the diagnosis of Wilms' tumor was made postoperatively by pathological examinations. A similar case was reported by Holbrook et al[6]. In our second case, a correct diagnosis was made preoperatively since we had the experience of a prior case in which there was a history of surgical removal of a Wilms' tumor. Since echocardiography demonstrated a right atrial mass, emergency surgery was performed. Obviously this patient's condition was more critical because it was complicated by the presence of jaundice and the pathological findings of a congestive liver.

During a nephrectomy acute tricuspid valve obstruction and pulmonary embolism in the renal veins and the inferior vena cava with no metastatic invasion of these veins have been reported.[12,13] Thus, during surgery this has to be taken into consideration.

The best approach to intracardiac extension of Wilms' tumor is open-heart surgery for removal of the mass and extirpation of the pedicule from the inferior vena cava as extensively as possible[3]. Luck et al[7] and Grosfeld and Weber[8] advise a thoraco-abdominal approach for removal of both the intracardiac mass and nephrectomy in one surgical operation[7-8]. The NWTS results show that the two year survival of 15 cases with intracardiac extension is the same as for the noncardiac cases of Wilms' tumor. Also,preoperatively, intraoperatively or postoperatively diagnosed cases did not differ in prognosis[3]. For this reason, the same therapy program that was used in cases without cardiac extension can be applied to patients diagnosed preoperatively, intraoperatively or postoperatively. However, a preoperative correct diagnosis is to the benefit of the patient.

Intracardiac extension of Wilms' tumor is a rare but treatable condition provided that it is diagnosed early by routine echocardiography. All cases of Wilms' tumor should be scrutinized for this possibility using echocardiography which has brought a new perspective to this tumor by its easy applicability as a noninvasive method. This is true not only for diagnosis which saves the patient from costly and potentially risky tests but also for follow-up reevaluations.

Summary

Two children who were brought to the Istanbul Children's Hospital with congestive heart failure caused by extension of Wilms' tumor to the right atrium are presented. In both cases a large mass was noted in the right atrium by

two-dimensional echocardiography. The tumors were successfully removed at open heart surgery, and chemotherapy and radiotherapy were started postoperatively. The patients are both alive and symptom-free; one, three and a half years and the other to years postoperatively.

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AGGRESSIVE KAPOSI'S SARCOMA IN CHILDREN: A CASE REPORT*

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Key words: Kaposi's sarcoma, pulmonary insufficiency

In 1872 Morictz Kaposi described an independent entity of "idiopathic multiple pigment sarcoma of the skin" in patients seen in the dermatology department[1]. The tumor was characterized by the development of skin nodules or plaques usually starting on the hands or feet but occasionally involving the viscera[2].

It has been recently reported in the United States that immunosuppressed patients[3-4], homosexual men[5], intravenous drug abusers. Haitian immigrants, hemophiliacs[6], and prision inmates[7] were especially at risk of developing Kaposi's sarcoma (KS). Recent reports of acquired immunodeficiency syndrome (AIDS) have called attention to KS in children[8]. In this article, we present a three year-old boy with aggressive KS.

Case Report

A three-year-old boy was admitted to the Dr. Sami Ulus Children's Hospital in October 1986, presenting with periorbital ecchymoses, palpebral edema, dyspnea, and fever of eight days' duration. There were no significant abnormalities pertaining to his prenatal, natal or early postnatal periods. His physical and motor development was normal. It was ascertained that BCG, DPT, and polio immunizations had been given to the patient at the appropriate intervals, and that he had not contracted mumps, measles, varicella or pertussis. The child, however, received various drugs for frequent upper respiratory tract infections and recurrent episodes of otitis media. His mother, aged 20, is a housewife in good health, and his father, aged 24, is a professional driver suffering from peptic ulcer. The parents had never been abroad, had never been recipients of blood

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transfusions, and were neither drug users nor homosexuals. The patient had a healthy seven-month-old sister. There was no history of abortion, stillbirth or death of a sibling in the family.

Physical examination revealed a child with a temperature of 39°C, dyspnea, and a respiration rate of 45 per minute. He had facial edema, periorbital ecchymoses and subconjunctival hemorrhages. There was a bilateral, fixed, hard mass measuring 7x7 cm in the mandibular area. Bilateral axillar cervical and inguinal nodes, the largest of which was 2x2 cm, were also palpated.

Ascultation of the chest revealed fine bilateral rales. The liver was palpable five cm and the spleen six cm below the arcus costarum in the midclavicular line.

Laboratory findings revealed a hemoglobin of 5.5 g/dl, white blood cell count 17200/mm^3, platelet count 75000/mm^3; the peripheral blood smear showed polychromasia, hypochromia, enisopoikilocytosis, 34 % segmented neutrophils, 28 % lymphocytes, 10 % monocytes, 1 % basophils, 20 % atypical lymphocytes, 7 % atypical monocytes. Examination of the bone marrow aspirate showed hypercellularity, slight megaloblastic changes in erythroid cells and an increase in promyelocytes. The BUN was 30 mg/dl, serum creatinine 0.7 mg/dl, total serum protein 5.5. g/dl, albumin 3.25 g/dl, total bilirubin 0.6 mg/dl, total lipids 830 mg/dl; total cholesterol 170 mg/dl, alkaline phosphatase 4.6 BU; SGOT 15 U; SGPT 30 U. The erythrocyte sedimentation rate was 50 mm/hr, PPD test negative, direct Coombs test negative, immunoelectrophoresis: IgG 1310 mg/dl (N: 929±228), IgM 138 mg/dl (N :56±18), IgA 62.9 mg/dl (N :93±27). Hemoglobin electrophoresis and the throat culture were within normal limits. The chest roentgenogram revealed a mediastinal mass and bilateral parenchymal infiltration. IVP and roentgenograms of the bones were normal.

The patient was transfused 350 ml of blood and combination therapy of ampicillin and gentamicin was initiated intravenously. A biopsy of the right inguinal node was obtained. The lymph node was pink and elastic and measured 1.2x0.5x0.4 cm. Microscopically, the structure of the lymph node was largely distorted and a malignant tumor was noticed. The tumor consisted of atypical fusiform endothelial cells which also formed vascular formations. Malignant tumoral infiltration of varying size and location was observed in the marginal sinuses which was defined as the metastasis of KS. In the patient's sera HTLV-III antibody was found to be negative by the ELISA method. The child died of progressive pulmonary insufficiency on the tenth day of hospitalization.

The following findings were obtained at postmortem examination: Microscopically, examination of the heart showed no significant findings except for left ventricular hypertrophy. Mucous membranes starting in the subepiglottic region and extending to where the main bronchi enter the lungs were hyperemic and

rough. Many irregular lesions of varying size, the largest, 1 cm in diameter, were observed on the visceral pleural sides of both lungs. There were many red lesions on the stomach and on the ascending colon including the cecum, the largest being 1.5 cm and 0.5 cm in diameter, respectively. Tumoral infiltrations ranging from 0.1 to 0.5 cm in diameter were detected in the lymph nodes of the cervical, mediastinal, paraaortic, celiac, mesenteric and inguinal regions.

Microscopically, examination of the epiglottis, trachea, bronchi, lungs, palatine tonsils, submandibular glands, stomach, liver, small intestine and bowel, thymus, spleen, and cervical, mediastinal, abdominal, and inguinal lymph nodes showed malignant tumoral infiltrations. Vascular structures composed of atypical endothelial cells were observed between the mucosa and submucosa. These cells varied in size, shape and staining characteristics. They were either round or notched, varied in diameter and some had red blood cells within their lumens. The presence of vascular structures was demonstrated by using silver and the Massoni trichome staining techniques (Figs. 1-3). On examination no significant pathological findings were detected in the radix linguae, testes, diaphragm, thyroid gland, skeletal muscles, skin, pancreas, medulla spinalis, bladder or surrenal glands. Histological evidence of *pneumocystis carinii* and cytomegalovirus infections was not found.

