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THE CORONA MORTIS: AN ANATOMIC CADAVER STUDY

Aysun Uz* • Çiğdem Erkuran* • Mehmet Cem Bozkurt* • İbrahim Tekdemir*

SUMMARY

In this study, we examined the anastomosis situated between the branches of the obturator and the external iliac arteries and veins that form the corona mortis in order to determine whether it is arterial, venous or both. Seven fixed cadavers (14 pelvic halves) were used. A communicating branch between the external iliac vein and the obturator vein over the superior pubic ramus was observed in all specimens. We called this branch the "communicating vein" ("v. communicans"). An accessory obturator artery was seen in two specimens. Our study showed that the corona mortis located over the superior pubic ramus and formed by the communicating vein is actually a venous anastomosis.

Key Words: *Anatomy, corona mortis, obturator artery, obturator vein, vascular anastomosis*

ÖZET

Corona Mortis Üzerine Anatomik Bir Kadavra Çalışması

Bu çalışmada, a. v. obturatoria ile a. v. iliaca externa'nın dalları arasında yer alan anastomozlar olarak tarif edilen corona mortis'in sadece arteriyel veya venöz mü yoksa her ikisi tarafından mı oluşturulduğu araştırıldı. Çalışmada 7 fikse kadavra (14 yarım pelvis) kullanıldı. İncelenen örneklerin hepsinde ramus superior ossis pubis üzerinde, v. iliaca externa ile v. obturatoria arasında birleştirici bir dal tespit edildi. Bu dal tarafımızdan v. communicans olarak isimlendirildi. İki örnekte ise a. obturatoria accessoria görüldü. Çalışmamız göstermiştir ki; ramus superior ossis pubis üzerinde yer alan ve v. communicans olarak isimlendirdiğimiz damarın oluşturduğu corona mortis aslında bir ven anastomozudur.

Anahtar Kelimeler: *Anatomi, a. obturatoria, v. obturatoria, corona mortis, vaskuler anastomozlar*

The vascular connection between the obturator and the external iliac systems is known as the "corona mortis" (1,2,3,4,5,6). Although detailed information is available on the arterial anastomosis of the corona mortis, a definition of the venous system is lacking. Classical anatomy textbooks describe a tiny anastomosis on the dorsal side of the pubic symphysis between the obturator and the external iliac arteries, but do not mention if this anastomosis can be life threatening (1,3,4,7,8). Nevertheless, it is stated that in cases where the obturator artery is not seen (20%-30%), the accessory obturator artery originating from the external iliac artery or its tributaries may present a risk (4,7,8). Tornetta et al. and Gilroy et al. confirmed some consequential connections between the veins situated on the superior pubic ramus (70%) (2,5). In surgical approaches, knowledge of this anastomosis, located over the superior pubic ramus between the arterial and the venous systems, gives confidence to the surgeon (1,2,3,4,6). In this work, we studied whether the anastomosis that forms the corona mortis is arterial, venous or both.

MATERIALS AND METHODS

Seven fixed cadavers (14 halves) were dissected. An incision beginning from the bony landmark of the anterior superior iliac spine to the pubic symphysis was performed, and the superficial soft tissues and abdominal wall muscles of the region were removed. The dissection proceeded to the anterior axillary line and to the costal margin. The anterior abdominal wall was then tipped over medially. Dissection clearly revealed the starting point of the inferior epigastric artery in the facia of the rectus abdominis muscle. Next, vas-

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cular structures that course vertically on the superior pubic ramus were uncovered and examined to determine whether they were arterial, venous or both.

A vernier caliper sensitive up to 0.1mm was used to measure the external diameters of the vessels that form the corona mortis and the distance from the pubic symphysis to the anastomosis.

FINDINGS

A venous anastomosis on the superior pubic ramus was a consistent finding in all cases. These venous connections between the external iliac and the obturator veins can be seen in Figure 1. The average external diameter of this "communicating vein" was 3.26 mm (2.17-4.87 range). This vein coursed vertically to inferior of the superior pubic ramus and connected to the obturator vein. This type of connection was detected inside the obturator foramen in some cases and outside the foramen in others (Figs. 1, 2).

In 12 of the cadaver halves, the obturator artery originated from the internal iliac artery and branched before entering the obturator foramen, or pubic ramus. This branch coursed to the dorsal side of the pubis and anastomosed with the pubic branch of the inferior epigastric artery. The average diameter of these connecting vascular structures was measured as 0.98 mm (0.60-1.24 range).

In two of the samples, the obturator artery originating from the internal iliac artery could not be found. Instead, an extension of the external iliac artery was observed in one sample and an accessory obturator branch from the inferior epigastric artery was observed in the other (Figs. 2, 3). This artery coursed from the superior pubic ramus vertically to enter the obturator foramen. The measured diameters of this vessel were 2.38 and 2.24 mm. An obturator vein (Fig. 2) could be seen in one of these two cases but could not be seen in the other (Fig. 3).

The average distance between the dorsal side of the pubis and the arterial or venous anastomosis was 40.44 mm (33.22-52.72 range).

It was observed that the venous arch over the superior pubic ramus was in close connection with the femoral ring and the lacunar ligament (Fig. 4).

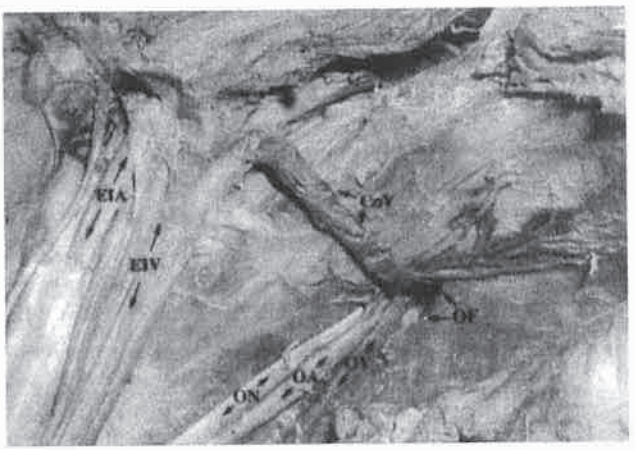

Figure 1: The "communicating vein" is situated between the external iliac and the obturator veins, left side upper view (EIA: external iliac artery; EIV: external iliac vein, ON: obturator nerve; OA: obturator artery, CoV: communicating vein; OV: obturator vein; OF: obturator foramen).

Figure 2: Accessory obturator artery originating from the inferior epigastric artery and two foramen tributaries of the communicating vein (CoV1 and CoV2), right side upper view (EIA: external iliac artery; EIV: external iliac vein; IEA: inferior epigastric artery; AOA: accessory obturator artery; CoV: communicating vein; CoV1: branch of the communicating vein; CoV2: branch of the communicating vein; OV: obturator vein; OF: obturator foramen).

DISCUSSION

The pubic branches between the inferior epigastric artery and the obturator artery are surgically significant. If the branches are thick, they may pose a great risk. Odar mentions that if the anastomosis between the obturator branch of the inferior epigastric artery and the pubic branch of the obturator artery is thick it may be injured during femoral hernia repairs (9).

McMinn and Grant document the accessory obturator artery on the superior pubic ramus in their well-known anatomy atlases (10,11). In the absence of the

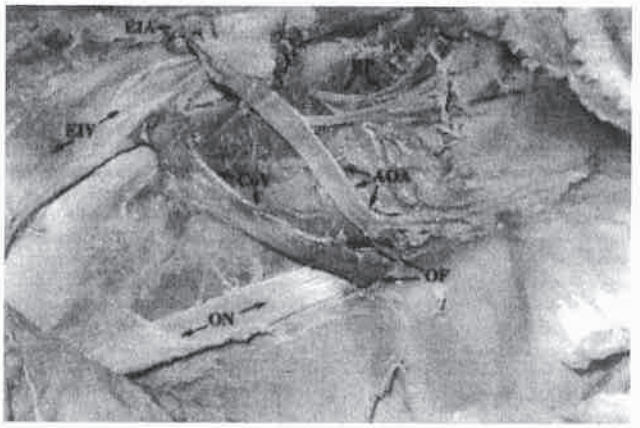

Figure 3: Accessory obturator artery orginating from the external iliac artery, left side upper view (EIA: external iliac artery; EIV: external iliac vein; CoV: communicating vein; AOA: accessory obturator artery; RP: pubic branch; ON: obturator nerve; OF: obturator foramen).

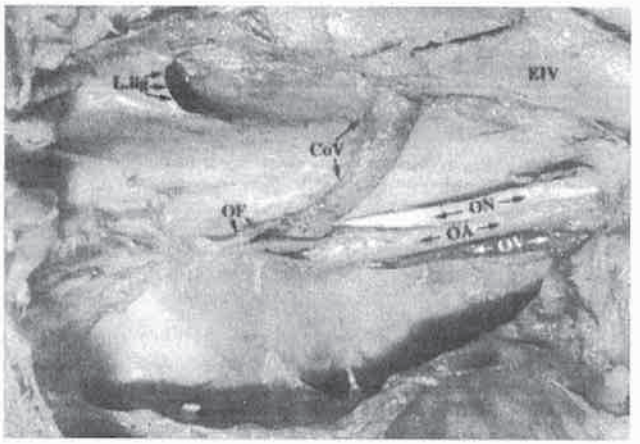

Figure 4: Close relationship between the lacunar ligament and the communicating vein, right side upper view (EIV: external iliac vein; L. Lig: Lacunar ligament; CoV: communicating vein; ON: obturator nerve; OA: obturator artery; OV: obturator vein; OF: obturator foramen).

obturator artery, several authors mention an unusual accessory artery that originates from the inferior epigastric artery or a thickened portion of the inferior epigastric artery (1,4,6,8,11). According to Moore, the incidence of this unusual or accessory vessel is 20% (4). Textbooks state that if the anastomosis is formed by a thick branch, surgery of this region may be risky. The tiny anastomosis behind the pubic symphysis, however, has not been defined (1,4,5,8,11,12). Only Mainland, Odar and Yıldırım considered these tiny structures as a part of the corona mortis (3,6,9). In our study, tiny connections between the obturator and the external iliac arteries were considered less important, since their average diameter is approximately 0.98 mm, and they are located away from the surgical field. On the other hand, there is a possibility of a surgical risk when the accessory obturator artery exists in place of the obturator artery. The diameter of this accessory artery, located on the superior pubic ramus, was found to be 2.88 mm in one case and 2.24 mm in another.

Classical anatomy textbooks pay less attention to the veins that form the communicating anastomosis in the area than to the arteries. Although Moore refers to the venous connection as the "accessory obturator vein", and Gray mentions a thick vessel relating to the obturator and the external iliac veins, they do not mention any risks posed in such cases during surgical operations (4,12). Lanz and Wachsmuth refer to the vein that originates from the external iliac vein and runs through the obturator canal, as "vv. comitantes" (13). In Studies describe the corona mortis anastomosis as a vascular structure that is 34% arterial, 70% venous and 20% both (5). In an anatomic cadaver study on South African blacks, Missankov et al. found 12 cadavers with arterial vascular structures, 26 cadavers with venous vascular structures and 12 cadavers with both (14). However, in dissections of 55 cadavers, Gilroy et al noted a relatively higher incidence of the obturator artery variations (70-80%) (2). In these studies, the incidence of venous anastomosis was higher than that of arterial anastomosis.

In our study, we observed a thick vein (3.26 mm diameter on average) between the external iliac and obturator veins in all cases. In the two cases in which an accessory obturator artery was seen, we referred to the vein coursing by this artery as the "communicating vein" rather than the "accessory obturator vein". But regardless of its designation as "unusual", "accessory", or "pubic branch", it is important to note that there is always a thick vein on the superior pubic ramus. The likelihood of the existence of a vein rather than an arterial connection should be noted by surgeons, in light of concerns over venous bleeding.

Tornetta et al. described a morphometric measurement of 60.20 mm (30-90 mm) for the distance from the pubic symphysis to the anastomosis in 50 pelvic halves (5). Our average measurement was 40.44 mm (33.22-52.72 mm). This distance should be taken advantage of in hernia repair (15) and in fixing unstable pelvic fractures.

In conclusion, a consistent venous connection between the external iliac and the obturator veins located on the superior pubic ramus may be called the "communicating vein". This structure forms the corona mortis. In cases when the obturator artery is missing, the accessory obturator artery joins the corona mortis (20-30%). This artery or vein reaches the obturator foramen passing by or over the femoral ring on the superior pubic ramus. Here it has a close relationship with the loose edge of the lacunar ligament and the neck of the femoral hernial sac. The surgeon, in dealing with direct or indirect inguinal and obturator hernia, should be aware of these anastomoses and their close relationship to the femoral ring.

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DIAGNOSTIC PERFORMANCE OF SERUM DIPEPTIDYL PEPTIDASE IV ACTIVITY IN DEPRESSION

Serenay Elgün* • Aytaç Keskinege* • Hakan Kumbasar**

SUMMARY

Dipeptidyl peptidase IV (DPPIV) is a T-cell associated enzyme which is known to possess an essential role in T-cell-mediated immune response. Serum DPPIV activity was shown to be significantly lower in major depressives in comparison to minor depressives. Since immune-inflammatory alterations have been repeatedly reported in depression, decreased serum DPPIV activities in depressed patients compared to healthy controls or in major depressives compared to minors, may reflect the impaired immune state in depression.

In this regard, we aimed to evaluate the diagnostic performance of serum DPPIV activity measurement as a discriminatory variable in depression. Receiver operating characteristics (ROC) curve which is used to estimate the quantitative performance of a test, revealed that the sensitivity and the specificity of the test was efficient in separating major depressives both from minor depressives and healthy subjects.

Key Words: *Dipeptidyl peptidase IV, depression, ROC curve*

ÖZET

Serum Dipeptidil Peptidaz IV Aktivitesinin Depresyondaki Tanısal Performansı

T hücre ile ilişkili bir enzim olan dipeptidil peptidaz IV (DPPIV)'ün T-hücre aracılı immün yanıtta esensiyal bir rol oynadığı bilinmektedir. Serum DPPIV aktivitesinin major depresyonlularda minör depresyonlulara göre anlamlı oranda düşük olduğu gösterilmiştir. Depresyonda immün-inflamatuar değişimler olduğu sıklıkla bildirildiğinden, depresif hastalarda sağlıklı kişilere kıyasla veya majör depresiflerde minörlere kıyasla daha düşük bulunan serum DPPIV aktiviteleri depresyonda immün durumun bozulduğunu gösterebilir.

Bu bakımdan, serum DPPIV aktivite ölçümünün depresyonda ayırdedici bir değişken olarak tanısal performansının değerlendirilmesine karar verildi. Bir testin kantitatif performansını belirlemek için kullanılan Receiver operating characteristics (ROC) eğrisi, testin majör depresifleri hem minörlerden hem de sağlıklı kişilerden ayırdetmek için yeterli sensitiflik ve spesifikliğe sahip olduğunu açığa çıkardı.

Anahtar Kelimeler: *Dipeptidil peptidaz IV, depresyon, ROC erisi*

DPPIV (CD26) (EC 3.4.14.5) is an exopeptidase which removes N-terminal dipeptides from peptides with a proline or alanine at the penultimate position. Within the hematopoietic system, DPPIV is identified as CD26, the T-cell activation antigen and is predominantly expressed on the cell membrane of human T lymphocytes and plays a key role in T-cell-mediated immune response (1). Serum DPPIV activity has been measured in several immune disorders with the assumption that it might reflect the immunological status (2,3).

Recent studies confirm the hypothesis that severe depression is accompanied with immune-inflammatory alterations (4,5,6). Serum DPPIV activity was measured and found to be decreased in depressed patients compared with healthy subjects suggesting a possible role (6,7,8). However, diagnostic performance of the test was not demonstrated.

There are numerous ongoing studies in search for a reliable biological marker which may be used in the evaluation of psychiatric illnesses. A ROC plot offers an improved capability to judge a test's performance to discriminate between diseased and non-diseased or between two different clinical states such as minor and major depressives. When evalauting the performance of a test, confusion is avoided by using the ROC curves instead of only accepting statements such as "the test is very sensitive or very specific". It has been ad-

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vocated that the area under the curve is a relative measure of a test's performance (9). Therefore, we decided to evaluate the diagnostic performance of an immune state variable, serum DPPIV activity measurement by ROC analysis, also as a discriminatory test in depressed patients and healthy subjects.

MATERIALS AND METHODS

Ninety-eight (54 major, 44 minor) depressed outpatients (mean age ± SD= 34.6 ± 7.2) who were admitted to the Department of Psychiatry, Faculty of Medicine, University of Ankara were included in the study. They were diagnosed and categorised according to DSM-IV criteria. The structured psychiatric evaluation was made on the basis of the National Institute of Mental Health Diagnostic Interview Schedule (10). They were free of any drugs known to affect immune or endocrine function and hormonal preparates including oral contraceptives for at least 1 month prior to blood collection. A diagnosis of major depression was made if within the past month the patient had 2 weeks or more of depressed mood or anhedonia, along with 2 weeks or more of 4 other DIS criterion symptoms. If for 2 weeks or more within the past month, the patient either experienced depressed mood or anhedonia and at least 1 other criterion symptom or, 3 or more criterion symptoms in the absence of depressed mood or anhedonia, it was diagnosed as minor depression.

Sixty-nine healthy control subjects (mean age ± SD= 32.7 ± 5.1) were assessed with the Structured Clinical Interview for DSM-IV, non-patient edition (11) and excluded for past, present and family history of psychiatric disorders. They were also free of any medication for at least 1 month prior to blood sampling. None had ever been taking psychotropic drugs.

All patients and controls had normal physical examinations and none of them reported any long lasting physical illness. Routine clinical laboratory analyses, i.e. blood determinations (liver function tests such as ALT, AST and GGT, renal function tests such as blood urea nitrogen and creatinine, thyroid function tests such as basal TSH, total and free T4, T3, hematologic tests, serum electrolytes and urine tests) were in normal ranges. They all agreed to participate in this study and gave us informed consent.

Sera were separated from blood samples taken at 0830h following an overnight fast and stored at –20°C until enzyme activity was measured spectrophotometrically. DPPIV activity was analysed by colorimetric determination of glycyl-prolyl-p-nitroanilide tosylate hydrolysis (12). Absorbances were read using a Unicam Helios α UV-VIS spectrophotometer (Cambridge, UK). Results were expressed as IU/L. The within-run and between-run precisions of the assay were 2.7% and 3.3%, respectively. All chemicals were purchased from Sigma Chemical Co. (St. Louis, Mo.).

Statistical analyses of data were performed using Student's *t*-test. In order to assess the diagnostic accuracy of serum DPPIV activity in depression, ROC (receiver operating characteristics) curves were plotted (13). ROC curves were generated by plotting the sensitivity (true positives) (y-axis) against 1-specificity (false positives) (x-axis) at various cut-off points of the tests.

RESULTS

Mean ± SD values for DPPIV activities of major, minor depressed patients and controls were 10.09±4.83, 18.58±6.25 and 20.12±8.48 IU/L., respectively. Serum DPPIV activity of major depressives was significantly decreased when compared with minors ($p<0.005$) and controls ($p<0.001$). No meaningful difference was found between the minor depressives and controls. Therefore, ROC analyses were employed in order to assess the separation of major depressed patients from minors and controls, using serum DPPIV activity as the discriminatory variable.

DISCUSSION

Decreased serum DPPIV activity in depressed patients may reflect the T-cell related alterations regarding the immune status, since CD26/DPPIV plays part in T-cell-mediated immune response (1). Besides, lowered serum DPPIV activity in major depressed patients in comparison with minor depressed ones might suggest that major depressives display a greater tendency to immune dysfunction. Assuming that this possible dysfunction in T-cell related immunity in depression might be used for the discrimination between depressed patients and healthy subjects, ROC analyses were performed.

ROC plot of a given test offers an improved capability to judge a test's performance to discriminate between diseased and non-diseased or between two different clinical states such as minor and major depressives. It has been advocated that the area under the

curve is a relative measure of a test's performance (9). When using ROC analysis, one can select different cut-off points to maximise either the diagnostic sensitivity or specificity, according to the clinical needs. We observed that a cut-off value of 15 IU/L gave a diagnostic sensitivity of 90% and a specificity of 80%, when used for the separation between major and minor depressives with a greater area under the curve (Figure 1a). The test was also found efficient for discriminating major depressives from healthy controls as displayed by the ROC curve (Figure 1b). Using the same cut-off value, a 89% sensitivity with a %81 specificity was obtained. Since there was no statistically significant difference between the minor depressives and controls, ROC analysis was not performed for these subgroups.

As a conclusion, serum DPPIV activity seems to be a promising biological marker both in the diagnosis of depression and evaluation of the immune status of depressed patients. As seen, the diagnostic performance of the test has proved to be satisfactory in separating major depressives from healthy subjects and minor depressives. This might also raise the possibility for the test to be included in the categorisation criteria of depression. Thus, the subject is relevant to more attention and further investigation in various aspects.

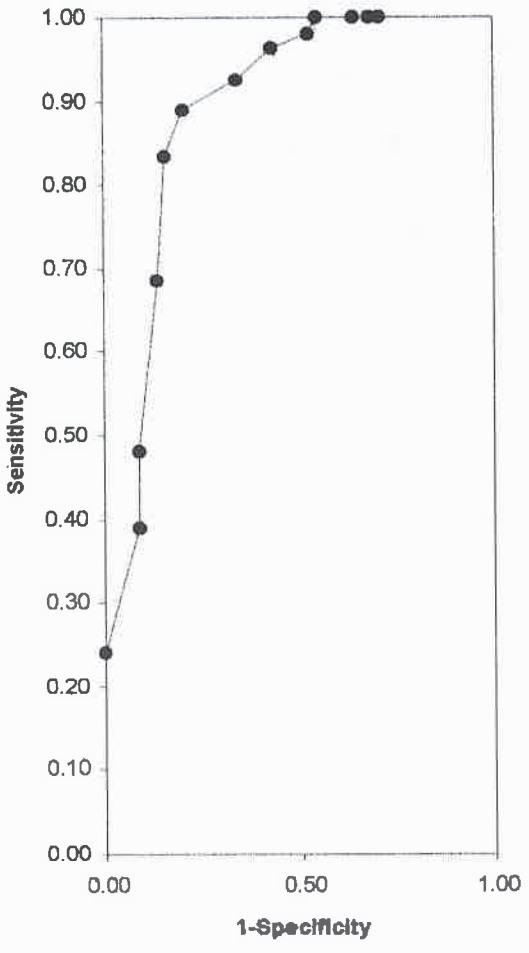

Figure 1(a)

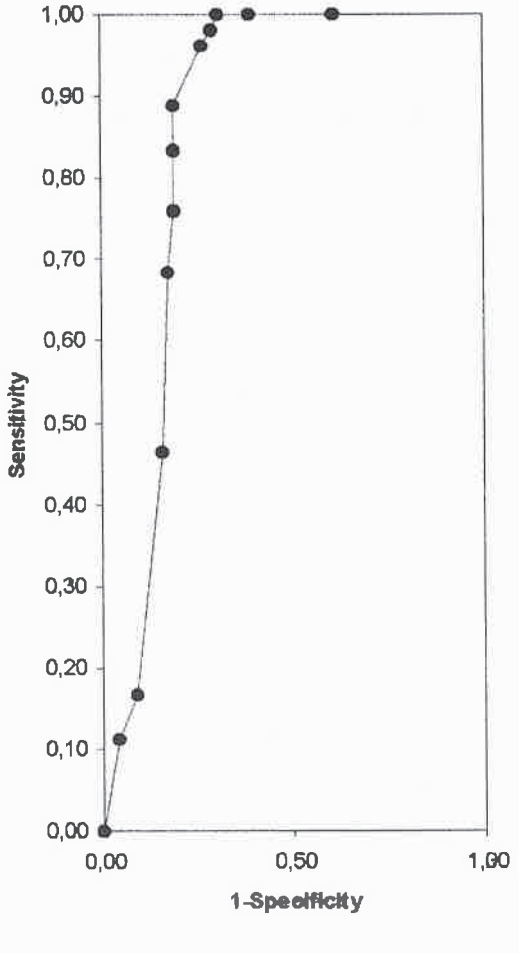

Figure 1(b)

Figure 1: ROC plots showing serum DPPIV activity discriminating between (a) major and minor depressives, (b) major depressives and controls.

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HEART RATE VARIABILITY IN HYPERTROPHIC OBSTRUCTIVE CARDIOMYOPATHY: ASSOCIATION WITH FUNCTIONAL CLASSIFICATION AND LEFT VENTRICULAR OUTFLOW GRADIENTS

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SUMMARY

The aim of this study was to investigate cardiac autonomic control in patients with hypertrophic obstructive cardiomyopathy (HOCM) and to assess the indices of heart-rate variability in relation to clinical and echocardiographic features. Twenty-three patients (17 male, 6 female; mean age 43±11) with HOCM and 18 healthy volunteers were included. M-mode and two-dimensional echocardiography and pulsed and continuous-wave Doppler studies were obtained. All patients and volunteers underwent continuous 24-hour ambulatory ECG monitoring. Time domain variables considered in this study were standard deviation of mean RR intervals (SDRR), root-mean squared successive difference (RMSSD) and percentage of cycles differing from the preceding one by more than 50 msec (PNN50%). Patients were compared to detect associations between indices of heart-rate variability, left ventricular outflow tract obstruction and clinical status. Age-corrected heart-rate variability parameters were also correlated with echocardiographic and clinical characteristics of the patients. New York Heart Association (NYHA) Functional Class III and IV patients had lower values of SDRR index, RMSSD and PNN50% when compared with NYHA Functional Classes I and II (p<0,05). Time domain heart-rate variability parameters were found to be significantly correlated with subaortic dynamic obstruction. In conclusion, heart-rate variability is reduced in HOCM and well-correlated with the degree of subaortic obstruction. Heart-rate variability indices are also sensitive markers of functional status.

Key Words: *Cardiomyopathies, heart rate, hypertrophy*

ÖZET

Hipertrofik Obstrüktif Kardiyomiyopatide Kalp Hızı Değişkenliğiyle Fonksiyonel Kapasitenin ve Subaortik Gradientin Karşılaştırılması

Hipertrofik kardiyomiyopatiye kardiyak otonom aktivitedeki değişikliklerin eşlik ettiği bilinmektedir. Çalışmamızda hipertrofik obstrüktif kardiyomiyopatide (HOKM) kalp hızı değişkenliği indekslerini klinik ve ekokardiyografik parametrelerle karşılaştırdık.

Çalışmamıza HOKM tanısı konulan 23 hasta alındı (17 erkek, 6 kadın, ortalama yaş:43±11). Kontrol grubu da benzer yaş ve cinsiyet özellikleri olan 18 sağlıklı bireyden oluşturuldu (16 erkek 2 kadın, ortalama yaş: 45±14). Tüm hastalara M-mode, iki-boyutlu ve pulse-Doppler ölçümlerinden sonra 24 saatlik Holter ve kalp hızı değişkenliği incelemeleri yapıldı. Çalışmada kalp hızı değişkenliği parametrelerinden sırasıyla SDRR (RR intervallerinin standard sapması), RMSSD (ortalama atım aralıklarını karelerinin karekökü) ve PNN50% 50 ms'den fazla farklılık gösteren atımların oranınına bakıldı. Hastaların kalp hızı değişkenliği parametreleri subaortik gradient ve fonksiyonel kapasiteleriyle birlikte incelendi. Fonksiyonel kapasitesi sınıf III-IV olan hasta grubunda kalp hızı değişkenliği parametrelerinde sınıf I-II olan hasta grubuna göre belirgin azalma saptandı. Zaman bazında yapılan kalp hızı değişkenliği parametrelerinin subaortik gradient ile istatistiki olarak anlamlı derecede korrelasyon gösterdiği bulundu.(SDRR: r=-0.6743, p<0.01; RMSSD: r=-0.4928, p<0.05, PNN50 : r=-0.5432, p<0.05).

Sonuç: Kalp hızı değişkenliği HOKM hastalarında kontrol grubuna göre anlamlı derecede azalmıştır. Bu hastalardaki subaortik gradient ve fonksiyonel kapasite ile kalp hızı değişkenliği parametreleri arasında kuvvetli bir korrelasyon olduğu bulunmuştur.

Anahtar Kelimeler: *hipertrofi, kalp hızı, kardiyomiyopati*

Measurement of heart-rate variability has been reported to be a useful non-invasive method for the general assessment of cardiovascular autonomic neural status (1,2). Altered autonomic nervous system function has been documented in hypertrophic obstructive cardiomyopathy (HOCM) and is associated with markers of adverse prognosis (3,4,5). A number of pathophysiological components of HOCM have been

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identified: (1) left-ventricular outflow obstruction, (2) diastolic dysfunction, (3) myocardial ischemia and (4) arrhythmia (6,7,8,9). The dynamic type of obstruction to left ventricular outflow exhibited by patients with HOCM (due to systolic anterior motion of the mitral valve and midsystolic contact with the ventricular septum) may show variability with consecutive two-dimensional echocardiographic measurements. Such variability in gradients may be associated with the autonomic dysfunction. The aim of this study was to evaluate cardiac autonomic control in patients with HOCM and to assess the indices of heart-rate variability in relation to the clinical, two-dimensional echocardiographic and Doppler echocardiographic features of the disease.

MATERIALS AND METHODS

Patient group: The study group consisted of 23 patients with HOCM and 18 volunteers in sinus rhythm not receiving cardioactive medication. Diagnosis was made 4±3 months before the study began and was based on echocardiographic features. All patients had left interventricular septum (IVS) hypertrophy of 1.5 cm or more on two-dimensional echocardiography and IVS/ PW (posterior wall) ratio ≥1.3 in the absence of a systemic cause. Systolic anterior motion of the mitral wall was also observed in all patients. Patients with systemic hypertension were excluded. None of the patients had diabetes mellitus or any disease that might be associated with cardiac hypertrophy. The majority of patients were symptomatic, with chest pain (n=3; 13%) or dyspnea (n=16; 70%). At the time of the study, five patients had never received any cardioactive medication; 12 patients discontinued beta-blockers or verapamil (n=6) for at least four half-lives before the study. Four patients had family histories of hypertrophic cardiomyopathy, and one patient had been resuscitated from ventricular fibrillation.

Data collection and processing: M-mode and two-dimensional echocardiography and pulsed and continuous-wave Doppler studies were obtained with a phased-array Doppler echocardiography unit (Wingmed, System Five) with a 2.5 Mhz duplex imaging transducer. Using established methods, we measured maximum interventricular septal thickness and maximum posterior-wall thickness (10). Left-ventricular outflow obstruction was evaluated by continuous Doppler, positioning the probe so that velocities in the left-ventricular outflow tract were recorded. Left-ventricular outflow tract gradient was measured according to a modified Bernoulli equation (gradient = peak velocity^2 x 4), with gradient in millimeters of mercury. All measurements represent the average of at least three cardiac cycles. All patients underwent continuous 24-hour ambulatory ECG monitoring. Solid-state recordings were analyzed with a Medilog Excel (version 4.1c., Oxford Medical Ltd) ECG software system. ECG data were sampled digitally from the Oxford Medilog scanner for analysis of heart-rate variability. The computer program automatically calculates all 24 hours RR interval series. Premature atrial and ventricular beats and subsequent intervals were excluded automatically by the analysis, and the automatic detection was also visually checked by the investigator for proper identification. Time domain variables considered in this study were standard deviation of mean RR intervals (SDRR), root-mean squared successive difference (RMSSD) and percentage of cycles differing from the preceding one by more than 50 msec (PNN50%).