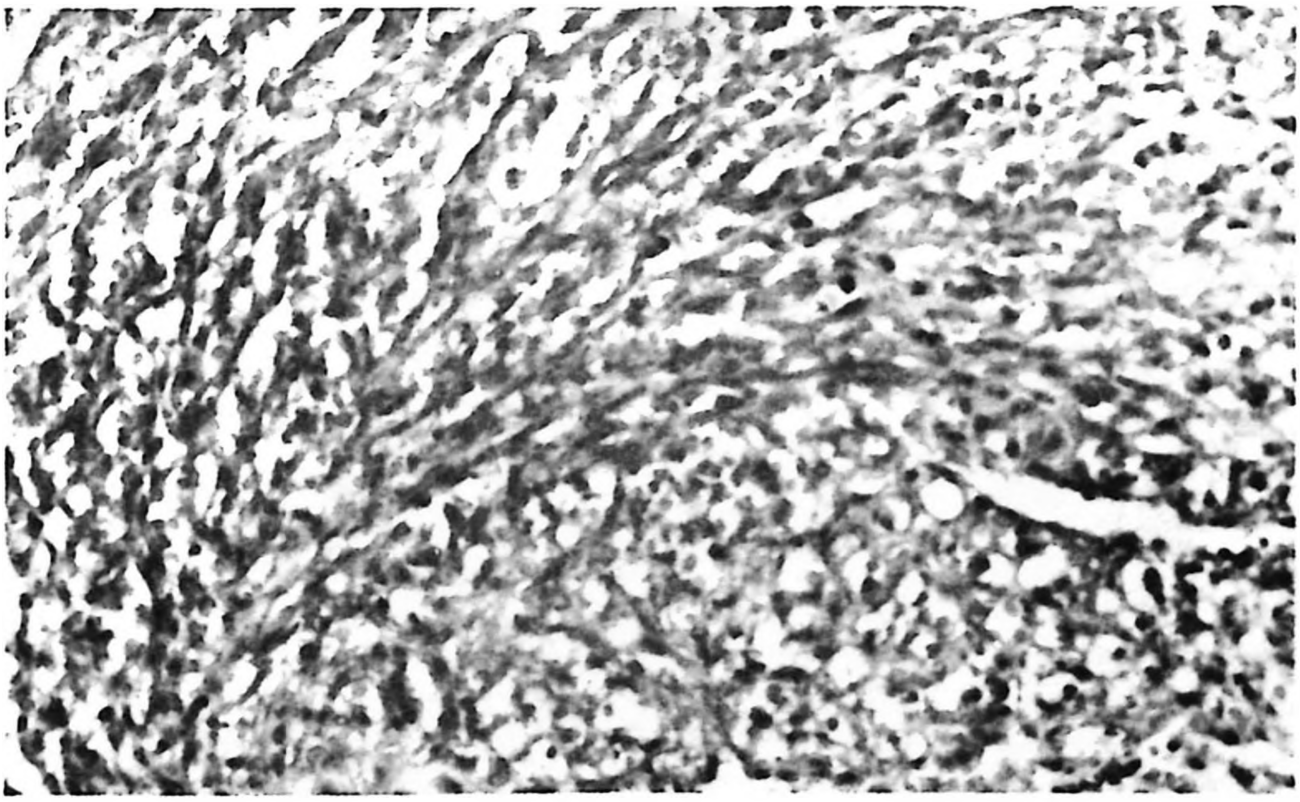

Fig. 1 a: Kaposi's sarcoma metastasis in the lymph nodes; atypical endothelial cells varying in size and shape. Hematoxylin and eosin (x 200).

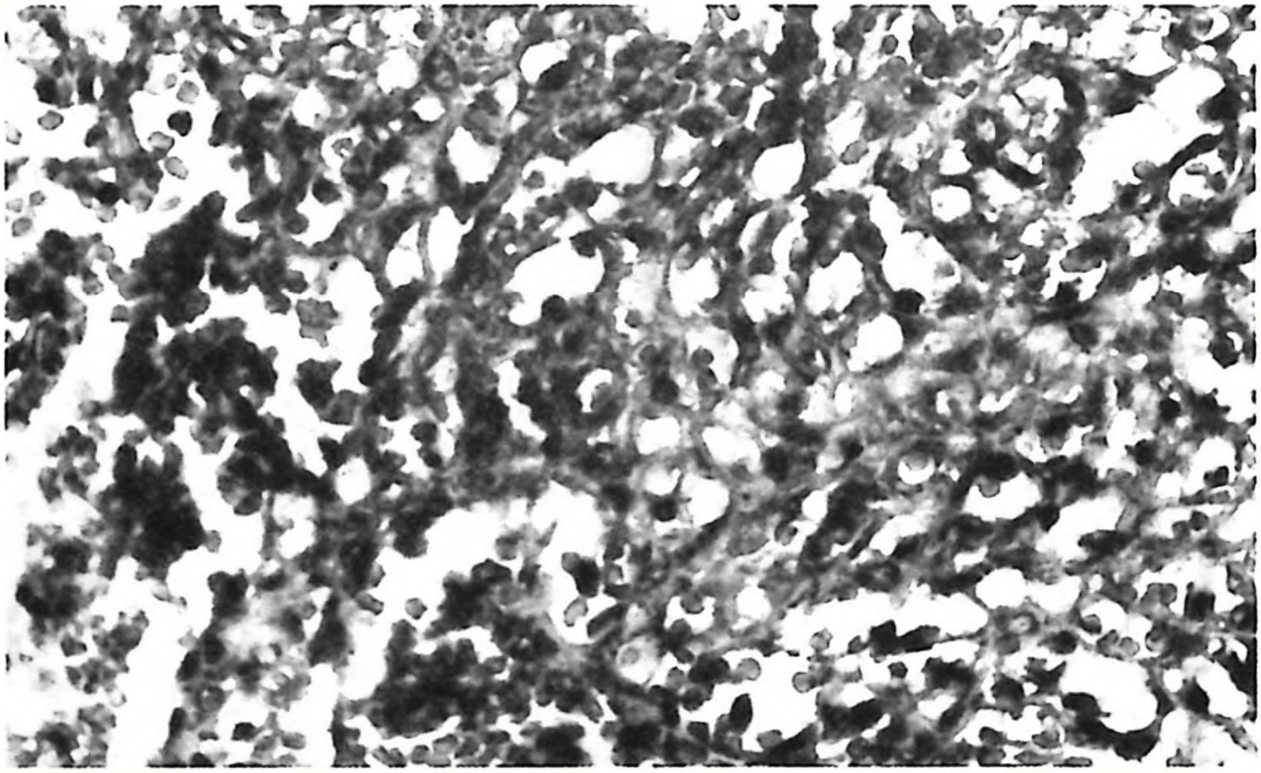

Fig. 1 b: Kaposi's sarcoma metastasis in the lymph nodes; atypical endothelial cells varying in size and shape. Hematoxylin and eosin (x 400).