Statistical analysis: Patients were compared to detect associations between indices of heart-rate variability, left-ventricular outflow tract obstruction and clinical status. The results were analyzed with the statistical package for social sciences. Continuous variables are presented as mean ± SD. Significance of changes were calculated by means of t test or Mann-Whitney U test, and when appropriate, chi-square analysis was performed for categorical variables. Age-corrected correlation coefficients were calculated between echocardiographic and heart-rate variability parameters. A value of $p<0.05$ was regarded as significant.

RESULTS

Twenty-three patients with a mean age of 43±11 year (17 male, 6 female) were included in the study population. We divided the patients into two groups according to NYHA functional capacity. Group I consisted of 10 patients with Class I-II clinical characteristics and Group II consisted of 13 patients with Class III-IV symptoms. Time domain parameters and echocardiographic findings were compared between the two groups. Age-corrected heart-rate variability parameters were also correlated with echocardiographic and clinical characteristics of the patients.

Eighteen age and sex-matched control subjects (16 male, mean age 45±14) had mean values of SDRR: 114±31 msec, RMSSD: 45±10 msec and PNN50: 13.4±5.2%. Heart-rate variability measurements were

significantly lower in patients with HOCM than in control subjects.

On cross-sectional echocardiography, mean values of left-ventricular septum thickness was 2.2±0.4 cm, mean ratio of interventricular septum to left-ventricular posterior wall was 1.7±0.3 in patients. Left-ventricular outflow tract obstruction was noted in all patients, with a mean peak instantaneous gradient of 67±39 mmHg. Mean ejection fraction was 76±6 %.

No difference was observed in measures of two-dimensional echocardiography between Group I and Group II. Patients in deteriorated functional class (group II) were detected as having significantly increased left-ventricular outflow tract pressure gradients when compared with Group I patients (Table 1). NYHA Functional Class III and IV patients had lower values of SDRR index, RMSSD and PNN50% when compared with NYHA Functional Classes I and II (p<0,05). Time domain heart-rate variability parameters were found to be significantly correlated with the degree of dynamic obstruction, even though two-dimensional echocardiographic measurements were similar. As seen in Table 2, we found a significant inverse correlation between time domain heart-rate variability parameters and mean instantaneous outflow pressure gradients. In other words, as the outflow pressure gradient increased, the heart-rate variability decreased.

Table 1. Comparison of patient groups according to NYHA functional classification.

	Group I (Class I-II) (n=10)	Group II (Class III-IV) (n=13)	P
Male (n)	8 (80%)	9 (69%)	NS
Age (year)	43±15	42±9	NS
Maximum gradient mmHg	27±11	93±18	<0.01
Mean gradient mmHg	13±6	48±8	<0.01
IVS cm	2.1±0.5	2,3±0,2	NS
IVS/PW	1.7±0.2	1.8±0.4	NS
EF %	76±6	77±6	NS
SDRR ms	54±19	22±12	<0.01
RMSSD ms	33±14	20±11	<0.05
PNN50 %	2.2±1.1	7.3±4.9	<0.05

IVS : interventricular septum
PW : posterior left ventricular wall
EF : ejection fraction
SDRR : standard deviation from the mean of RR intervals
RMSSD : root-mean square of successive RR differences
PNN50 : proportion of RR intervals more than 50 msec different

DISCUSSION

Mechanisms by which subaortic gradients are produced in patients with HOCM have been scrutinized, and numerous studies have focused on defining contributions of several morphologic and physiologic factors, including (1) reduced systolic outflow tract dimensions; (2) substantial hypertrophy involving the anterior ventricular septum; (3) anterior displacement of mitral valve and papillary muscle within the ventricular cavity; (4) increased size and length of mitral leaflets; (5) hyperdynamic left-ventricular ejection producing a high velocity jet that streams through a narrowed outflow tract, pulling the mitral leaflets toward the septum; and (6) primary geometric abnormalities of the papillary muscle-mitral valve apparatus responsible for altered distribution of tension to the mitral leaflets (11,12,13). In addition to these factors, autonomic influence on the heart measured by heart-rate variability might have the potential to provide additional insight into physiologic and pathophysiologic conditions of patients with HOCM.

This is the first study to show the correlation between heart-rate variability and subaortic pressure gradients (SDRR; r:-0.6743, p<0.01; RMSSD; r:-0.4428, p <0.05, PNN50%; r:-0.5432, p<0.05). It may be that sympathetic predominance measured by decreased heart-rate variability causes subaortic gradients by supernormal activation of mechanoreceptors. Findings also indicated the importance of neural mechanisms in the clinical presentation of HOCM patients. RMMSD and PNN50% and time domain measures considered to represent parasympathetic modulation of heart rate were lower in NYHA Functional Class III and IV patients.

Ajiki et al. and Bonaduce et al. also found decreased vagal control in hypertrophic cardiomyopathy (3,14). Counihan et al. found a strong association between adverse family history and increased heart-rate variability. Interestingly, they found no correlation

Table 2. Age-corrected correlation coefficients between mean instantaneous pressure gradients and time domain heart-rate variability parameters

	Mean instantaneous pressure gradient	P
SDRR	r: –0.6743	<0.01
RMSSD	r: –0.4428	<0.05
PNN50%	r: –0.5432	<0.05

SDRR : standard deviation from the mean of RR intervals
RMSSD : root-mean square of successive RR differences
PNN50 : proportion of RR intervals more than 50 msec different

between altered heart-rate variability and the presence or magnitude of the left-ventricular outflow gradient (15). However, Simantirakis et al. demonstrated that long-term pacing in HOCM patients restores the sympathovagal balance in the heart rate by increasing vagal activity (16).

The sympathetic dominance on the heart is mediated by the release of epinephrine and norepinephrin. Activation of beta-adrenergic receptors result in cAMP-mediated phosphorylation of membrane proteins, which affects ventricular performance and electrophysiology (17). Symptomatic improvement by beta-adrenergic blockers shows the exact nature of autonomic imbalance, which can be demonstrated with 123I-metaiodobenzy guanidine (MIBG) myocardial scintigraphy.

In conclusion, heart-rate variability is reduced in HOCM and well-correlated with the degree of subaortic obstruction. Heart-rate variability indices are also sensitive markers of functional status, and there is a significant relationship between the autonomic nervous system and physiological correlates in HOCM.

Limitations: We did not consider the relation of SDRR index (mean of standard deviations of normal R-R intervals for all 5-minute segments of a 24-hour ECG recording) and SDARR (standard deviation of average normal R-R intervals for all 5-minute segments of 24-hour ECG monitoring) since there was no demonstrated advantage of these two parameters over SDRR and RMSSD.

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ANXIETY AND DEPRESSION THROUGHOUT THE HEMATOPOIETIC CELL TRANSPLANTATION PROCESS

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SUMMARY

In this study, 27 patients (9 male, 18 female) undergoing bone marrow transplantation were evaluated using Beck Depression Inventory, State Anxiety Inventory and Trait Anxiety Inventory tests. Beck Depression Inventory and State Anxiety Inventory tests were performed three times at three successive stages of the transplantation procedure: immediately prior to the start of the transplantation procedure (Stage 1); at the beginning of the aplasia period (Stage 2); and immediately after engraftment (Stage 3). A Trait Anxiety Inventory was taken only at Stage 3 of the procedure. In Stage 1, 26% of patients were found to be suffering from depression. This rate increased to 48% at Stage 2 and 29.6% at Stage 3. State anxiety at a clinical level was discovered in 70.3% of patients at Stage 1, 63% at Stage 2 and 63% at Stage 3. None of the patients were found to have trait anxiety at a clinical level. A statically significant difference ($p<0.05$) in average Beck Depression Inventory scores was recorded between Stage 2 and Stage 3. No statistically significant difference was found in average State Anxiety Inventory scores among the three stages. Our findings indicate a high prevalence of depression and clinical anxiety among bone marrow transplant patients at every stage of the transplantation process.

Key Words: *Anxiety, depression, hematopoietic cell transplantation.*

ÖZET

Hematopoietik Hücre Transplantasyonu İşlemi Sırasında Anksiyete ve Depresyon

Bu çalışmada kemik iliği transplantasyonu yapılan 27 hasta (9 erkek, 18 kadın), Beck Depresyon Ölçeği, Durumluk Anksiyete Ölçeği ve Süreklilik Anksiyete Ölçeği ile değerlendirildiler. Beck Depresyon Ölçeği ve Durumluk Anksiyete ölçeği transplantasyon işleminin birbirini izleyen üç safhasında olmak üzere üç kez gerçekleştirildi; transplantasyon işlemi başlangıcından hemen önce (1. aşama), aplazi periyodunun başlangıcında (2. aşama), engraftmandan hemen sonra (3. aşama). Süreklilik Anksiyete Ölçeği sadece üçüncü aşamada uygulandı. Depresyon birinci aşamada %26, ikinci aşamada %48 ve üçüncü aşamada %29.6 olarak bulundu. Klinik durumluk anksiyete birinci aşamada %70.3, ikinci aşamada %63 ve üçüncü aşamada %63 idi. Hastaların hiçbirinde klinik seviyede süreklilik anksiyetesi bulunmadı. İkinci aşama ve üçüncü aşama ortalama Beck Depresyon Ölçeği sonuçları arasında istatistiksel olarak belirgin farklılık vardı ($p<0.05$). Üç aşamadaki ortalama Durumluk Anksiyete Ölçeği sonuçları arasında istatistiksel olarak belirgin farklılık bulunmadı. Bulgularımız kemik iliği transplantasyonu yapılan hastalarda transplantasyon sürecinin her safhasında depresyon ve klinik anksiyete prevelansının yüksekliğini göstermektedir.

Anahtar Kelimeler: *Anksiyete, depresyon, hematopoietik hücre transplantasyonu*

Psychological stress is extremely high in patients with oncological diseases. Psychiatric disorders such as depression, anxiety and delirium occur at a significant rate in cancer patients, particularly as the disease advances and treatments become more aggressive (1). While many of the psychological problems connected with cancer are well-known, new therapeutic strategies such as bone marrow transplantation, which require settings similar to intensive care, may result in additional acute stress.

Bone marrow transplantation is increasingly being used to treat children and adults with a variety of life-threatening diseases. Although bone marrow transplantation is in many instances a life-saving intervention, it is a high-technology procedure that is both aggressive and life-threatening and that is associated with

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an array of physical and psychological stressors. Psychiatric and psychosocial research and intervention can greatly contribute to the understanding and management of stress in bone marrow transplantation recipients, donors and their families.

Patients undergoing bone marrow transplantation experience unique coping problems that differentiate them from other cancer patients. Structuring time is particularly difficult for patients awaiting the success or failure of their transplant in isolation. They may suffer from numerous psychological problems directly related to the transplantation procedure itself. Individual phases of bone marrow transplantation (qualification of patients for operation, pre-transplantation and post-transplantation periods, final phase) reveal varied disturbances and difficulties, indicating the need for full diagnosis, psychotherapy and, in certain cases, psychiatric intervention during treatment.

PATIENTS AND METHOD

In this study, 27 patients undergoing bone marrow transplantation were evaluated using Beck Depression Inventory, State Anxiety Inventory and Trait Anxiety Inventory tests. Nine (33.3%) of the patients were female and 18 (66.7%) were male. Beck Depression Inventory and State Anxiety Inventory were performed three times at three successive stages of the transplantation procedure:

Stage 1: Immediately prior to the start of the transplantation procedure.
Stage 2: At the beginning of the aplasia period.
Stage 3: Immediately after engraftment.

Trait Anxiety Inventory was taken only at the third stage of the procedure.

Ages of patients varied between 15 and 49 years of age, with the mean age 33.2. The length of time from the onset of the disease varied from five months to seven years, with the mean length 19.8 months. Twenty-one of the 27 patients (78%) underwent allogeneic-type transplantation and eight (22%) underwent autologous-type transplantation. The diagnoses of the patients were as follows:

Hodgkin's disease	: 1 (3.7%)
T-cell lymphoma	: 1 (3.7%)
Aplastic anemia	: 1 (3.7%)
Myelodysplastic syndrome	: 1 (3.7%)
Breast carcinoma	: 1 (3.7%)
Acute lymphoblastic leukemia (ALL)	: 2 (7.4%)
Non-Hodgkin's lymphoma	: 2 (7.4%)
Acute myeloblastic leukemia	: 8 (29.6%)
Chronic myeloid leukemia	: 10 (37.0%)

RESULTS

Depression throughout the bone marrow transplantation procedure

Beck Depression Inventory scores were used to evaluate depressive signs and symptoms. Patients who scored 13 points or below were considered to have no depression, those who scored between 14 and 22 were considered to have mild depression, those scoring 23 to 34 points were considered to have moderate depression and those scoring 34 or above were considered to have severe depression.

Beck Depression Inventory scores at Stage 1 varied from zero to 26, with a mean score of 9.88. A total of seven (26%) of the patients were found to be in depression, with five (18.5%) suffering from mild depression and two (7.4%) from moderate depression. Beck Depression Inventory scores at Stage 2 varied from zero to 46, with a mean score of 12.92. A total of 13 (48%) of the patients were found to be in depression, with 12 (44.4%) suffering from mild depression and one (3.7%) suffering from severe depression. Beck Depression Inventory scores at Stage 3 varied from zero to 22, with a mean score of 8.9. A total of eight (29.6%) of the patients were found to be in depression, all of them suffering from mild depression.

The above results indicate that depression is quite prevalent among patients undergoing bone marrow transplantation. It is most prevalent during Stage 2, when nearly half of the patients registered depression scores above the cut-off point of 13.

One-sided variance analysis for repeated measurements was performed to discover if there were differences among Beck Depression Inventory scores during the three successive stages. The results showed a statistically significant difference ($p<0.05$) between Stage 2 and Stage 3 scores only. Although the rate of depression was higher at Stage 1 than Stage 2, the differences were not statistically significant. While these results may seem confusing, they are due to the fact that some patients scored lower in Stage 2, despite the overall high rate of depression during this stage. It should be noted that depression was quite prevalent in this population, becoming more so during the aplasia

period (Stage 2) and decreasing immediately after engraftment.

Anxiety throughout the bone marrow transplantation procedure

State Anxiety Inventory was used to evaluate anxiety signs and symptoms at the moment the test was given. Patients scoring 40 or above were considered to have state anxiety at a clinical level.

State Anxiety Inventory scores at Stage 1 varied from 17 to 53, with a mean score of 40.8. Nineteen (70.3%) of the patients were found to have state anxiety at a clinical level.

State Anxiety Inventory scores at Stage 2 varied from 20 to 56, with a mean score of 41.4. Seventeen (63%) of the patients were found to have state anxiety at a clinical level.

State Anxiety Inventory scores at Stage 3 varied between 22 and 54, with a mean score of 41.1. Seventeen (63%) of the patients were found to have state anxiety at a clinical level.

The above results indicate that clinical state anxiety is quite prevalent among patients undergoing bone marrow transplantation and is more prevalent than depression at all stages of the transplantation procedure.

One-sided variance analysis for repeated measurements was performed to discover if there were differences among State Anxiety Inventory scores during the three successive stages. No statistically significant difference was found.

Trait Anxiety Inventory was performed to estimate the long-term anxiety levels of patients. Those who scored 60 points or above were considered to have trait anxiety at a clinical level. Scores varied between 30 and 58. Thus, none of the patients was found to have trait anxiety at a clinical level.