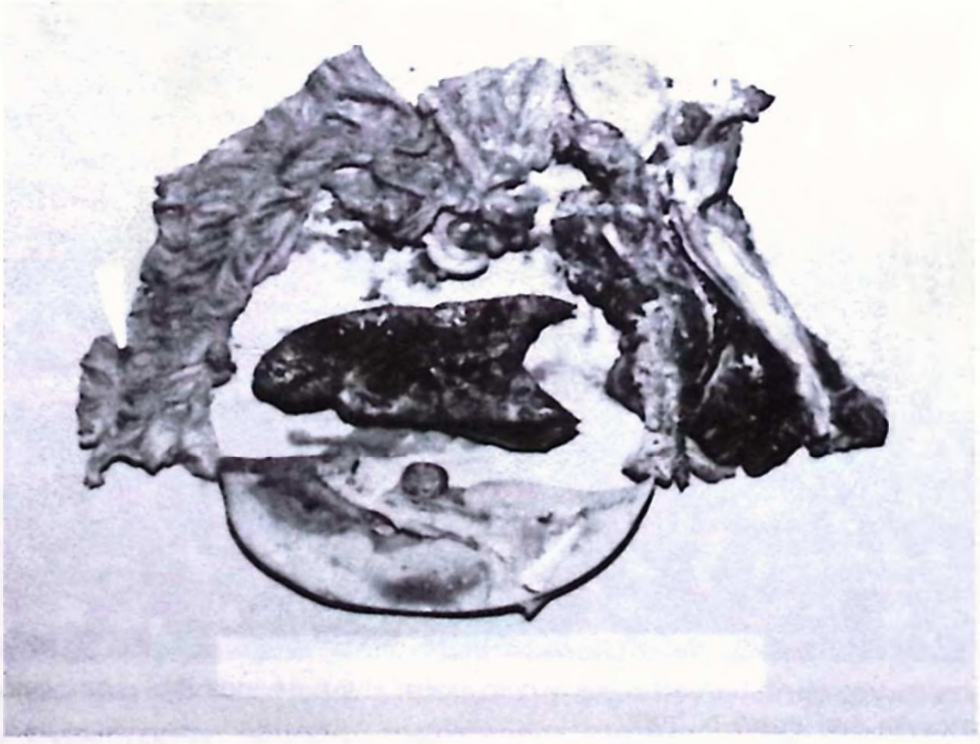

Fig. 2: Thymus, palatine tonsils, mediastinal and paratracheal lymph nodes, lungs, liver, and colon of the patient.

Fig. 3: Tumoral infiltration in the lung (macroscopical).

Discussion

Kaposi's sarcoma, a very rarely encountered tumor in children[8,9] has been reported in central east Africa, Europe and America.[10-12] Especially in Black African children the tumor is usually aggressive and pursues a fulminant course. Black African children with KS often have prominent lymph node enlargement. Visceral involvement develops in up to 20 percent of cases during the course of the disease. The lymph nodes and gastrointestinal tract are the most common sites of deep-seated disease but pulmonary involvement is also seen in disseminated cases.[13]

Recently KS has been regarded as an epiphenomenon of AIDS[14]. Skin or lymph node involvement may occur in KS associated with AIDS but patients suffering from progressive disease usually have multiple organ involvement particularly of the gastrointestinal tract and pulmonary parenchyma. Most of these patients have positive serologic evidence for HTLV-III antibody. However, two cases of AIDS with negative HTLV-III antibodies but positive HTLV-III antigens have been reported, one of these patients had KS[15]. Asymptomatic individuals at risk of developing AIDS who carried HTLV-III in their blood and/or saliva without detectable antibodies have been[16] previously reported. Although in endemic areas KS is thought to be independent of HTLV-III infection, in the United States a diagnosis of KS is usually thought to be synonymous with the diagnosis of AIDS but some cases of primary visceral KS unrelated to AIDS have also been reported[17].

Our patient had generalized Kaposi's sarcoma. When questioned, the family denied having had any contacts either at home or abroad with individuals at risk of developing AIDS. They also disclosed that they had not been recipients of blood transfusions and had not taken intravenous injections of drugs. Postmortem examination did not reveal an opportunistic infectious agent which was also a finding that did not correlate with AIDS. Therefore, we diagnosed our patient as having aggressive primary KS.

Summary

A three-year-old-boy with generalized Kaposi's sarcoma (KS) is presented. The child died of progressive pulmonary insufficiency on the eighteenth day of the course of his illness, the tenth hospital day. On postmortem examination diffuse KS infiltration was observed in the respiratory and gastrointestinal tracts, lymph nodes, liver, spleen and thymus. The patient was considered to be a case of KS unrelated to AIDS because of his negative HTLV-III antibody and epidemiologic characteristics, and therefore was believed to have primary aggressive KS.

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PERICARDIAL MESOTHELIOMA*

A Pediatric Case Report

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Key words: malignant mesothelioma, pericardium, childhood

Pericardial mesothelioma is an extremely rare tumor originating from mediastinal cells. A total 120 cases were reported with this tumor by 1985.[1] This tumor is most commonly seen in the third and fourth decades of life; males outnumbering females by a ratio of two to one.[2] Anorexia, weight loss, fatigue, fever and cardiac symptoms related to the localization of the tumor comprise the clinical picture which closely resembles pericarditis. In 75 percent of cases, correct diagnosis has been established at postmortem examinations[1]. Morphologically, these tumors may be either localized or diffuse. Dawe et al[3] have defined three histological subtypes of pericardial mesothelioma: pure epithelial, spindle cell, and mixed. Metastases to the pleura, adrenal glands and skin have been noted in 25 percent of cases[4]. The prognosis of the disease is poor. Surgical excision is usually impossible, and treatment with irradiation and chemotherapy generally lead only to temporary improvement[4]. The mortality rate is 60 percent within six months following the appearance of clinical symptoms[5].

We decided to present our case because the number of childhood cases of this type of tumor diagnosed preceding death is extremely rare.

Case Report

A nine and a half year old boy was admitted to the Istanbul University Children's Hospital with symptoms of cough, dyspnea and mild fever of one month's duration. The history did not reveal any pertinent information such as exposure to asbestos fibers. Physical examination revealed dyspnea, and crepitations were heard in the lower lobes. Cardiac dullness was found to be enlarged. The heart sounds were muffled.

Laboratory studies which included peripheral blood counts, serum glucose, urea, creatinine and electrolytes were all within normal limits except for an elevated

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erythrocyte sedimentation rate of 90 mm/h. The chest teleradiogram revealed a cardio-thorax index of 0.7, and the left cardio-phrenic angle was obscured. The ECG showed negative S – T waves in the left precordial leads. Echocardiography revealed a significant collection of fluid and a large cystic mass located on the left side and posteriorly within the pericardium (Fig. 1). Axial computerized tomograms of the thorax and abdomen revealed a normal abdomen but a mediastinal tumoral mass occupied a substantial part of the left hemithorax (Fig. 2). Cytologic

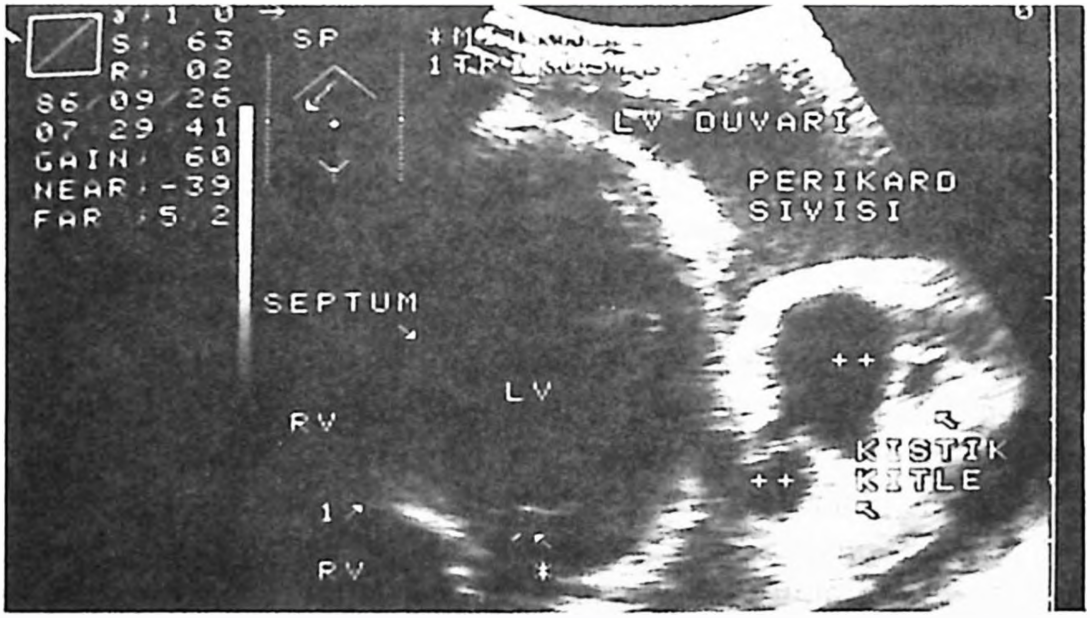

Fig. 1: The appearance of pericardial fluid and cystic mass on parasternal short axis examination