DISCUSSION

Patients undergoing bone marrow transplantation procedures are considered to be at obvious risk of developing psychiatric problems. Suffering from a malign disease, uncertainty about the outcome of treatment, distressing side effects during and after treatment and various associated psychosocial stressors are all factors that could contribute to bone marrow transplantation patients' susceptibility to psychiatric problems. The disorders most likely to develop among these patients are affective and anxiety disorders.

Baker et al (2) studied a sample of 437 patients who were being evaluated for bone marrow transplantation to assess their psychosocial adjustment. Nearly a third (31%) of the patients showed some degree of depression on the Center for Epidemiological Studies Depression Scale. Scores on the Profile of Mood States Scale also indicated that these transplantation candidates were experiencing a high level of psychological distress. Authors found indications of this distress in low scores on the Self-Rated Karnofsky Performance Scale and on scales measuring mastery and dispositional optimism.

Syrjala et al (3) found that bone marrow transplant recipients suffered from depression at a rate of 27% and elevated anxiety at a rate of 41% during the pretransplant period. Leigh et al (4) found rates of 22% for depression and 41% for anxiety, respectively, during the same period.

Prieto et al (5) compared the quality of life of 145 bone marrow transplantation survivors to that of a British reference population, discovering the most important differences in the areas of physical mobility, work and sex life. They also found psychiatric morbidity in bone marrow transplantation survivors to be higher than in a general Spanish population.

Colon et al (6) found that bone marrow transplantation patients suffering from depression, regardless of their specific psychiatric diagnoses, had poorer outcomes for recovery.

Chao et al (7) found bone marrow transplantation patients suffered from difficult sleeping (34%) and poor appetite (33%) 90 days after transplantation. Rates one year after transplantation were 5% and 0%, respectively. Andrykowski et al (8) found sleep difficulty among 51% of bone marrow transplantation patients 12 months after transplantation. They found no significant change in the sleep difficulty rate among the same patient population 40 months after transplantation.

Wolcott et al (9) report 15-20% of bone marrow transplantation recipient survivors to have a degree of psychological distress that might benefit from specific psychological/psychiatric intervention.

Rodrigue et al (10) assessed 51 bone marrow transplantation candidates before hospitalisation. The authors found little support for previous anecdotal reports hypothesising increased incidences of negative affect during the pre-admission period. However, pa-

tients' use of a passive coping style was found to be significantly correlated with higher degrees of negative affect and psychopathology.

McQuellon et al (11) found no significant differences in quality of life measure, mood scores and social support among female breast cancer patients before and after transplantation.

A question exists as to psychiatric differences between patients who have undergone bone marrow transplantation and patients who have been treated with conventional chemotherapy. Wellisch et al (12) compared leukemia patients who had undergone bone marrow transplantation to leukemia patients who had received conventional chemotherapy. Overall, no significant differences were found between the two groups in regard to depression symptoms, multi-focal psychiatric symptomatology or on any sub-test evaluating problems and rehabilitation needs of cancer patients. No significant differences in quality of life were found between the treatment groups.

Lesko et al (13) found no significant differences in quality of life between leukemia patients who had undergone bone marrow transplantation and leukemia patients who had received conventional chemotherapy. However, they did find both groups had significantly higher levels of distress than those observed in normal, physically healthy samples.

From a different perspective Gregurek et al (14) found the level of state and trait anxiety at the beginning of isolation to be significantly higher in patients who subsequently developed acute grade II-IV GVHD as compared to patients with GVHD grade 0-, irrespective of age, sex or stage of the disease prior to bone marrow transplantation.

Finally; Jenkins et al (15) examined the influence of factors such as depression and anxiety upon length of stay, survival, psychosocial adjustment and negative prognostic attitudes in patients who underwent bone marrow transplantation. In contrast to other studies, they found psychiatric illnesses had little influence on physical outcome variables. However, they did find psychiatric illnesses to affect psychosocial outcome.

Our study found a high rate of depression among bone marrow transplantation patients during all three stages of the transplantation period, including the third stage, when a low rate of depression might be expected. Rates of depression were found to be 26% at Stage 1, 48% at Stage 2 and 29.6% at Stage 3. The fact that depression was most prevalent at the beginning of the aplasia period (Stage 2) may be due to the psychological stress caused by aplasia. This period is marked by waiting, expectation and passivity. The helplessness patients may experience during this period may make them prone to depression. The high rate of depression during Stage 3 may be due to exhaustion resulting from the entire transplantation process, regardless of its success.

Our study found clinical level state anxiety to be even more prevalent than depression. Clinical level state anxiety was found at a rate of 63% at Stage 1 and 70% at Stage 2. It was also 63% at Stage 3, despite reasonable expectations that it would be lower at this stage. In contrast to clinical level state anxiety, clinical trait anxiety was not found at any stage. This finding reveals anxiety to be a state-dependant phenomenon in this patient population.

In conclusion, our study indicates that bone marrow transplantation patients are under great risk of developing depression and anxiety during all stages of the transplantation process. The emphasis on stages differentiates our study from previous ones. Post-transplantation psychosocial outcome may be considered more important by some, but we believe that psychological problems throughout the transplantation procedure are equally important. The bone marrow transplantation procedure is very difficult to cope with for all patients, and clinicians must remain alert to signs and symptoms of anxiety and depression in this population. Defining the frequency and intensity of psychological problems at every stage of the transplantation process can provide valuable guiding information that will enable clinicians to provide help for their patients with psychological problems.

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POSTERIOR URETHRAL DEFECTS REPAIRED WITH HUMAN AMNIOTIC MEMBRANE IN THE RABBIT MODEL

Hüseyin Dindar*

SUMMARY

Posterior urethral trauma and their treatment with urethroplasties using various grafts lead ultimately to stricture formation. With the hope of decreasing morbidity, a posterior urethral defect was created and reconstructed with human amniotic membrane. Posterior prostaticomembranous urethra was prepared by transpubic approach in fifteen New Zealand male white rabbits. The defect created at the anterior part of the posterior urethra was repaired with human amnion patch. Repaired segments were removed at postoperative first week and first month respectively in three rabbits for every groups and fixed in formalin. Renal scintigrafies , excretory urograms and urethrocystograms were studied on the rest of the rabbits on the third postoperative month.

An abscess formation with a urethrocutaneous fistula and a fistulae were detected in two rabbits. Upper urinary tract dilatation or stasis, and urethral stenosis were not detected in the rest. Renal shapes, renal perfusion and excretion were normal. Early histopathological evaluation demonstrated fibrosis and ulceration, but a complete epithelization and minimal fibrosis was demonstrated at the third month in the rest.

***Conclusion:** Human amniotic membrane can be used as a biological graft material due to its antiscarring and anti-inflammatory features.*

***Key Words:** Amnioticmembrane,posterior urethra, repair,trauma*

ÖZET

Posterior Üretra Yaralanmalarında İnsan Amniotik Membran Kullanımı

Posterior üretra yaralanmaları genelikle darlıkla sonuçlanmakta ve darlık çeşitli üretroplasti yöntemleri ile giderilmeye çalışılmaktadır. Karmaşaları ortadan kaldıran bir yöntem geliştirilememiştir. Tavşan modelinde insan amniyotik membranının darlık gelişimi ve yara iyileşmesi üzerine etkilerini araştırmak amacı ile bu çalışma yapılmıştır. Üç aylık 15 Yeni Zellanda tipi erkek tavşanda transpubik yaklaşımla posterior üretra ortaya kondu ve anterior kısmında 2x0.5 cm boyutlarında oluşturulan defekt aynı boyuttaki insan amniotik membranı ile 6/0 prolen yardımıyla onarıldı. Ameliyat sonrası 1. hafta ve 1. ayda 3'er denek öldürülerek onarılmış üretral segmentler çıkarıldı ve histopatolojik inceleme yapıldı. Geri kalan tavşanlara ameliyat sonrası 3. ayda statik ve dinamik böbrek sintigrafileri ve ekskretuar renogramları ve üretrosistografileri yapıldı. Çalışma grubunda ve beş normal denekte plazma elektrolitleri ve kan gazları çalışıldı.

İki denekte birinde retropubik apse ile beraber olmak üzere üretrokütanöz fistül gelişti. Bu iki denekte aynı zamanda mesanede taşlar oluştu, sistogram ve cerrahi eksplorasyonda üretranın kısmen oblitere olduğu gözlendi. Diğer deneklerde sistoüretrografi ve İVP'de normal kalbreli üretra olduğu,darlık gelişmediği gözlendi.Yapılan dinamik ve statik böbrek sintigrafileri kontrol gruplarıyla karşılaştırıldığında normal olarak değerlendirildi. Üretrada darlık izlenen deneklerde hafif renal aktivite retansiyonu gözlendi. Histopatolojik olarak 3. ayın sonunda epitelizasyonun tamamlandığı ve fibrotik aktivitenin çok azaldığı görüldü.

Üretral yaralanmalarda insan amniyotik membranı epitelizasyonu hızlandırıcı ve özellikle inflamasyonu ve fibrozisi azaltıcı özelliklerinden dolayı biyolojik bir greft materyali olarak uygulanabilir.

***Anahtar Kelimeler:** Amniotik membran, Posterior üretra, yaralanma, onarım*

The most common cause of membranous or supramembranous stricture of the urethra in children is partial or complete urethral disruption, which occurs secondary to the shearing forces of pelvic fractures. The incidence of urethral injury occurring in association with a pelvic fracture varies from 4.7 to 25 per cent and is predominantly seen in male subjects. Even though urethral injury is repaired by primary urethroplasty or urethral realignment, urethral stricture develops at a rate of 40-62 percent. Yet these strictures may

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not respond to dilatation (1,2). Difficult urethral strictures, especially of the bulbous and posterior urethra may be effectively treated today by one of the many sophisticated methods of urethroplasty and internal urethrotomy (1,3). Unfortunately, in addition to recurrent strictures, other forms of late complications such as impotence, incontinence of urine and urinary fistula occur in greater frequency when urethroplasty is applied (3).

A multitude of different graft materials has been used for reconstruction of the genitourinary tract. Most synthetic materials undergo extrusion or cause stone or fistula formation. At present, intestinal tissue is the substance most commonly used for reconstruction. However, the insult to the gastrointestinal tract associated with obtaining the tissue may in itself lead to gastrointestinal complications (4).

The unique healing properties of placental membranes were recognized as early as 1910(5). Freedom from infection in clean or sterile wounds, a marked decrease in pain and an increased rate of re-epitelization of the traumatized skin or mesenchymal surface were observed when the amniotic membrane was used as a wound dressing (6,7,8,9). Fortunately, the possibility of rejection is minimal due to its hypoallergicty (10). For these reasons, a posterior urethral defect was created and reconstructed with human amniotic membrane in a rabbit model. Epithelization and stricture formation were evaluated,and the effect of the amniotic membrane on the wound healing of posterior urethral injuries was investigated in this experimental study.

MATERIALS AND METHODS

Three-month-old sixteen New Zealand male white rabbits were anesthetized with administrating 10 mg/Kg pentothal (Na-5-ethyl-5-(1-methyl-buthyl)-2-thiobarbitura-te, Abbott) via the dorsal ear vein. Lower abdomen and both inguinal areas were depilated and painted with betadine and covered with sterile drapes. The pubic symphisis was incised and separated with a knife and was prepared the posterior prostaticomembranous urethra. Two thirds of anterior part of the posterior urethra was excised for two-cm length. The defect was repaired with human amnion patch of 2x0.5 cm using 6/0 prolene suture. Human amniotic membrane was kept in 100mL of normal saline with 1g cephobid. The urethral lumen was checked with 8 Fr Nelaton sound and removed after completion of repair. The pubic symphisis was approximated with 2/0-prolene suture and the skin was closed with 2/0 silk sutures. A prophylactic use of 400 IU penicillin procaine was administered by intramuscular injection. Patched urethral segments were removed at the postoperative first week, and first month respectively in three rabbits for every group and fixed in formalin. Static and dynamic renal scintigraphies followed by excretory urograms and urethro- cystograms were evaluated on the rest of the rabbits at the third month. Plasma electrolytes and blood pH were measured in the study group and five normal rabbits.

Renal perfusion studies were performed using scintiview imaging console and pho gamma IV camera equipped with a low energy, all purpose, parallel hole collimator. The energy setting was centered at 140 KeV with a window of 25%. Images were obtained using posterior projections with the rabbits in supine position. The detector was kept parallel to the back of the rabbit and 1 mCi (37 MBQ) Technetium 99m DPTA (Dietylene triamine pentaacetic acid) was injected as a compact bolus via the dorsal ear vein. Imaging was commenced promptly. Serial images were taken after injections for every 2 seconds during the following 30 minutes resulting in dynamic images. 100 000 counts were collected with the same camera at 15, 30, and 60 minutes after injections for static evaluation. Static evaluation revealed the shape, activity and excretion and drainage of the tracer as a curve of time. All images were interpreted qualitatively by two experienced observers without prior knowledge of the study.

Excretory urograms were obtained by urografin injection (3,5-Bis acetamido-2, 4,6-triiodobenzoic acid-Na and Meglumine, Schering AG) in a bolus dose of 2mg/Kg via the dorsal ear vein. Urograms were obtained at 5,15,30,45 and 60 minutes after injections.

Urethrocystographies were taken after urografin administration via an indwelling 8 Fr Nelaton sound indwelling the urethra and anteroposterior and lateral projections were obtained. The animals were anesthetized and killed with overdose Pentothal and the whole urethra with bladder neck was removed and fixed in 10 percent formalin. Then embedded in paraffin wax and sections 4 to 6 micron thick were cut and stained with hematoxylin and eosin and evaluated in light microscopy.

RESULTS

There was an abscess formation located retropubically and extending to the right femoral area in one of the rabbits. Urethro-cutaneous fistulae were detected in this rabbit. Another rabbit had also a urethrocutaneous fistula. Those two rabbits also had bladder stones in 3-15 mm diameter. Both cystography and surgical exploration revealed fistulae with minimal urine discharge, while urethrae were partially obliterated (Figure 1). Cystography and IVP did not reveal any upper urinary tract dilatation or stasis, and cystourethrograms did not show any urethral stenosis in the rest of the animals (Figure 2). Blood pH and plasma electrolytes were not different when compared with controls ($p>0.01$) (Table 1). Renal shapes, renal perfusion and activity and excretion were normal at scintigraphic studies performed in experimental groups and in controls. A significant activity retention in both kidneys in the animal with abscess formation and a slight renal activity retention in only right kidney in the one of the rabbits with fistulae formation were detected (Table 2).

Histopathological evaluation at the end of first month showed ulceration at the patched site, scanty epithelization areas and moderate fibroblastic activity and fibrosis under the amniotic membrane. However, the specimens obtained at the end of the third month revealed that in the most of the animals epithelization was complete and fibrotic activity under the neoepithelium was minimal (Figure 3).

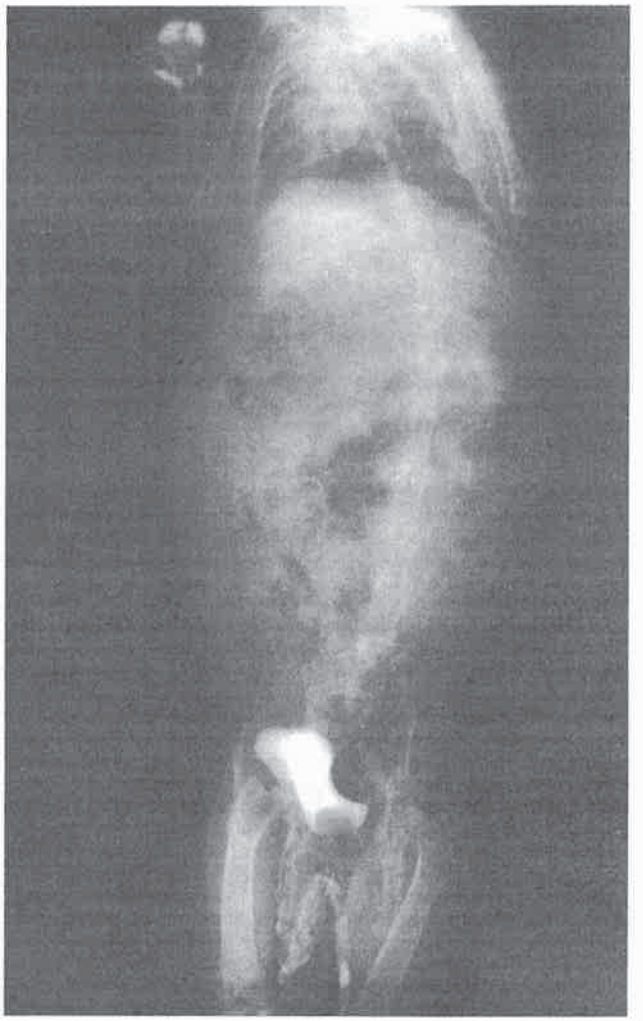

Figure 1: Posterior urethra repaired with amniotic membrane obstructed with abscess formation.

DISCUSSION

Various grafts have been used in the treatment of genitourinary tract defects and strictures such as, peritoneum, seromuscular grafts, and bovine pericardium as organic ones and silicon and Teflon as inorganic ones. Patients' own tissues such as bladder mucosa, prepucial, scrotal and inguinal skin are used as an autograft in the repair of the posterior urethral defects and stenosis (3,4,11). But these frequently cause urolithiasis and fistula formation (2,4,11). When intestinal tract has been used in bladder reconstruction, gastrointestinal problems, hyperchloremic acidosis, excessive mucus, diverticula formation and malignancy may develop (1,3,11).

An ideal graft should have features such as being biologically degradable, forming a good skeleton for regeneration, nonrejectable, easily available and cost-effective (8,12).

Table 1. Whole blood chemistry of control and study groups.Statistical analysis made by Anova in Minitab programe

	PH	Crea mg/dl	BUN mg/dl	Na mEq/L	Cl mEq/L
Study(n:16)	7.38+-0.13	1.61+-0.31	21.2+-2,31	144.01+-1.21	98.75+-1.57
Control(n:5)	7.36+-0.11	1.59+-0.32	20.6+-3.20	144.09+-1.30	99.04+-1.34
	NS(p>0.1)	NS	NS	NS	NS

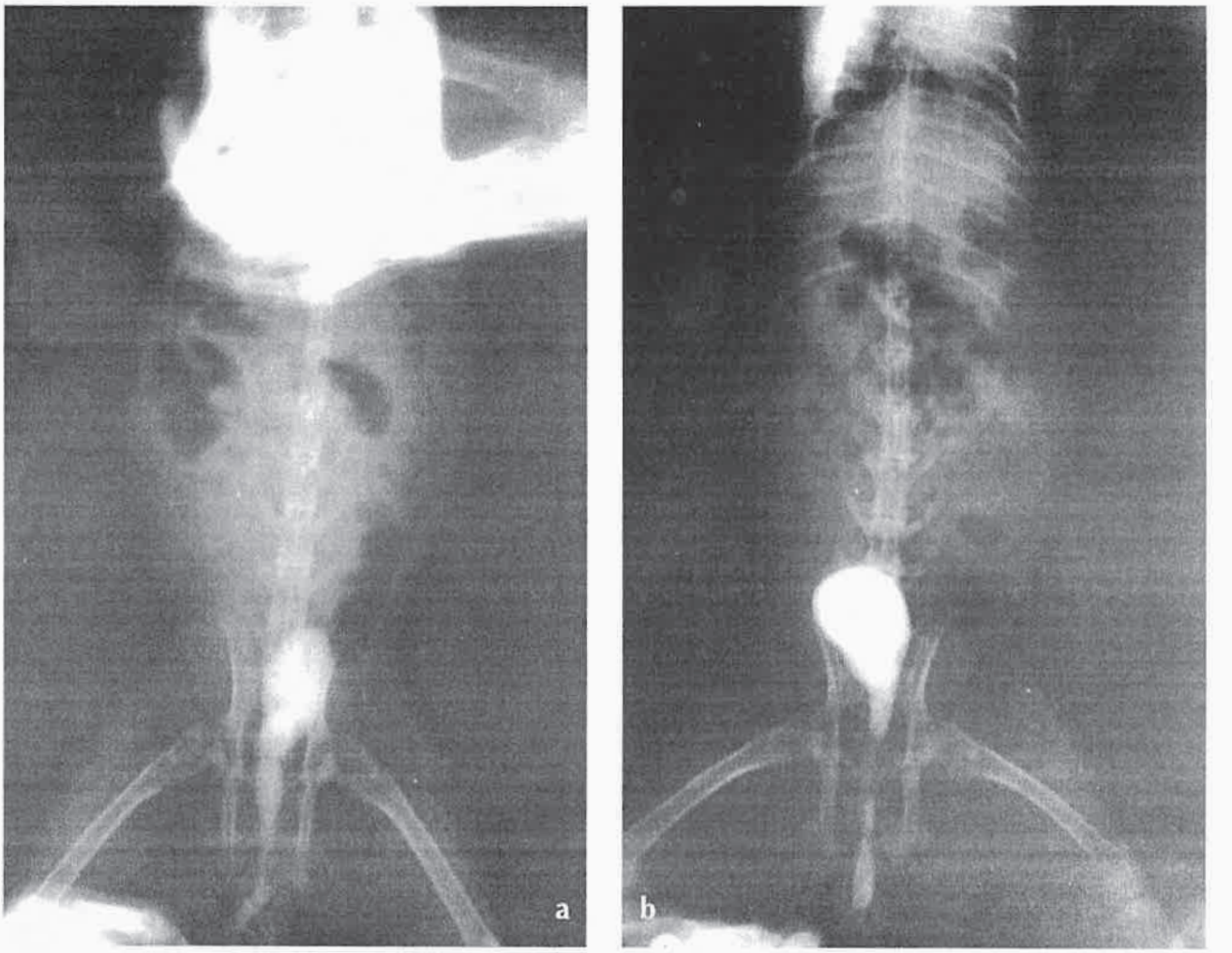

Figure 2: A normal urethrocystogram (a) and a straight urethra without stenosis after repair(b).

Table 2. Scintigraphic,radiologic and histopathologic findings three months after urethral repair. Early histopatolhogic findings of six rabbits were not presented.

Rabbit	Scintigraphy		X-Ray	Histopathology
	Perfusion	Retention	Urethral Caliber	Epithelization
1	Normal	None	Normal	Sufficent
2	Normal	None	Normal	Sufficent
3	Normal	None	Normal	Sufficent
4	Normal	None	Normal	Sufficent
5	Normal	None	Normal	Sufficient
6	Normal	None	Normal	Sufficient
7	Normal	None	Normal	Sufficent
8	Normal	Yes(b)	Decreased	Ulceration
9	Normal	Yes®	Decreased	Ulceration
10	Normal	None	Normal	Ulceration
11 (Control)	Normal	None	Normal	Normal*

(b):Retention in the both of the kidneys
®: Retention in only right kidney
*:Control specimens were obtained from five of the study groups during posterior urethral repair

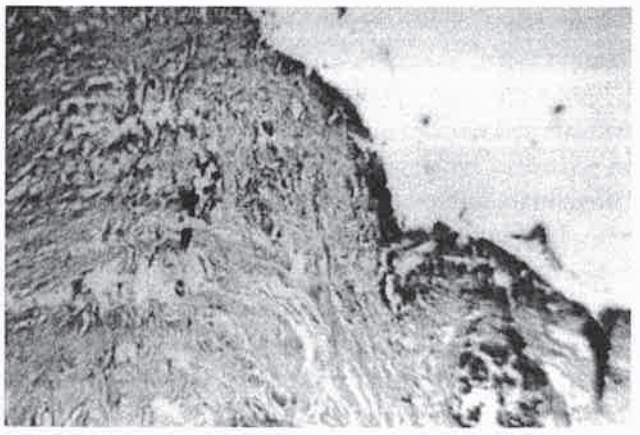

Figure 3: Epithelization of the patched urethra with minimal fibrosis at third month. Hematoxylin and eosin (4x10).

Human amniotic membrane expresses mRNA's for a number of growth factors and contains several growth factor proteins. High levels of EGF, KGF, HGF and bFGF in the amniotic membrane with amniotic epithelium as compared to the amniotic membrane without amniotic epithelium suggest an epithelial origin for these growth factors. EGF, KGF and HGF in particular might play important roles in wound healing especially for epithelization after amniotic membrane transplantation (13). Clinical studies in burn care, gastrointestinal surgery, and application of amniotic membranes on graft donor sites of split-thickness skin grafting and on chronic leg ulcers and oral cavity reconstruction with pectoralis mojor muscle covered with amniotic membrane have demonstrated that amniotic membrane provide a rapid epithelization (14,6,7,8).

On the other hand, amniotic membrane contains basement membrane components and various proteinase inhibitors. When used as a graft, the basement membrane of amniotic membrane could block inflammatory insults to a damaged tissue (15). Clinical and experimental studies in ocular surgery revealed that immediate intervention for acute alkaline burns with amniotic membrane as a temporary patch promotes wound healing by inhibiting proteinase activity and polymorphonuclear leukocyte infiltration. This feature leads to less fibrosis, which is important in corneal and skin wound healing (15,13,16). Reported data from clinical and experimental studies indicate that amniotic membrane transplantation in ocular surgery facilitates rapid healing with recovery of a normal epithelial phenotype (without haze formation) in the epithelium and reduces inflammation, vascularization, and scarring in the stroma (15,13,16).

Down-regulation of the transforming growth factor-beta (TGF-beta) signaling system is a strategy for preventing scarring during wound healing. Human corneal and limbal fibroblasts cultured on the stromal matrix side of preserved human amniotic membrane revealed that an amnionic membrane matrix can suppress the TGF-beta signaling system, DNA synthesis, and subsequent myofibroblast differentiation. This action explains in part the antiscarring results of amniotic membrane transplantation used for ocular and other surface reconstruction. It may also explain in part why fetal wound healing is scarless (17).

Antiscaring features of amniotic membrane was clinically and experimentally also confirmed by constructing tubular structures such as common bile duct, ureter and vaginal reconstructions in patients with vaginal agenesis and vascular graft interposition (18,19,20,21,22).

Human amniotic membranes were used to repair bladders after supratrigonal cystectomies in experimental animals. The membranes maintained the integrity of the bladders until healing and reepithelialization occurred. There was no significant loss of bladder capacity or decreased renal function postoperatively. Calcification did not occur on the membranes but was noted on chromic sutures retaining the membranes in a few bladders. Histologic examinations revealed evidence of regeneration of normal appearing smooth muscle along the path of a retracting placental patch, and thus of reconstitution of a normal-appearing and functioning bladder (23,24).

Though early histologic evaluation demonstrated modarate fibrosis and ulceration, this feature was disappeared in the third month in the present study. The membrane did not lead to a significant foreign body reaction and new uroepithelium covered the defect in three months. However, any muscular development was not detected in the presented study. Stone formation probably due to foreign body reaction of the stitches used in this setting, which led to abscesses formation and fistula was developed in only three of the 16 rabbits. In the rest a straight urethra without stenosis was achieved. Though we gave only one dose antibiotic for preventing infections, as a foreign body extending up to the bladder neck, amniotic membrane has

not caused to infection or related reactions, except in three rabbits. This indicates antibacterial features of amniotic membranes.

In the conservative treatment of omphalocele the surrounding epidermis grows under the amniotic membrane over the peritoneum in less than one month. A similar growing model does run, and neouroepithelum covered the patched area was identical with original ones. Minimal fibrosis detected by histopatological examination is considered to be a result of down regulation of the transforming growth factor-beta signaling system and inhibiting of inflammatory insult by proteinase inhibitors. This decreased fibrosis was also confirmed by a straight urethra without stenosis by urethrograms.

Human amnion having a surface electrical property as high as human skin provides early adherence to the wound. Early adherence of a skin substitute to the wound surface is paramount if it is to function as a skin equivalent (12). However, marked fibrosis at early period in this setting may be a result of insufficient adherence of the amniotic patch to the periurethral tissue because we do not used a stent or tissue adhesive materials, or continuing urine flow might prevented early adherence.

Cystography and IVP have not revealed any upper urinary tract dilatation or stasis, and cystourethrography has not showed any urethral stenosis in the present study. Sintigraphic studies performed in experimental groups and in controls, renal shapes, renal perfusion and activity and excretion were normal when compared to controls. However, in animal with abscess formation there was significant activity retention in both kidneys and in the rabbit with fistula formation a slight renal activity retention in only right kidney was detected. These results indicate that urethra repaired with amniotic patch does not develop any urinary stasis, urine retention and infection in most of the animals.

Amniotic membrane, which is derived from the epiblast and which appears before the embryonic plate is formed, remains in its primitive state and fails to differentiate further. This primitive state or less complete differentiation is considered to be the cause for hypoallergicity and their antibacterial activity. On the other hand, it is forwarded that amniotic membrane has a glycoprotein, which inhibits the lymphocytes and lyphoblastogenesis and prevents rejection and inflammatory reaction. The bactreiostatic activity of the amnion is said to be due to the presence of antibodies, possibly allantoin and lysozyme. It is not affected by the process of drying, irradiation, or storage or by the removal of the chorion (20).

Human amnion possesses several characteristics that make it attractive as a bioprothesis. Amnion creates a mild immune response and minimal or no class I human leukocyte antigen reaction. This graft produced much less and a more delayed inflammatory response than xenograft (23). The delayed resorption of the amniotic membrane allows re-endothelialization of the naked patch by natural urinary mucosa. The early epithelization of urinary tract mucosal defect in the prevention of late restricturing as in the biliary tract has been well known. Microscopic examination of the patched urinary tract showed re-endothelialization of the graft access without development of a fibrotic stricture.

We recommended that immediate injury could be repaired with amniotic patch in a similar fashion with the better results as achieved with urethroplasties and repair with autografts. Repair of the defect of tubular structures with amniotic membrane could be a more effective and important especially for its antiscaring feature.

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ECTOPIC ADRENAL GLAND TISSUES IN YOUNG BOYS

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Selim Erekul** • İ. Haluk Gökçora*

SUMMARY

This article reviews the subject of ectopic adrenal tissue along the spermatic cord as an incidental finding during operations on boys for inguinoscrotal problems such as undescended testis, inguinal hernia, hydrocele and varicocele.

Between January 1985 and January 1999, 1,691 inguinal and 220 congenital gastrointestinal system malformation operations were performed on patients whose ages ranged from two days to 10 years (mean 3 years). Twenty-one ectopic adrenal tissue nodules were detected in 16 patients, all of whom were males. Ten of the inguinoscrotal pathologies were right-sided and, in most instances, unilateral single nodules. There were no bilateral occurrences. A resected transverse colon of a newborn with meconium ileus with pseudocyst formation had immature testicular and ectopic adrenal tissue present within. While one of the nodules contained adrenal medullary tissue, the remainder contained only cortical tissue.

Ectopic adrenal tissue is of potential clinical significance because its association with congenital adrenal hyperplasia could lead to treatment difficulties and poor prognosis. It may also evolve into a neoplasm or the site of production of excessive adrenal hormones, particularly after bilateral total adrenalectomies.

Nodules consisting of ectopic adrenal tissue, which are of only a few millimeters in diameter, should be removed whenever incidentally detected, but a routine search should not be mandatory.