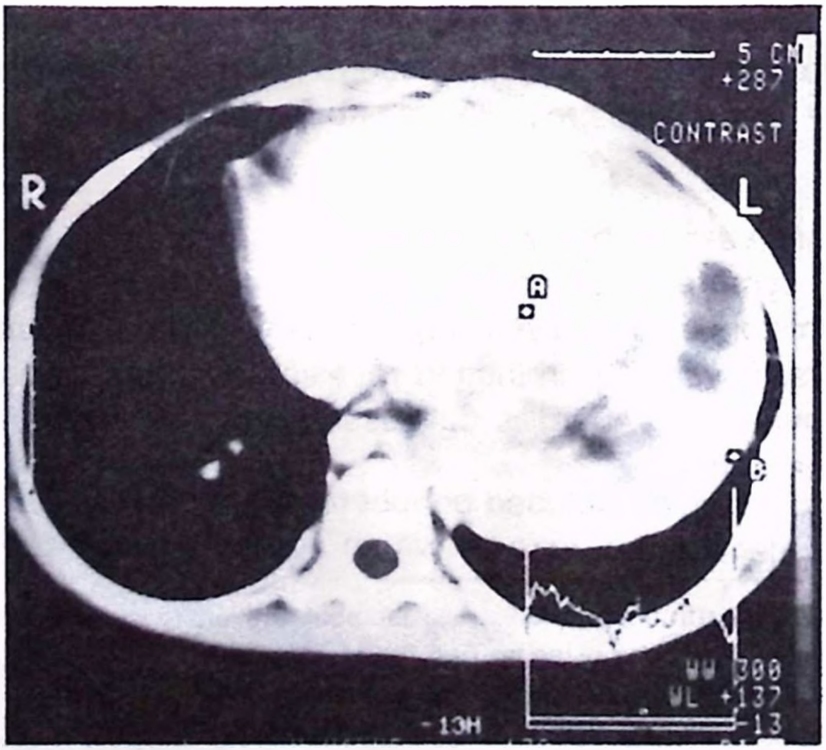

Fig. 2: Computerized axial tomogram of the thorax showing solid tumoral matter starting from the left upper mediastinum and covering a substantial portion of the front and central sections of the left hemithorax, extending down on to the left diaphragm, and containing necrotic areas

examination of the pericardial fluid disclosed copious atypical mesothelial cells. An open pericardial biopsy showed a diffuse, well-differentiated, tubulopapillar, malignant epithelial mesothelioma. Combination chemotherapy with cytoxan actinomycin D and dacarbazine was initiated[6]. No apparent clinical improvement was obtained and the patient's condition continually deteriorated. He died fifteen months after his admission. At postmortem examination a pericardial tumor weighing 2460 g and measuring 22 x 19 x 14 cm. was detected. The tumor also involved the heart. The mass was soft, hemorrhagic, greyish-yellow and could easily be separated from the adjacent tissues. It was partially necrotic and contained many cysts (Fig. 3). A small section of the tumor had invaded the

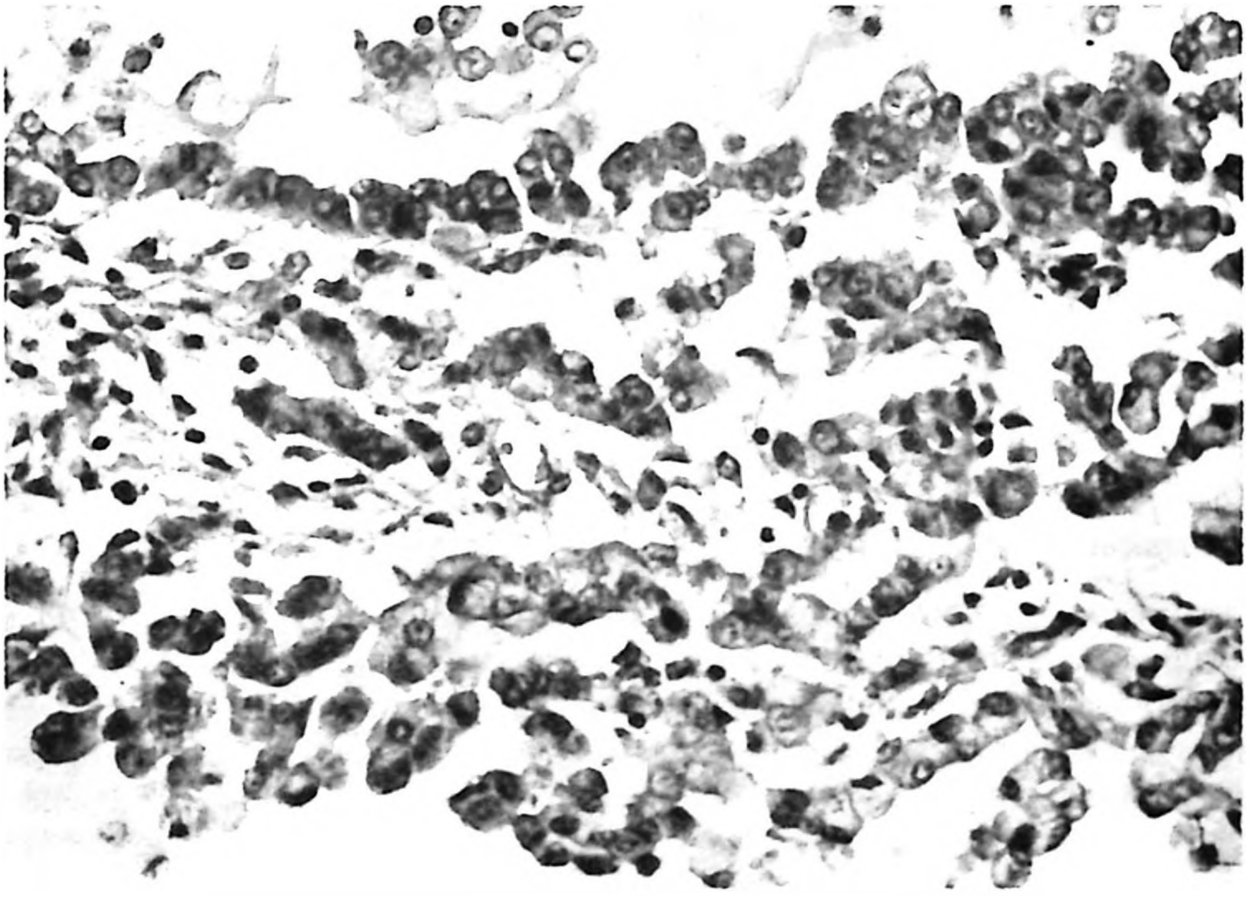

Fig. 3: Epitheloid type mesothelioma of tubulopapillar structure

myocardium. No tumoral formation was seen in the hilar, bronchial or mediastinal lymph nodes. Light and electron microscopy confirmed the diagnosis of a malignant epitheloid mesothelioma, and tubulopapillar in type, as identified in the biopsy (Fig. 4).