Key Words: *Inguinoscrotal, ectopic adrenal tissue, neuroblastoma.*

ÖZET

Çocuklarda Ektopik Adrenal Dokular

Ektopik adrenal dokusu inmemiş testis, kasık fıtığı, hidrosel ve varikosel gibi inguinoskrotal bölge sorunlarının cerrahi tedavileri sırasında spermatik kordon boyunca raslantısal olarak bulunabilen bir ektopik dokudur.

1985-1999 yılları arasında yapılan 1691 inguinal bölge, 220 konjenital gastrointestinal sistem malformasyon cerrahisi sırasında 16 olguda 21 adet nodül saptanmıştır. Olguların tamamı erkektir. İnguinoskrotal patolojilerin 10 tanesi sağ tarafta yerleşmiştir. Olguların çoğunda tek taraflı soliter nodül saptanmış, bilateral nodül varlığı saptanmamıştır. Mekonyum ileusu nedeniyle transvers kolon rezeksiyonu yapılan bir olguda da immatür testiküler ve ektopik adrenal dokusuna raslanmıştır. Nodüllerden bir tanesinde sadece medüller yapı saptanırken geri kalanlarında kortikal yapı histopatolojisi gözlenmiştir.

Ektopik adrenal dokular potansiyel bir klinik önem taşımaktadır. Neoplaziye dönüşebilecekleri gibi fazla hormon yapım ve salınımına neden olabilirler. Bilateral adrenalektomi sonrası adrenal bezlerin görevlerini üstlenebilirler.

Birkaç milimetre çaplı bu nodüllere raslandığında çıkartılması uygun olur, ancak özellikle aranması zorunlu değildir.

Anahtar Kelimeler: *İnguinoskrotal, ektopik adrenal doku, nöroblastoma*

This article reviews the subject of ectopic adrenal tissue along the spermatic cord as an incidental finding during operations for inguinoscrotal problems such as undescended testes, inguinal hernia, hydrocele and varicocele (1,2).

Nodules consisting of ectopic adrenal tissue should be removed if they are a few millimeters in diameter should be removed whenever incidentally detected, but a routine search should not be mandatory (1,3).

Ectopic adrenal medullary and cortical tissues are potential sources of neoplasia-neuroblastoma or of hormone production after adrenalectomy. This condition is mostly seen in the retroperitoneum and hilium of the gonads. It has also been documented to appear in various other sites (3,4,5).

Neuroblastomas, on the other hand, are the most common solid malignant lesions in infants, with a reported incidence of 1 in 10,000 live births. This tumor

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may occur at any tissue site originating from the neural crest. The most common sites of origin are the adrenal medulla and associated sympathetic ganglia. Neuroblastoma may originate at other sites, including the neck, mediastinum and pelvis and may in fact arise from ectopic adrenal tissue (6).

PATIENTS AND METHODS

Between January 1985 and January 1999, 1,691 inguinal and 220 congenital gastrointestinal system malformation surgeries were performed in the Department of Pediatric Surgery at the Ankara University School of Medicine. A retrospective analysis was performed to evaluate the patients by age, sex and ectopic adrenal tissue. Histopathologic findings and the association of congenital adrenal hyperplasia or any other malignancies were examined.

RESULTS

Twenty-one nodules of ectopic adrenal tissue were detected in sixteen patients, all of whom were males. Ten of the inguinoscrotal pathologies were right-sided and, in most instances, unilateral single nodules. There were no bilateral occurrences. A resected transverse colon of a newborn with meconium ileus with pseudocyst formation had immature testicular and ectopic adrenal tissue present within. During operation, yellowish nodules of 1-4 mm in diameter were detected on the spermatic cord and removed from the 15 inguinoscrotal pathologies. Their histology demonstrated ectopic normal adrenal tissue. One nodule contained medullary tissue and the rest contained cortical tissue (Figure 1and 2).

Nine adrenal malignancies, three ganglioneuromas, five neuroblastomas and a ganglioneuroblastoma were further operated on during the same period. Three were detected retroperitoneally; two were abdominal and one pelvic on the course of the vessels. The pelvic one was not clearly defined as originating from ectopic adrenal tissue or from the sympathetic ganglions. One was located at the posterior mediastinum and the rest originated from the adrenal medulla. Although reported in the literature, no paratesticular neuroblastoma were discovered among these cases.

Cases with ectopic adrenal medullary and cortical tissues were evaluated retrospectively with reference to the recent literature.

DISCUSSION

Ectopic adrenal tissue along the spermatic cord is a sporadic finding during routine surgical procedures in the inguinal region of infants and children (1,3). Its incidence seems to be rising (1).

Morgagni (2) in 1740 was the first to recognize the characteristic yellowish nodules of the adrenal in the near vicinity of the gland. Since then, ectopic adrenal tissue has been reported in such diverse locations as the brain, lungs, liver, gallbladder, kidney, pancreas, transverse colon, celiac plexus, broad ligament, ovaries, testes, epididymis and retroperitoneally along the course of the vessels to the gonads (1,7,8,9). The coeliac plexus is the most distal area in which ectopic adrenal medullary tissue has been found. Ectopic adrenal tissue has also been discovered more distally (1,7,10). In the present series, 21 ectopic adrenal tissues were detected along the course of the spermatic

Figure 1: Adrenal cortex and medulla tissue presented separetely. The cortical cells are arranged in a nearly normal pattern (H.E 40X magnification).

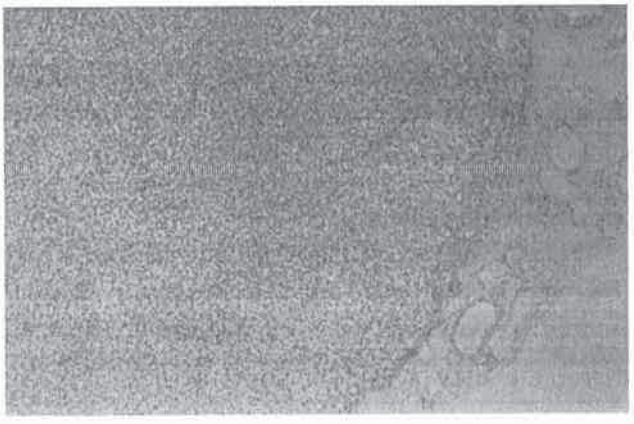

Figure 2: Only the medullary cells are seen. The cells show no organisation (H.E 40X magnification).

cord and on the wall of the pseudocyst formation along the transverse colon.

Though most often located in the vicinity of the adrenal gland, the presence of adrenocortical tissue has been reported in the apex of the hernial sac in 22 out of 771 (2.85%) operations for inguinal hernia in children, whereas in the subgroup operated upon for undescended testes an incidence of 9.3% was observed (1). There is a tendency for predilection of the right side. The present series revealed 0.76% ectopic surrenal tissue in inguinoscrotal problems, and 77% of them were right-sided. Bilateral occurrences were not detected in the present series or in the literature survey (1,11).

The adrenal gland has a double origin: The cortex develops from the mesoderm of the Wolfian ridge, whereas the medulla originates from the ectoderm of the primitive ganglionic crest. The medulla penetrates the cortex along the central vein and becomes enveloped by the adrenal cortical tissue. During this penetration, small fragments, mostly consisting of this cortex, separate and form the accessory adrenal structures. Most of these ectopic adrenals are situated near the normal adrenal, but some of them are displaced during the migration and descent with the gonadal structure. In general, when these accessory glands are formed at a distance removed from the parent glands they are composed of cortical tissue only, while those closer to the adrenal gland may contain medullary substances as well. It has been concluded that the ovarian vein might contribute to fragmentation of the adrenal cortex as the vein develops over the surface of the gland, bringing an accessory nodule of adrenal tissue with it during descent of the gland. An alternative but not as widely accepted theory is that ectopic adrenal tissue develops from pluripotent cells at the spot where they are encountered (1,2,3,7,10,12,13).

Ectopic adrenal tissue is associated with the gonads because adrenal cortical tissue develops in the region of the urogenital ridge, and foci of the developing cortex may be carried with the descending gonad and thus lie in proximity with it. The separate development of the medulla from the neuroectoderm makes it less likely to be in proximity to the gonads in the adult position. Ectopic adrenal cortex in hernia sacs is likely due to the incomplete descent of cortical cells accompanied by a descending testis (3,5,7).

Habuchi et. al. (8) reported the simultaneous occurrence of epididymal abnormality and ectopic adrenal tissue as incidental findings during surgical operations for inguinoscrotal problems. Mininberg and Dattwyler (14) reported that ectopic adrenal tissue can cause neonatal spermatic cord torsion.

Ectopic adrenal tissue is of potential clinical significance because of its association with congenital adrenal hyperplasia. It may also occur in untreated or poorly controlled congenital adrenal hyperplasia and may lead to treatment regulation problems and poor prognosis (15). Bilateral testicular masses in children with adrenogenital syndrome may mimic Leydig cell tumors, which are also a common cause of precocious puberty and which appear to be derived from cells of possible adrenal origin stimulated by adrenocorticotrophic hormones (16). It may also evolve into a neoplasm or the site of production of excessive adrenal hormones, particularly after bilateral total adrenalectomies (4,8,10,12,17). In the present series, there was only one retroperitoneal pelvic neuroblastoma detected on the course of the vessels, but it was not clearly defined as originating from ectopic adrenal tissue or from the sympathetic ganglions. There were no paratesticular neuroblastoma found in this series.

The occurrence of adrenal rest cells in paratesticular sites were noted in 15 testes of 100 infants examined at autopsy. These rests may become clinically significant when they manifest as scrotal masses in patients with elevated levels of adrenocorticotropic hormone. The belief that adrenal rests within or near the testes can be stimulated to undergo tumorous hyperplasia by continuously excessive levels of adrenocorticotropic hormone is supported by the frequent occurrence of unilateral or bilateral testicular tumors in male patients with congenital adrenal hyperplasia (3,4,17).

Bilateral appearances of neuroblastomas are rare and are often considered to represent metastatic spread rather than simultaneous primary malignant lesions. The incidental finding of a nodular mass in the inguinal canal in children usually occurs during surgical exploration for pathologies in the region. A case of bilateral neuroblastoma occurring simultaneously in the inguinal canals of an infant with no evidence of metastatic disease has been reported (6).

The functional significance of ectopic adrenal tissue is due to its ability to undergo adenomatous hyperplasia associated with the production of endocrine dyscrasias and its compensatory functional

hypertrophy following destruction or ablation of the adrenal glands (1). Computer tomography and scintigraphy provide the first line of investigation for identifying possible ectopic tumors or recurrences (18,19).

Although ectopic adrenal tissue tends to atrophy and disappear during childhood and rarely undergoes adenomatous or neoplastic changes, removal of aberrant adrenal tissue is warranted whenever encountered incidentally (1,3). It is especially important in congenital adrenal hyperplasia because of the difficulty in treatment when adrenal remnants are present (15,16). It is generally agreed, however, that surgical dissection of the spermatic cord for these nodules may outweigh the benefits and should not be performed as a routine measure.

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INITIAL AMNIOCENTESIS CASES FROM ANKARA UNIVERSITY OBSTETRICS AND GYNECOLOGY PRENATAL DIAGNOSIS LABORATORY

Fulya Tekşen* • Acar Koç**

SUMMARY

The aim of this study was to investigate chromosomal abnormalities, fetal loss rates, mosaicism, complications and rates of false positive or negative results in patients who underwent amniocentesis. Included in the study were 125 women with prenatal diagnosis indications at 16-20 weeks of gestation. Cytogenetic investigation produced three abnormal karyotypes, giving a chromosomal abnormality rate of 2.4 percent. No mosaicism, complications related to the procedure or false positive or negative results were observed. The study concluded that amniocentesis is a safe and reliable diagnostic procedure for second-trimester high-risk pregnancies when performed by an experienced team.

Key Words: *Amniocentesis, Fetal Loss Rate, Mosaicism*

ÖZET

Ankara Üniversitesi Kadın Hastalıkları ve Doğum Prenatal Tanı Laboratuvarında İlk Uygulanan Amniyosentez Vakaları

Bu çalışmanın amacı, amniyosentez uygulanan hastalardaki; kromozom anomalileri, fetal kayıp oranları, mozaisizm, işleme bağlı komplikasyonlar ile yalancı pozitif ve yalancı negatif sonuçların incelenmesidir.

Çalışmaya, prenatal tanı endikasyonu taşıyan 16-20 haftalık gebe 125 kadın katılmıştır.

Sonuçta; kromozomal anomali oranı, 3 patolojik karyotip ile % 2.4 olarak bulunmuş, mozaik bulguya rastlanmamıştır. Ayrıca işleme bağlı komplikasyon ortaya çıkmamış ve yanlış pozitif veya negatif sonuçlara rastlanmamıştır. Böylece, deneyimli bir ekip tarafından

gerçekleştirildiğinde amniyosentezin , yüksek risk taşıyan gebeliklerde rahatlıkla uygulanabilen, güvenilir bir prenatal tanı yöntemi olduğu kanısına varılmıştır.

Anahtar Kelimeler: *Amniyosentez, Fetal Kayıp Oranı, Mozaisizm*

Possibilities for treating, or, ideally, avoiding hereditary diseases have increased enormously with the rapid and radical developments in the field of molecular biology (1). Today, by the use of routine sampling and diagnostic testing procedures such as amniocentesis, chorionic villus sampling and cordocentesis, in utero and even pre-implantation diagnosis, termination of pregnancy in the early weeks of gestation is possible (2). Amniocentesis has been a routine test for high-risk women since the early to mid-1980s. (3). The procedure has great advantages of high diagnostic reliability and low fetal loss rate related to the procedure. In addition to chromosome analysis, levels of enzymes, hormones, amino acids and metabolic products detected in the amniotic fluid are used in the prenatal diagnosis of Mendelian and multifactorial genetic diseases (4,5). This study describes our experience in genetic amniocentesis in a group of 125 high-risk pregnancies.

MATERIAL AND METHODS

The study included 125 high-risk women with fetuses at 15-22 weeks' (17.5 mean) gestational age. Ages of these women ranged from 17-44 years (32.8 mean). Indications for inclusion in the study were: advanced maternal age (n=61); previous child with chromosomal abnormality (n=13); pathological USG (n=9); suspicious triple test results (n=23); Mendelian genetic disease in the family (n=10); previous child with neural tube defect (n=5); previous child with mental retardation (n=3); maternal pathology (n=1) (Table 1). Amniocentesis was performed by the same team of obstetrician, genetician, sonographers and laboratory personnel in each case. Under guidance of ultrasonography, a 20-gauge needle was used to take 20 ml of amniotic fluid from each patient at between 16-22 weeks (17.5 mean) of gestation. Three of the specimens taken were bloody, but this did not affect the growth of cells in

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Table1. Indications of women undergoing amniocentesis

INDICATION	n
Advanced maternal age	61
Previous child with chromosomal abnormality	13
Pathological USG	9
Suspicious triple test results	23
Mendelian disease in the family	10
Previous child with NTD	5
Previous child with mental retardation	3
Maternal pathology	1
TOTAL	**125**

Table 2. Cytogenetic results and follow-up after amniocentesis

KARYOTYPE	n	OUTCOME
46,XX	67	Normal liveborn
46,XY	55	Normal liveborn
47,XX,+21	3	Induced
TOTAL	**125**	

the culture. After 10-15 days, amniocyte cultures were harvested, chromosomes were G-banded and cytogenetic analyses were performed.

RESULTS

There was no fetal loss related to the procedure. Three abnormal karyotypes were observed, giving a pathology rate of 2.4 percent. The abnormal karyotypes were trisomy 21 (n=2) and Klinefelter syndrome (n=1). All of the abnormal fetuses were induced. In the follow up, it was observed that all the pregnancies with normal karyotypes resulted in live births (Table 2). There was no culture failure, and no mosaicism was observed. There were no false positive or false negative results.