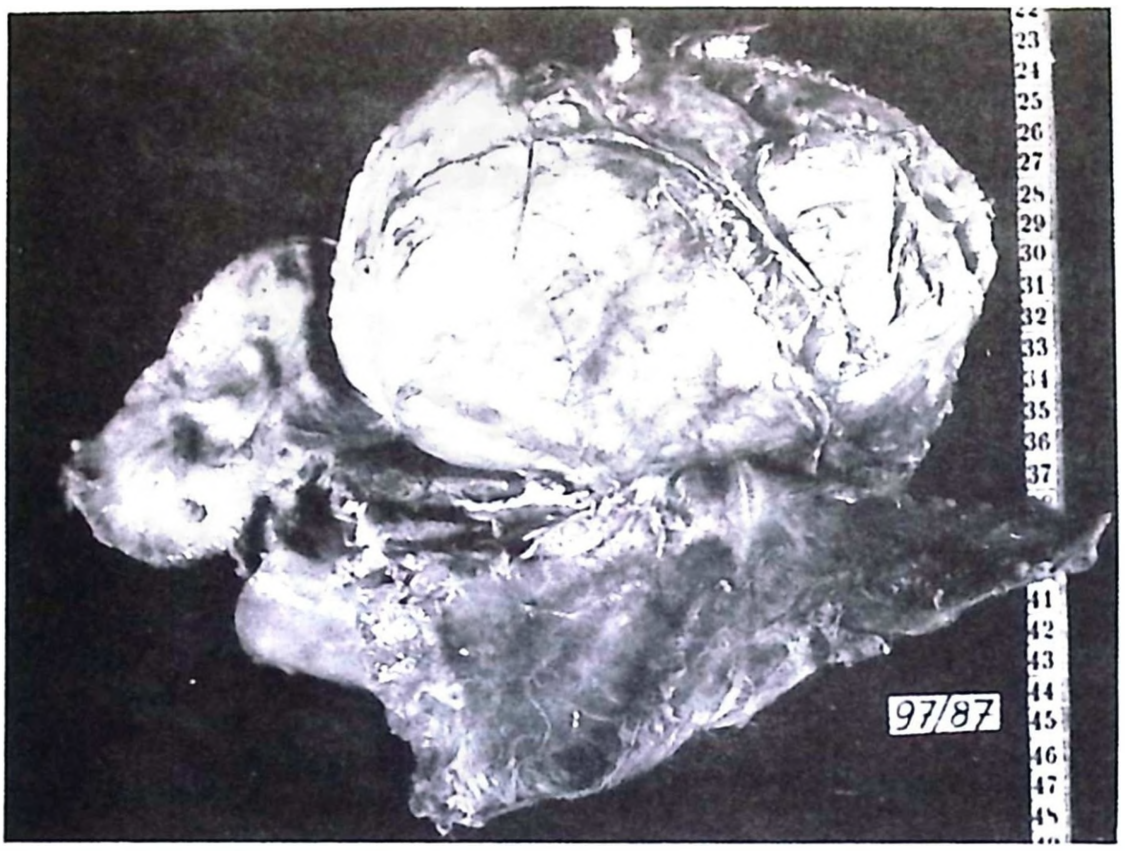

Fig. 4: Tumoral matter which can easily be separated from the pleura, and with no penetration to the parietal pericardium

Discussion

Primary pericardial mesothelioma is a very rare neoplastic disease. Pleural mesotheliomas are reported usually to be associated with pulmonary asbestosis[7]. The etiologic factors in pericardial mesotheliomas are yet unclear. The family and personal histories of this case disclosed that there had been no previous exposure to materials containing asbetos fibers. Besides, it has been reported that a period of latency ranging from 12 to 38 years after exposure to asbetstos fibers is necessary for this tumor to develop.[8]

Primary pericardial mesothelioma is an occasional diagnosis in all age groups but it is still rarer in children. In a review of the relevant literature, we were able to find only six pediatric cases reported to date[8-13].

The majority of the cases present as pericarditis[4]. Telecardiographic and ECG findings of our patient were also highly suggestive of pericarditis, but the echocardiographic examination revealed a retrocardiac cystic mass. It is also sometimes difficult to distinguish between malignant mesothelial cells and reactive cells on cytologic examination. Since a homogenous pericardial mass may be mistaken for fluid in echo imaging, CAT examination is more valuable in clinical diagnosis.[5]

It should also be noted that in 74 percent of cases pleural mesotheliomas involve both the pericardium and myocardium, and they must be carefully excluded in diagnosing primary pericardial mesothelioma[14]. In our case, postmortem examination revealed that the pleura was free of tumoral involvement. Our findings were in complete agreement with the criteria devised by Andersen and Hansen[9] which include limitation of the disease only to the pericardium, no tumoral penetration of the parietal pericardium, only regional lymph node involvement, if at all, and the verification of these criteria at postmortem examination.

Summary

A nine and a half year old boy was brought to the hospital because of a cough, dyspnea and mild fever. He was well-nourished and had an uneventful history. His chest X-ray and electrocardiographic findings suggested pericarditis but further examinations and an open pericardial biopsy revealed a mass histologically diagnosed as pericardial mesothelioma, a very rare tumor in this age group.

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ECTOPIC THORACIC KIDNEY*

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Key words: ectopia, kidney, thoracic kidney

Ectopic intrathoracic kidney is a very rare developmental anomaly which is usually asymptomatic and is an incidental finding on chest radiographs taken for other reasons. In a series of 15,919 autopsies performed on children, twenty-two cases of ectopic kidney were reported and only one case was diagnosed as intrathoracic.[1] Most intrathoracic kidneys which occur predominantly in males, are located in the left hemithorax. About sixty cases of this anomaly have been reported to date.[1-5] Other congenital abnormalities may, however, be associated with ectopic intrathoracic kidney.[4] In this paper we report a case of intrathoracic kidney, the purpose of which is three-fold:

(1) To draw the attention of the clinician to the existence of intrathoracic kidney in the differential diagnosis of low chest densities. (2) To report the youngest female case of intrathoracic kidney, of which, up until now, there have been no published accounts in the literature. Incidentally, our case was that of a female which is in contrast to the reports demonstrating male preponderance of this anomaly. (3) To stress that these types of kidneys function very well and that there is no need for medical therapy or surgical intervention after the correct diagnosis is made.

Case Report

A five-month-old female infant was hospitalized with the diagnosis of bronchopneumonia. The infant was febrile and auscultatory findings were consistent with bronchopneumonia. Plain chest radiograph showed parahilar and paracardial infiltrates supporting the clinical diagnosis. There was an additional dome-shaped density on the left diaphragm superimposed on the cardiac silhouette (Fig. 1).

Ultrasonography demonstrated that the dome-shaped density was a kidney with normal anatomical structures. For further clarification, intravenous urography (Fig. 2), scintigraphy (Fig. 3), and computerized tomography (Fig. 4) were performed which all verified the existence of an abnormally located left kidney.

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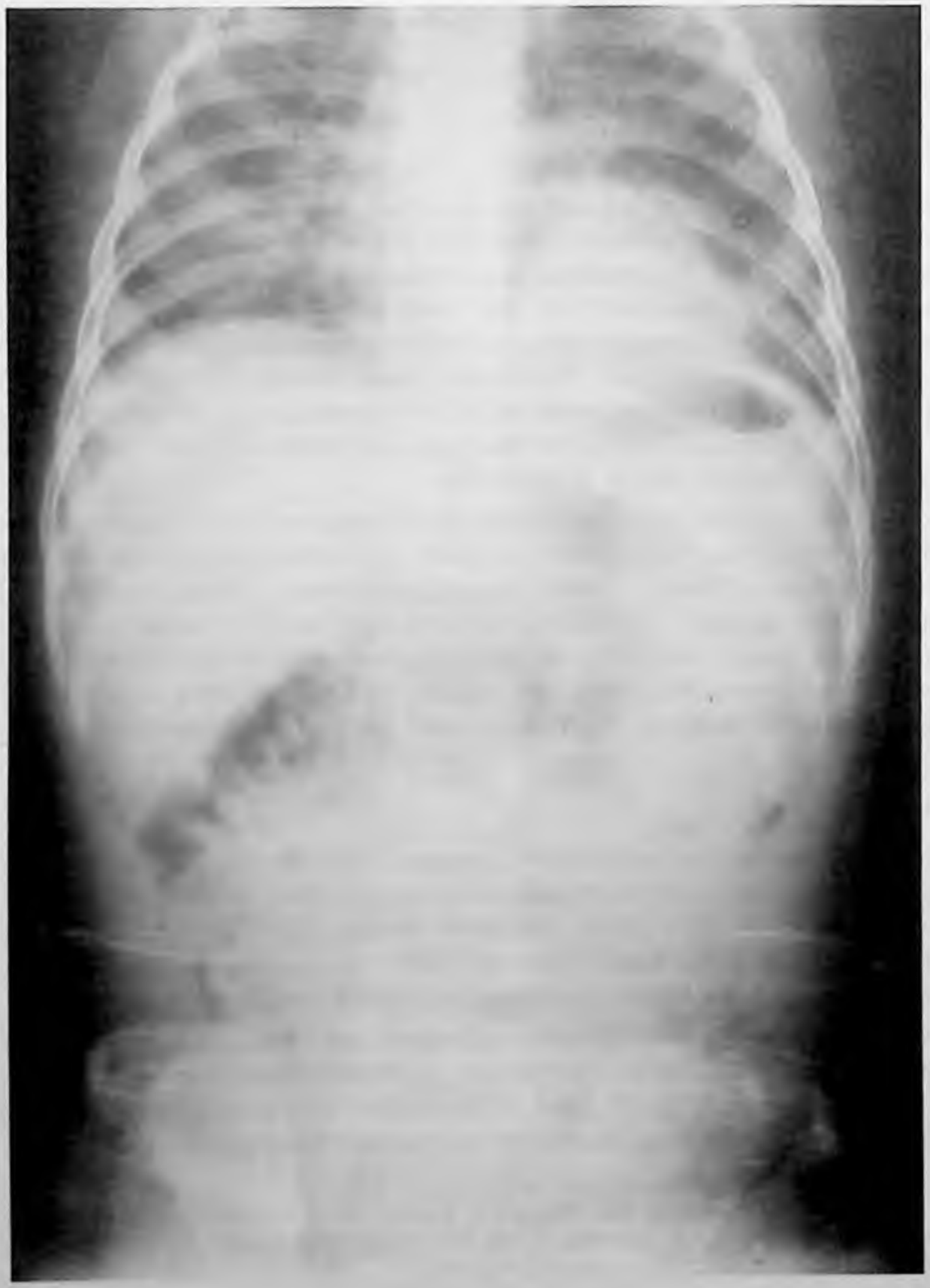

Fig. 1: Plain chest and abdominal radiographs of the patient. Note the dome-shaped density on the left diaphragm superimposed on the cardiac silhouette.

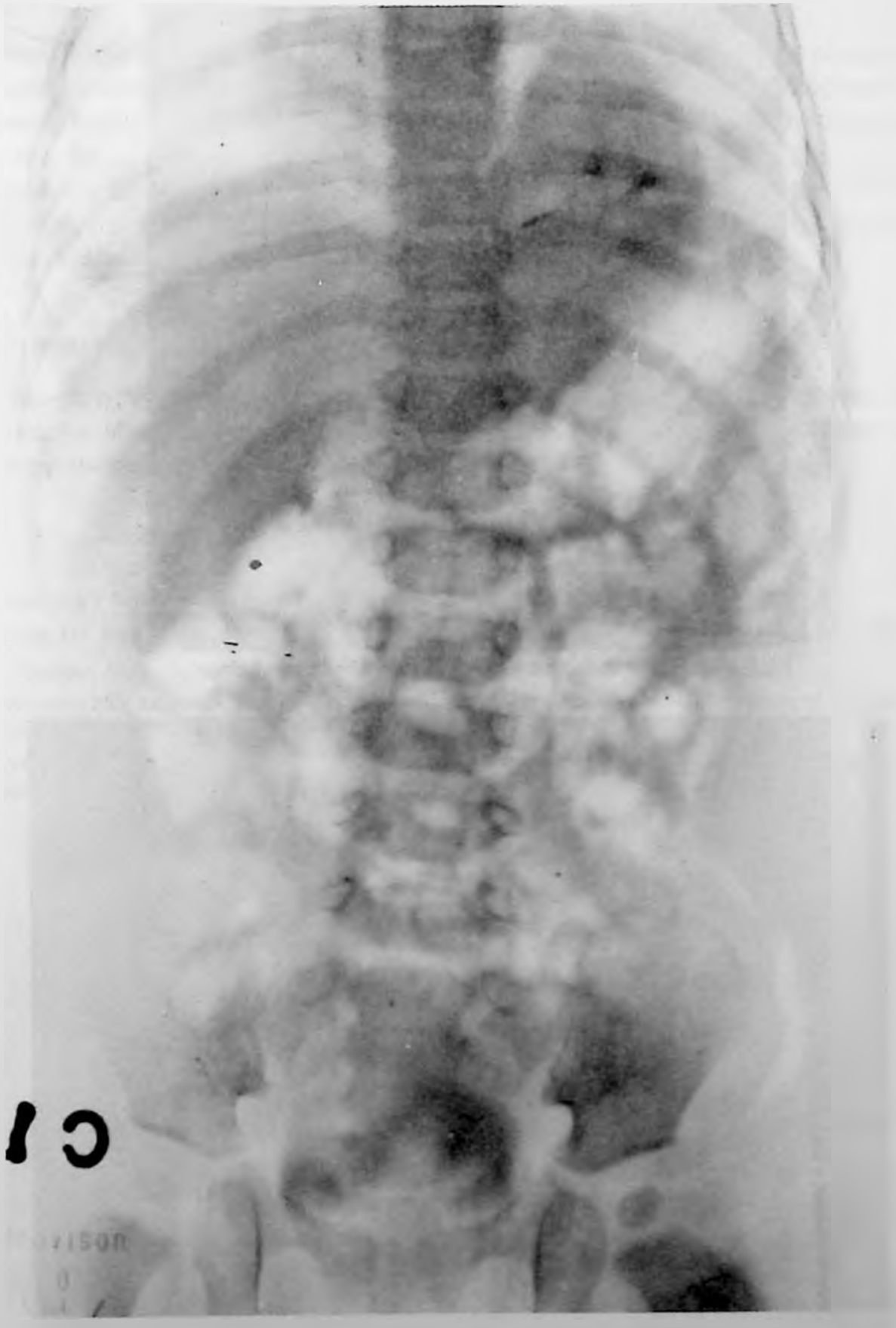

Fig. 2: Intravenous pyelogram of the patient.