DISCUSSION

Amniocentesis performed in the second trimester of pregnancy by experienced hands provides great advantages to high-risk women. However, both maternal and fetal risks related to the procedure have been reported. Maternal risks include bleeding, infection, amniotic fluid embolism and blood-group sensitization secondary to the procedure (6,7,8,9). Risks to the fetus are spontaneous abortion, puncture and induced malformations (10,11).

Studies have shown spontaneous abortion rates after the procedure have ranged from 0.2-1.5% (8,10,11,12,13). Other comparative studies have shown the added risk of spontaneous abortion from amniocentesis as only 0.03 % (13,14) when compared with control groups with no predisposing factors and a history of spontaneous or induced abortions as well as bleeding, maternal age, smoking and alcohol consumption (15), the technique of puncture and placental site (16). In our study of amniocentesis cases, no spontaneous abortions were observed.

In some studies, obtaining fluid free from contaminating red blood cells was found to be important for the success of cell culture (17). The use of USG has been found to significantly reduce the number of blood-tinged specimens (12). In our study, fluid samples containing blood did not affect the success of the cultures. Culture success have been reported at 96.7-99.7% (6,12,18,19). We did not observe any culture failure and were able to produce cytogenetic results for all patients on whom the procedure was applied.

Another problem faced in amniocentesis is mosaicism. This finding may be indicative of a fetal anomaly, which is defined as the existence of more than one cell line in the same individual. The abnormal cell line may be restricted to extra-embryonic tissue or may be the result of an in-vitro event (20). Cases of mosaicism at a rate of 0.001-0.4% have been previously reported in the literature (18,19,20,21). We did not observe any mosaicism in our study.

Our pathological case rate of 2.4% is comparable with results of other centers (2.6-6.4%) for chromosomal anomalies (6,22,23,24).

Our study concluded that amniocentesis is a safe and accurate procedure when performed by experienced hands to high-risk women in the second trimester of pregnancy.

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CLINICAL SIGNIFICANCE OF LVOT OBSTRUCTION CAUSED BY SEPTAL HYPERTROPHY: ASSOCIATED AND DISTINCTIVE POINTS BETWEEN THE AGING PROCESS AND OTHER CARDIAC DISEASES

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SUMMARY

Septal hypertrophy is one cause of left ventricular outflow tract (LVOT) obstruction. It has been suggested that this morphological finding may develop with age along with other cardiac pathologies. Some hypothetical approaches have been produced and added into the literature. Recent advances in real-time three-dimensional imaging have been helpful in evaluating myocardial hypertrophy caused by various mechanisms. In this review, similarities and differences in hypertrophic septa are discussed, and potentially significant imaging features, including recent advances, are evaluated.

Key Words: *Septal hypertrophy, left ventricular outflow tract obstruction, real-time 3-dimensional echocardiography*

ÖZET

Septal Hipertrofinin Neden Olduğu Obstruksiyonun Klinik Önemi: Yaşlılık ve Diğer Kardiyak Hastalıklarda Ayırıcı ve Birlikte Olan Noktalar

Septal hipertrofi sol ventrikül çıkış yolu daralmasının nedenlerinden biridir.Bu yapısal bulgunun kalp hastalıkları haricinde yaşlanma ile de gelişebileceği öne sürülmüştür.Bu konuda bazı hipotezler üretilmiş ve literatüre geçmiştir. "Real-time" 3 boyutlu ekokardiyografide son gelişmeler farklı mekanizmalarda oluşan myokard hipertrofisinin değerlendirilmesinde yararlı olmuştur.Bu derlemede,hipertrofik septumdaki benzerlikler ve farklılıklar tartışılmış ve yeni ilerlemeler ile birlikte önemli görüntüleme özellikleri değerlendirilmiştir.

Anahtar Kelimeler: *Septal hipertrofi,Sol ventrikül çıkış yolu darlığı, "real-time" 3 boyutlu ekokardiyografi*

Left ventricular outflow tract (LVOT) obstruction has been classically observed in association with hypertrophic obstructive cardiomyopathy (HCM). In this setting, the LVOT obstruction-producing pressure gradient is due to asymmetric septal hypertrophy and systolic anterior motion (SAM) of the mitral valve. SAM is related to the anterior position of the mitral valve in HCM (1). Decreased mitral anular motion, possibly due to altered myocardial function, has been observed in HCM using real-time three-dimensional echocardiography (3-DE) and complex annular reconstruction methodology.

Whether the increased terminal velocities represent measurable pressure gradients associated with an obstruction has been a point of controversy in the HCM literature for many years (3,4). We observed LVOT area obstruction in HCM patients using real-time 3-DE, with a meaningful correlation between three-dimensional LVOT volume and LVOT gradients (5).

LVOT obstruction has been shown to occur in some clinical conditions including concentric hypertensive hypertrophy (6), excessive sympathetic stimulation (7) and pericardial tamponade (8) and after aortic valve replacement for aortic valve stenosis (9).

The occurrence of a dynamic LVOT obstruction has recently been described in the setting of acute myocardial infarction (MI) (10-12). The proposed mechanism for this occurrence in MI patients has been apical infarction with compensatory hyperkinesis of the residual, normally perfused basal segments of the myocardium. This compensatory hyperkinesis decreases the systolic LVOT cross-sectional area, resulting in acceleration of blood flow through the LVOT (13).

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In the normal heart, the left border of the septum is continuous with the anterior wall of the aorta, with a smooth, gentle curvature. Anatomical studies have shown that in the aged heart the ascending aorta moves to the right and the septum becomes located below the aortic valve (14).

Another cause of LVOT narrowing is proximal septal bulge (PSB). The anatomic change in septal position in PSB produces a dynamic ventricular ejection, in that outflow tract velocity is increased; this is comparable with HCM and LVH groups. It has been suggested that focal hypertrophy may be secondary or contributory to the enhanced ventricular dynamics in a manner different from that of primary cardiomyopathy (15). In the pathologic study of Goor et al. (16), the protrusion of the septum was clearly a function of age, but hypertrophy was not found. It is known that the angle between the midseptum and aorta is more acute in sigmoid septum, while a more obtuse angle is seen in normal as well as cardiomyopathic patients (17,18). On the other hand, in subjects with PSB, a more acute angle developed only in systole (15).

We recently observed smaller LV midbasal and basal segment volumes in patients with secondary forms of LVH by deriving a quantitative index of LV geometry using real-time 3-DE (19). This finding suggests that basal LV hypertrophy may be caused by increased afterload in LVH patients with aortic stenosis or hypertension. Similarly, increased afterload resulting from arteriosclerosis due to aging may be one cause of PSB in the elderly. Increased afterload imposed by shearing stresses on the focal area of the septum is associated with the development of septal angulation, which means that the focal hypertrophy effect may be seen predominantly in aged patients (15).

In cases with protruding angulated septa, impact pressure due to kinetic pressure combined with lateral pressure has been described as occurring in the high-velocity stream of the narrowed outflow tract, whereas other walls are subject to static lateral pressure only (20). The distortion of the flow stream as the septum ages may produce increased shearing stresses (21) along the walls of the outflow tract, which might induce selective hypertrophy of the focal area.

It is usually accepted that cardiac hypertrophy is associated with increased pressure and volume overload, resulting in increased wall stress (22). In PSB patients, increased velocity is associated with convective acceleration that is almost always seen as decreased hydrostatic pressure to the wall (15). Using real-time three-dimensional volume data in patients with LVH, we observed increased mitral annulus longitudinal and circumferential motion, suggesting hyperactivity in the LV basal segment (2). Similarly, the contraction of the ventricle moves the angulated basal portion of the septum more transversely across the short axis of the LV toward the base of the mitral valve, narrowing the outflow tract in PSB patients, while the basis of the septum descends markedly toward the apex in HCM patients (15).

LVOT velocity pattern in PSB and LVH patients may be differentiated. Subvalvular flow acceleration is detected in LVH with aortic stenosis before (23) or after (9) aortic valve replacement, while development of high velocity as the outflow tract narrows is more consistent with convective acceleration (24).

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CONGENITAL COMPLETE DEFICIENCY OF GH, TSH, AND PRL IN TWO SIBLINGS (Case Report)*

İffet Bircan ** • Serap Semiz *** • Sema Akçurin ****

SUMMARY

Congenital defects of the pituitary gland include autosomal recessive, autosomal dominant and an x-linked mode of inheritance. Mutations of pituitary-specific transcription factors Pit-1 and Prophet of Pit-1 (PROP1) are well known causes of the clinical entity of combined pituitary deficiency. Several newly discovered pituitary genes have been identified that regulate hypothalamic and pituitary development and are candidates for hypopituitarism in humans.

We describe two siblings with combined growth hormone, thyrotropin and prolactin deficiency. No genetic mutation for Pit-1 or PROP1 could be detected in the molecular genetic study of the cases and their parents. Our cases were found to have the same genotype for a new locus, of which additional, tightly linked markers should be sought.

Key Words: *Combined pituitary hormone deficiency, Pit-1, PROP1*

ÖZET

GH, TSH ve PRL'nin İki Erkek Kardeşte Konjenital Yokluğu

Hipofiz bezinin doğumsal defektleri; otozomal resesif, otozomal dominant ve X' e bağlı geçiş gösterir. Hipofizer spesifik farklılaşma faktörleri Pit-1 ve Prophet Pit-1 (PROP1) mutasyonları, kombine hipofizer yetmezliğin iyi bilinen klinik antitelerdir. Hipotalamik ve hipofizer gelişimi düzenleyen birkaç yeni hipofizer gen tanımlanmıştır ve insanlarda hipopituitarizm tanısı için adaydırlar.

Büyüme hormonu, tiroid stimulan hormon ve prolaktinin kombine eksikliği olan iki erkek kardeşi tanımladık. Olgular ve ailelerinin moleküler genetik çalışmalarında, Pit-1 ya da PROP1' e ait genetik mutasyon saptanmadı. Olgularımız, yeni lokusla ilgili olarak aynı genotipe sahiptiler; bu yeni lokus için ek-sıkı ilişkili "marker" ların araştırılması gerekmektedir.

Anahtar Kelimeler: *Kombine hipofizer hormon eksikliği, Pit-1, PROP1*

Specific hormones, such as growth hormone (GH), prolactin (Prl), thyrotropin (TSH), adrenocorticotropic hormone (ACTH), luteinizing hormone (LH), and follicle stimulating hormone (FSH), are secreted from numerous specialized cells in the pituitary gland (1). Pituitary function depends on the integrity of the hypothalamic-pituitary axis, so any defect in the development and organogenesis of this gland may result in a form of combined pituitary hormone deficiency (CPHD), which indicates an impaired production of GH and the lack of one or more of the other hormones produced in the anterior pituitary gland (1,2).

CPHD is a clinical entity with autosomal recessive, autosomal dominant or an x-linked mode of inheritance (1). Pituitary-specific transcription factors Pit-1 and Prophet of Pit-1 (PROP1), and their target genes are well known to cause the clinical situation of combined pituitary deficiency (3). Dominant and recessive mutations in the Pit-1 cause CPHD with severe deficiencies of GH and Prl and variable deficiency of TSH (4-7). Many other homeodomain and transcription factors have been identified as being involved in different developmental stages, such as P-Lim, P-OTX, ETS-1, and Brn 4 (8-10). Most recently, a novel, tissue-specific, paired-like homeodomain transcription factor, termed PROP1, has been identified as the cause of the Ames Dwarf mouse phenotype. Thereafter, different PROP1 gene alterations have been found in humans with

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CPHD (11,12). PROP1 gene mutations of considerable high frequency are reported in families with CPHD (12-14).

Two siblings with a combined deficiency of GH, TSH and Prl are presented in this article. Genetic studies of the family have been done and the literature has been reviewed.

CASE REPORT 1

An eight-day-old boy was admitted to our hospital with jaundice. He was the first-born child of nonconsanguinous parents. He showed developmental delay, puffy face and dull expression. The anterior and posterior fontanels were widely open, the forehead was prominent, and the bridge of the broad nose was depressed. He had a micropenis. Radiological study of the knees revealed no epiphyseal center. 3,5,3'-Triiodothyronine (T_3), thyroxine (T_4) and TSH levels were found to be 0.36 ng/ml, 2.3 mg/dl and 0.01 mU/ml, respectively. TSH and Prl responses to thyrotropin releasing hormone (TRH) were inadequate (peak: 0.04 mU/ml and peak: 0.01 ng/ml, respectively). Central hypothyroidism was diagnosed and L-T_4 replacement therapy was begun. He was readmitted when he was 4 years old (Figure 1). His bone age was 1.6, height was 73 cm, height standard deviation score was -6.8 and growth velocity was 2 cm/year. Peak GH responses to L-Dopa and insulin tolerance test (ITT), while he was euthyroid, were 0.3 ng/ml and 0.2 ng/ml, respectively. Complete GH deficiency was diagnosed. Cortisol response to insulin induced hypoglycemia was normal (peak: 48 mg/dl) but Prl response could not been detected. Computerized tomography (CT) of the sella revealed an empty sella. GH treatment was begun.

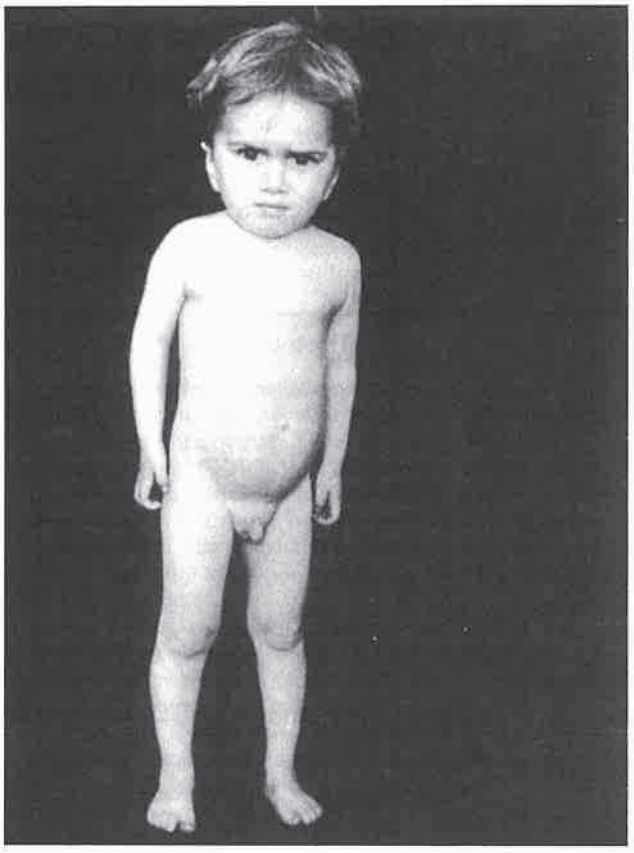

Figure 1: Patient 1, at age 4: dull expression, depressed bridge of the broad nose and micropenis are apparent.

CASE REPORT 2

The second child, also male, was admitted to our hospital at the age of 48 days. In addition to the physical findings present in his older brother, he had an umbilical hernia (Figure 2). His knee radiography revealed no epiphyseal center. T_3, T_4 and TSH levels were 0.01 ng/ml, 1.5 mg/dl and 0.1 mU/ml, respectively. TSH and Prl responses to TRH were insufficient (peak: 0.1 mU/ml and peak: 0.01 ng/ml, respectively). Central hypothyroidism was diagnosed and L-T_4 treatment was begun. At the age of six months, while he was euthyroid, GH provocation tests were done. Peak GH responses to L-Dopa and ITT were 1.1 ng/ml and 0.5 ng/ml, respectively. Complete GH deficiency was diagnosed and GH replacement therapy was begun. The cortisol response to insulin induced hypoglycemia was normal (peak 38 mg/dl), Prl response could not be detected. A CT of the pituitary gland was normal.