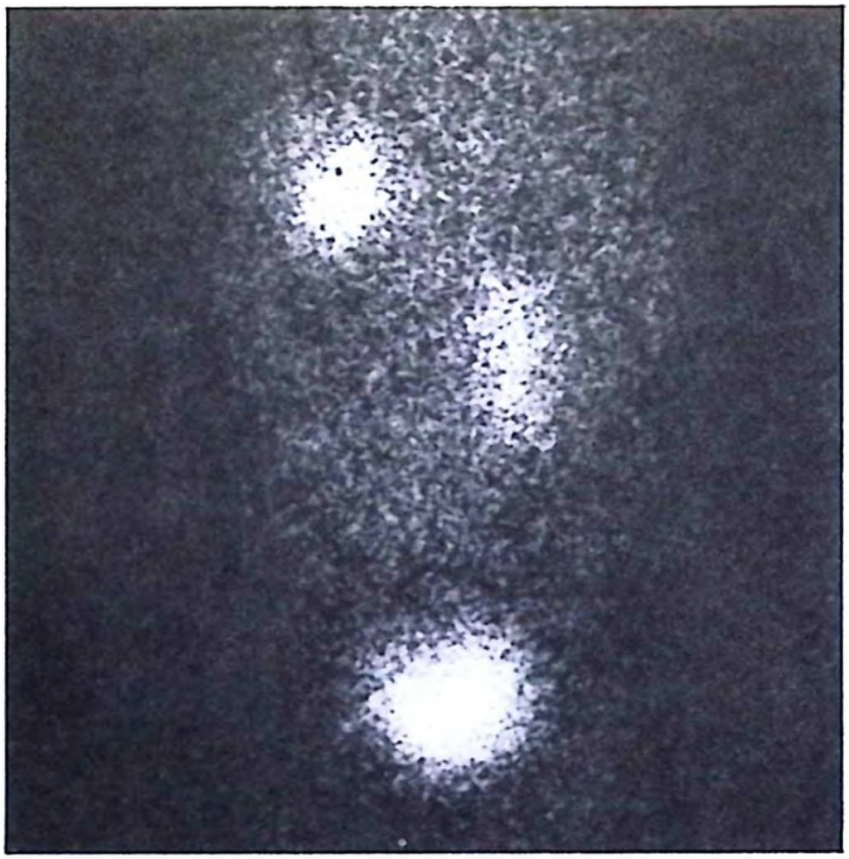

Fig. 3: Renal scintigram demonstrating ectopic kidney.

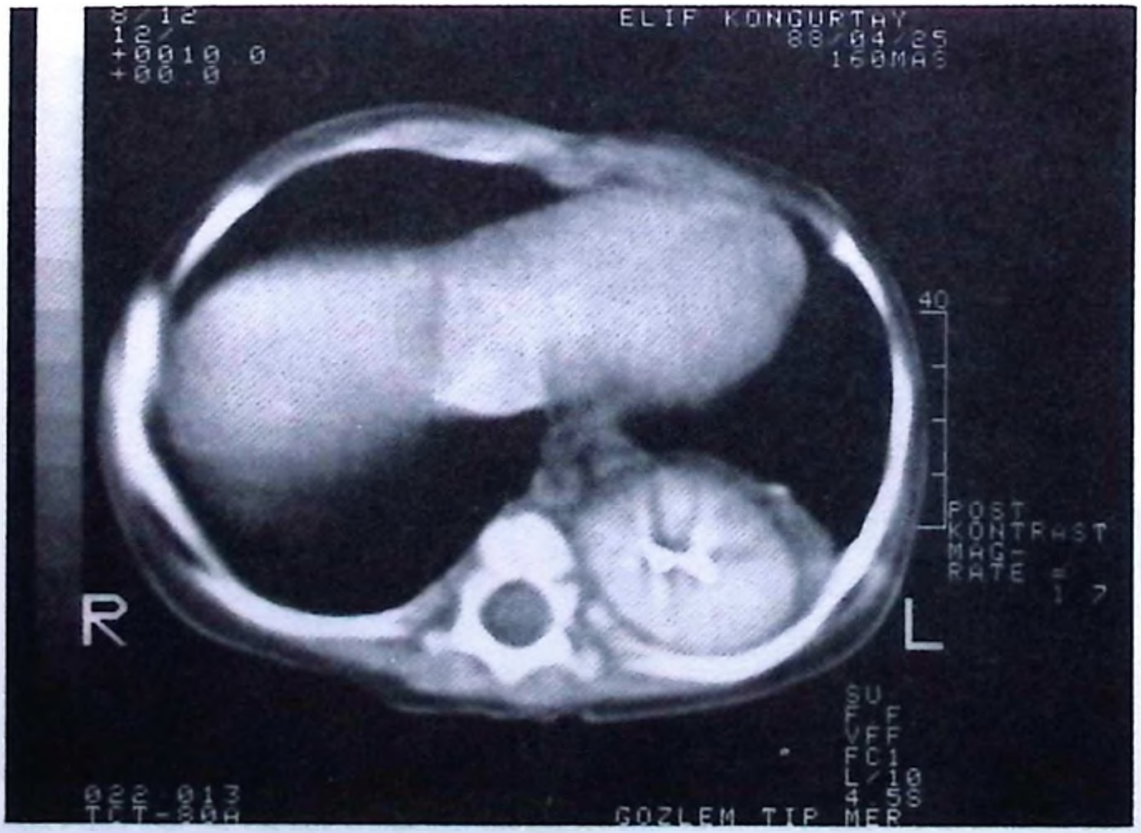

Fig. 4: Computerized tomogram of the patient.

Discussion

Intrathoracic kidney is a very rare congenital anomaly occurring at all ages. It is usually encountered during the evaluation of routine chest radiographs. The density suggesting intrathoracic kidney is usually a dome-shaped shadow masked by the heart and is sometimes interpreted as a pathology of the lung. It is necessary to distinguish this anomaly from a mass lesion. Although low ectopic kidneys are frequently prone to infection and stone formation, intrathoracic kidneys are usually asymptomatic and function normally.[1-5]

Summary

A five-month-old female infant was hospitalized for bronchopneumonia. Ultrasonography and other studies demonstrated the presence of an ectopic thoracic kidney with normal anatomical structures.

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ERYTHROBLASTOPENIA AND LEUKOPENIA IN THE PATIENT WITH SEVERE HERPES ZOSTER TREATED WITH INTRAVENOUS ACYCLOVIR*

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Key words: acyclovir, herpes zoster, erythroblastopenia, leukopenia

Herpes zoster is an acute infection characterized by crops of vesicules, usually confined to a dermatome, and by pain in the same area. Postherpetic secondary bacterial infections may occur. Antiviral agents such as vidarabine (adenine arabinoside) have been used to treat patients with severe or disseminated zoster. Acyclovir (Zovirax, a product of Wellcome Foundation, Ltd) is well-known as having in vitro activity against the Herpes group of viruses[1-2]. In addition, acyclovir has been shown to be effective in herpes zoster[3, 4].

We present a patient with severe herpes zoster in whom transient erythroblastopenia and leukopenia were observed on the second day of therapy with acyclovir. As far as we know, this is the first such case to be reported in the literature.

Case Report

A seven-year-old girl was admitted to Dr. Sami Ulus Children's Hospital with complaints of severe thigh pain and eruptions. There was no history of varicella.

Physical examination revealed dense, erythematous macular and vesicular eruptions on the left thigh, lower left back and left labium majora, which became sparse at the midline level (Fig. 1). Other findings were normal.

Laboratory studies revealed a throat culture yielding group A beta hemolytic streptococci. Urinalysis was normal. Hemoglobin was 12.4 g/dl, red blood cells 4.34 million per mm^3, hematocrit 34.6 %, white blood cell count 6800 per mm^3 with 38 % neutrophils, 60 % lymphocytes, and 2 % band forms. The erythrocyte sedimentation rate was 6 mm per hour. The varicella-zoster virus was demonstrated by cytopathic effects on the cell culture in the Department of Virology, Hifzisihha Institute, Ankara.

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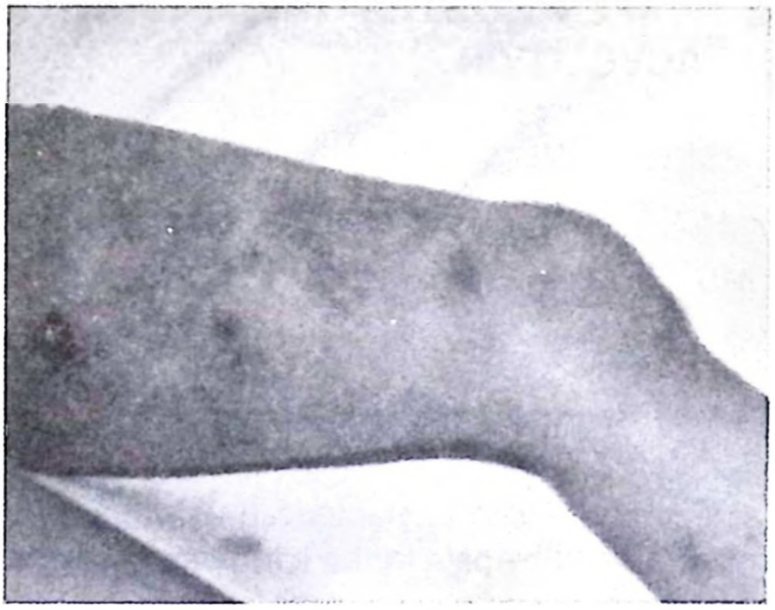

Fig. 1: Hemorrhagic and necrotic vesicles on the left thigh.

Intravenous acyclovir infusion in doses of 5 mg/kg every eight hours was begun. Each vial of Zovirax used for I.V. infusion was reconstituted by the addition of 10 ml physiologic saline. This provided a solution that contained 25 mg acyclovir per ml. 120 mg of acyclovir (5 mg x 24 kg of body weight) were added to 100 ml 0.9 % NaCl, which was given within an hour.

On the second day of therapy no new eruptions were seen. The vesicles were demarcated, and some began to form crusts. Hemoglobin was 10.5 g/dl, hematocrit 31 %, red blood cells 4.3 million per mm^3, and white blood cell count 5000 per mm^3. On the third day, the hemoglobin fell to 9.9 g/dl, red blood cells were 3.2 million per mm^3, and white blood cell count 4000 per mm^3. The erythrocytes were normochromic and normocytic. Bone marrow aspiration showed a decrease in the number of erythroblasts and a relative increase in the number of promyelocytes and myelocytes (Fig. 2). Phenoxymethyl penicilin

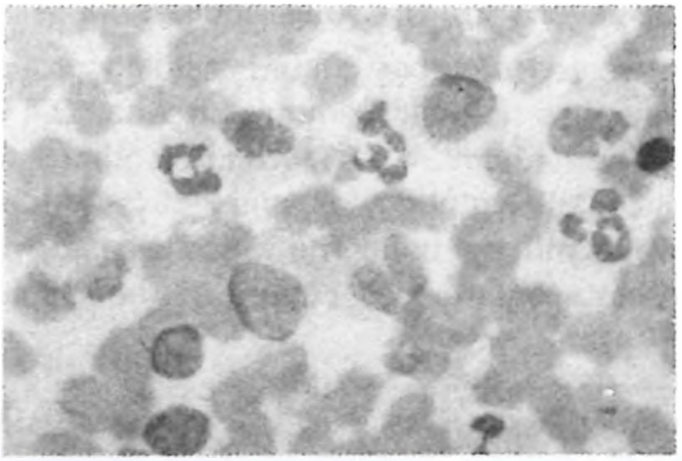

Fig. 2: On the third day, myelocytes and promyelocytes increased and erythroid precursors decreased in the bone marrow aspiration.

(penicillin V) 50,000 U/kg p.o. was started because of a positive throat culture. At the end of the third day of therapy the body temperature dropped to normal and all the vesicles had formed crusts. On the fifth day of therapy hemoglobin was 9.9 g/dl, red blood cells 4 million per mm^3, and white blood cell count 2800 per mm^3. Therapy was discontinued at the end of the fifth day. On the seventh day, hemoglobin, red blood cells, and white blood cells were normal. During the course of therapy, platelets, serum creatinine, creatinine clearance and serum transaminases were normal; direct Coombs test, and cold and warm agglutinins were negative. Normal bone marrow morphology was seen in the control aspiration in the second week. The clinical and hematological courses of the patient are shown in Table 1.

TABLE I. Summary of the Hematological Findings of the Patient

DAYS	1	2	3	4	5	6	7
Hemoglobin (g/dl)	12.4	10.5	9.9	9.9	9.9	11	12
Red blood cells (million/mm^3)	4.34	4.3	3.2	3.5	4	4.5	4.3
Hematocrit (%)	34	31	26	26	29	32	34
White blood cell count (per mm^3)	6800	5000	4000	3800	2800	3600	5800

Discussion

Acyclovir is converted to its monophosphate by the herpes virus enzyme, thymidine kinase. Host cell enzymes add a second and third phosphate group to form acyclovir diphosphate and acyclovir triphosphate. Acyclovir triphosphate is both a competitive inhibitor and a substrate for viral DNA polymerase, but shows little interaction with normal cell DNA polymerase[5].

Instances of transient rises in blood urea and creatinine have been reported after the administration of intravenous acyclovir[6]. The changes have been reversible on cessation of therapy and have sometimes resolved even while therapy was continued. A transient rise in serum transaminases has also been seen. A limited number of local reactions at the injection site has been reported[7].

Evidence of hematopoietic suppression has not yet been observed.[8-10] Acyclovir does not inhibit hematopoietic recovery after marrow transplantation when compared with a placebo[8]. In our patient, we observed transient erythroblastopenia and leukopenia on the second day of therapy. This may have been related to viral infections or the drug. It is known that viruses commonly causing leukopenia include hepatitis A and B, respiratory syncytial influenza A and B, measles, rubella and varicella. However, in the afore-mentioned infections erythroblastopenia has not been observed to be associated with leukopenia[11-12].

Drug induced neutropenia and leukopenia are not usually associated with an enlarged spleen, segmented or band neutrophils in the peripheral blood or generalized hyperplasia of the bone marrow; this may be an associated transient erythroblastopenia. These changes may be due to either immune-mediated destruction or progenitor failure[13]. We observed a relative increasing number of myelocytes and promyelocytes and an absolute decreasing number of erythroid progenitors in the bone marrow aspiration on the third day of therapy.

The transient erythroblastopenia and leukopenia observed in our patient may be related to the administration of acyclovir. We could not explain this transient hematological change due to any other cause. Fortunately, changes in the hematopoietic tissue were transient but this observation prompted us to monitor the hematological findings during acyclovir therapy.

Summary

A seven-year-old girl with transient leukopenia and erythroblastopenia which developed after the administration of acyclovir is presented. Ayclovir infusion was given in a dose of 5 mg/kg/every eight hours. On the third day of therapy the hemoglobin level fell to 9.9 g/dl, the hematocrit was 26 %, the white blood cell count 4000 percent/mm^3, red blood cells 3.2 million percent/mm^3. Bone marrow aspiration showed a decrease in the number of erythoblasts and a relative increase in the number of promyelocytes and myelocytes. Therapy was discontinued on the fifth day, and on the seventh day the findings were normal including the bone marrow aspiration.

We could not find any other reason which would cause transient erythroblastopenia and leukopenia in our patient.

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