METHODS

Hormonal studies

The T_3, T_4, and TSH were determined by using the 'two - side sandwich immunoassay' method (ACS 180, CHIRON). The serum GH and cortisol were determined by chemiluminescence enzyme immunoassay (DPC Immulite 1000 and ACS 180, CHIRON, respectively). The Prl was determined by using an alkaline phosphatase kit, L2PRA2 (Immulite 2000).

Genetic studies

Genetic studies of the patients and their parents were done at the Division of Genetics, Department of Pediatrics, Vanderbilt University, Nashville, USA. The

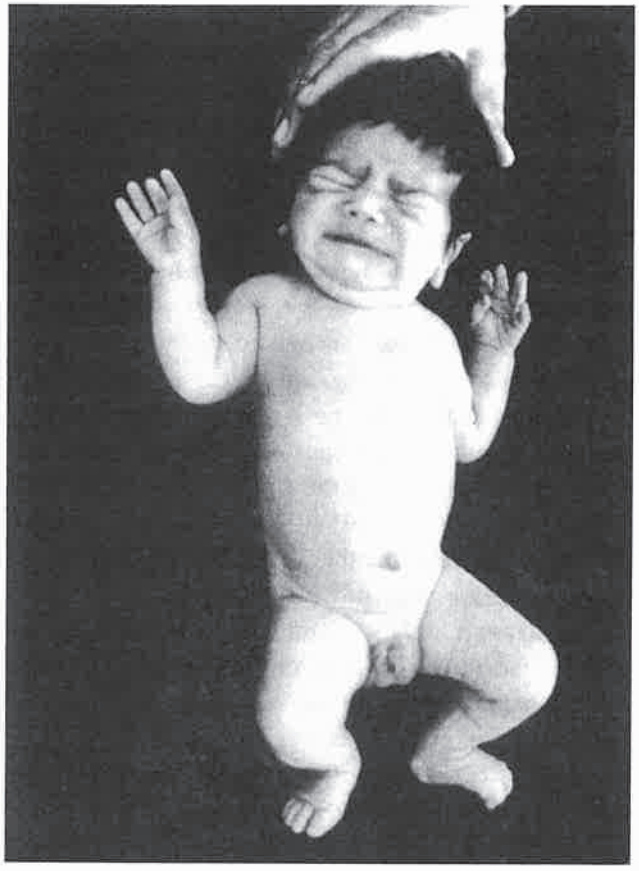

Figure 2: Patient 2, at the age of 48 days: puffy face, depressed bridge of the broad nose, micropenis and umbilical hernia are noted.

methods used by the investigators have been explained below.

Genomic DNAs were genotyped for two dinucleotide repeat polymorphisms, D3S1559 and D5S408, linked to the Pit 1 and PROP 1 genes, respectively. Genomic DNA (200 ng) was added to a 50 ml reaction mixture of 10 mM Tris- HCl (pH 8.3), 1.5 mM $MgCl_2$, 25 mM KCl, 200 mM/L of each dNTP, 1.5 pmoles of 5'-end- labeled forward oligonucleotide primer, 1.5 pmoles reverse oligonucleotide primer, and 2.5 U Taq Polymerase (Gibco- BRL, Gaithersburg, MD). The forward and reverse primers for D3S1559 were 5'-CACCCAAAGTGCTGAGATTAC-3' and 5'-CCTTAAGAGCATGATGATCCTTTT-3', respectively. The forward and reverse primers for D5S408 were 5'-ACAACTTCCAACCCTGAGAT-3' and 5'-ACTGTGCCTAGCCTTCATTT-3', respectively. The PCR reaction mixture was denatured for 3 min at 94C and cycled 32 times (94 C, 30 sec; 55 C, 30 sec; 72 C, 30 sec), followed by a 10 min extension at 72 C. The products were separated on a 6% denaturing polyacrylamide gel and visualized by autoradiography.

RESULTS

The genetic investigators reported that the PROP1 gene has been ruled out, as the genotypes for the two affected siblings were different. With respect to the Pit-1 locus, the family was not fully informative with the related markers (Because the father was homozygous for the Pit-1 marker and the mother was homozygous for another new locus marker). The family pedigree, with the segregation results for Pit-1, PROP1 and the new locus marker, is shown in Figure 3. The genetic researchers informed us that the new locus appeared to segregate, but they did not have a gene for this region yet, so further study was not possible.

DISCUSSION

The anterior lobe of the mature pituitary gland is populated by at least five highly differentiated cells that are progressively refined by the expression of additional activating / or restricting factors, such as Pit 1

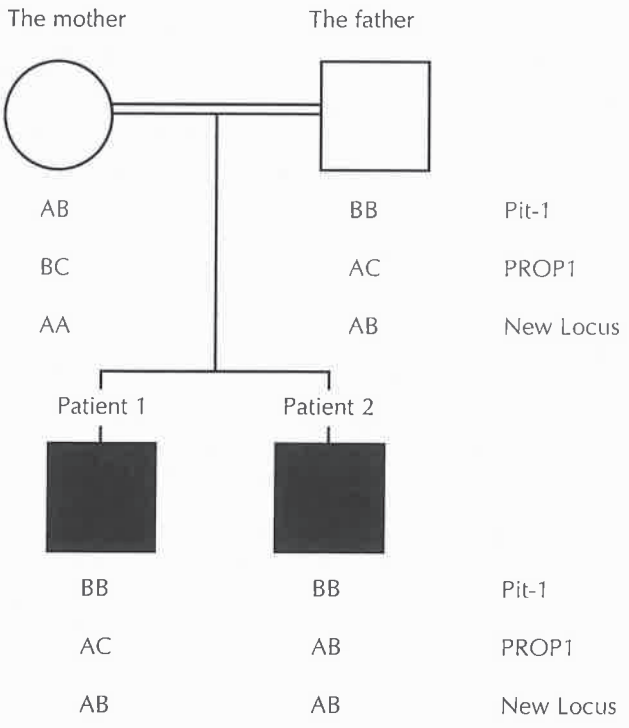

Figure 3: The family pedigree with the segregation results for pit-1, PROP1 and the new locus marker.

and Prop1. Pit-1, expressed in thyrotrops, somatotrops, and lactotrops, is required for the continued expression of the Pit-1 gene itself, and for the proliferation and survival of three cell types (15,16). Aside from the congenital complete GH and Prl, and the complete or partial TSH deficiency, the normal genital structure, spontaneous pubertal development, and the variable anterior pituitary size, typical findings in cases with Pit-1 gene mutation resemble the phenotypic characteristics seen in Laron's Syndrome or isolated GH deficiency type 1A (1). The occurrence of these different deficiencies varies, but the patients became symptomatic, presenting with severe growth retardation and failure to thrive, before the age of 12 months, and were normally diagnosed before the age of 2 years (17). Multiple pituitary hormone deficiency due to Pit-1 mutations is inherited either dominantly or recessively, depending on the DNA binding properties of the mutant protein (18). PROP1, a pituitary–specific, paired-like homeodomain transcription factor, has been shown to be important for determining the Pit-1 lineages, as well as the gonadotrope differentiation in the pituitary gland (11). PROP1 is expressed earlier than Pit-1 and known to contribute directly to Pit-1 transcription activation (3). Phenotypes of the two mutations are normal in heterozygous cases (3).

Clinical and laboratory findings in the cases presented here were thought to have Pit-1 or PROP1 gene mutations. The initial presentation in both patients was that of growth retardation and failure to thrive caused by TSH and GH deficiency. Because the patients in our cases had not yet reached the pubertal period, spontaneous puberty and LH and FSH responses to GnRH, could not be evaluated. Phenotype variability also applies to pituitary size in our patients. Magnetic resonance imaging of the sellar regions showed variable sizes of pituitary glands, which are generally hypoplastic in this disorder (2). Partial empty sella in the older brother has been interpreted as a primary empty sella due to intrinsic pituitary hypoplasia.

Pit-1 gene mutation has been detected in some families with the same characteristics seen in CPHD, and families with PROP1 gene mutation have been reported with increasing frequency in recent years (12-14). Furthermore, 3/4 of the CPHD families reported had a 2-bp deletion (301-302 del AG) in Exon2 of PROP1, suggesting that the 301-302 del AG mutation may be a major cause of CPHD (12,19).

The patients and their family have been genotyped with the most tightly linked markers for CPHD. Molecular genetic study of the siblings with CPHD, and of their family, could not detect Pit-1 or PROP1 gene mutation. Nevertheless, it has been concluded that our cases have the same genotype for a new locus, and additional tightly linked markers must be sought for this new locus.

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A CASE OF LIVE BORN TRIPLOIDY WITH 69, XXX KARYOTYPE

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SUMMARY

In this study, a case of triploidy with 69,XXX karyotype is presented. The infant was born at 32 weeks of gestation and lived for 5 hours. The post mortem autopsy revealed a hydrophilic placenta and polycystic kidneys. In addition, the mother of the proband had intrahepatic cholestasis of pregnancy (ICP).

The importance of prenatal diagnosis in such cases is emphasized.

Key Words: *Triploidy, hydropic placenta, polycystic kidneys, intrahepatic cholestasis*

ÖZET

69 XXX Karyotip Triploidli Yeni Doğan Vakası

Bu çalışmada 69 XXX karyotip bulunan triploidli bir vaka takdim edildi. 32 haftalık bir kız çocuğu olarak doğdu ve 5 saat yaşadı. Post mortem çalışmada, otopsi ile hidropik plesenta ve polikistik böbrekler tespit edildi. Keza annesinin gebeliğinde intrahepatik kolestaz geçirdiği saptandı. Bu tip vakalarda prenatal tanının önemi ortaya konmuştur.

Anahtar Kelimeler: *Triploidi, hidropik plesenta, polikistik böbrek, intrahepatik kolestaz*

Triploidy is a chromosomal abnormality with three sets of haploid chromosomes (3n) totaling 69. In general, about 1-3 % of all human conceptions are triploid (1). Nearly 50 percent of all first-trimester spontaneous abortions are either genetically or structurally abnormal and 7-28.9 % of them are triploid (2). Triploidy is a uniformly lethal condition (3). Infrequently, triploid infants survive birth after 28 weeks of gestation, but they die shortly thereafter (3).

The origin of an extra set of chromosomes may be either via fertilization of the ovum by two spermium (dispermi) (4) or from the failure of one of the maturation divisions in the ovum (digyny) (2) or sperm (diandry) (1,2).

Controversy remains regarding the risk of recurrence of triploidy and there is no data to indicate an increased risk of recurrence.

CASE REPORT

A 28-year-old woman was admitted to the Ankara University, School of Medicine, Department of Gynecology and Obstetrics at 30 weeks of gestation with complaints of pruritus and abdominal distention. She suffered from influenza, emesis, and bleeding during the first trimester of her pregnancy. In addition, the patient had thyroid gland problems and had previously taken Levotron for this condition. During this pregnancy, however, she refused to use any drug. Her obstetric history was as follows: gravida 3, parity 1 and abortus 1.

The ultrasonographic examination revealed *polyhidroamnios I cannot find this word in the medical dictionary!*, a gross placenta and polycystic kidneys. Laboratory investigations of the patient, including a hemogram, a urine examination, hepatic, renal, and thyroid function tests, and serum glucose level, were all normal. The patient had plantar and palmar pruritus without any dermatic lesions. She was diagnosed with intrahepatic cholestasis and given three times 4 grams of cholestiramin per day for the relief of her symptoms.

A cordocentesis was done due to abnormal ultrasonographic findings. Fetal blood (tested by APT test) obtained from the umblical cord was cultured for 72 hours and then harvested. 20 G-banded metaphases were counted and three of them were analyzed and kar-

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yotyped. In the cytogenetic evaluation, the 69 XXX chromosome constitution was obtained in all metaphases.

The proband was born at 32 weeks of gestation to non-consanguinous parents. No other individual in the family was reported to have a chromosomal anomaly. The infant lived for 5 hours. She was 44 cm in length and weighed 2100 gr. In the physical examination, no gross anomaly was found, but the autopsy revealed a hydrophilic placenta and polycystic kidneys.

DISCUSSION

Triploidy is one of the most devastating chromosomal disorders to occur as it allows no life expectancy for the fetus and leads to severe obstetrics problems in the mother.

Fetal defects include holoprosencephaly (3), posterior fossa cysts, exomphalos and other central nervous system anomalies (5), limb anomalies (6), cardiovascular system anomalies (3,6), respiratory system anomalies, (6), genito-urinary system anomalies (6), facial dysmorphism such as nasal malformations (6), skeletal deformities, hypoplastic internal organs, hypotonicity and deficiencies of the gall bladder. In most of these cases, decreased amniotic fluid volume, intrauterine growth retardation (3,7), cystic placental changes (5,7) and nuchal translucency (5) are common ultrasonographic findings.

In our case, *polyhydramnios*, an abnormal placenta, cardiovascular defects and polycystic kidneys were observed.

Although pregnancy induced, hypertension (3,4) with eclamptic seizures that are seen in the second trimester (5), at approximately 22 weeks of gestation, and a partial hydatidiform mole frequently coexist with triploidies. In our case, a partial hydatidiform mole was observed and confirmed by a pathological examination, but the mother did not have hypertension.

The mother of the proband also had intrahepatic cholestasis of pregnancy. Low T3 levels associated with intrahepatic cholestasis association have previously been reported (8). The cause of cholestasis of pregnancy is unknown. Some clinical observations suggest its pathogenesis to the effects of hormones (9). A significant change in some hormones such as unconjugated estrogen, beta-human chorionic gonadotropin and alpha-fetoprotein is also common. Deviations from normal levels of these hormones after 16 weeks of gestation may be related to the chromosomal anomalies of the fetus. This condition is used as criteria for performing the triple test to screen for chromosomal disorders. For example, an elevated maternal serum alpha-fetoprotein (MSAFP) is frequently noted in triploidy cases and is caused by associated fetal anomalies like omphalocele or by an excessive transfer of AFP related to increased placental size. In addition, human chorionic gonadotropin levels were found to be high in triploid cases at 10-14 weeks of gestation.

This is an unusual case of severe cholestasis of pregnancy with triploidy. Although it is difficult to comment conclusively about this association, it may represent a pathogenetic relationship. More studies are needed to investigate this phenomenon.

There are many reports of stillbirths attributed to ICP, but the chromosomal constitution of these cases is unknown. It is estimated that 4-5 percent of stillbirths have chromosome aberrations. Therefore, it is important to determine the karyotype of stillbirths related to ICP in order to determine the possible relationship between them. Cytogenetic studies should be done routinely in all cases of stillbirth.

In the prenatal diagnosis of triploid pregnancies, an ultrasonographic examination, the measurement of maternal serum human chorionic gonadotropin and alpha-fetoprotein, the determination of the DNA content of placental stromal cells by flow cytometry or image cell analysis, and a microscopic examination of the placenta with the standard criteria are recommended. In order to confirm the diagnosis, a karyotype analysis should routinely be done. A non-invasive method with a FISH analysis of isolated nucleated red blood cells from the maternal peripheral circulation at 12 weeks of gestation by X and Y probes are shown, (10) and a detection of the serum markers of pregnancy-associated plasma protein A (PAPP-A) and free beta chain of chorionicgonadotropin (free-beta hCG) in the same blood sample is reported (10).

In conclusion, appropriate genetic counseling and a prenatal diagnosis should be offered to women with triploid conceptus in their obstetric history and attention should be paid to cases of intrahepatic cholestasis of pregnancies. An early diagnosis of this abnormality is especially important for the appropriate obstetric intervention and prevention of maternal complications due to triploidy.

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THE COEXISTENCE OF PEMPHIGUS VULGARIS AND MULTIPLE BASAL CELL CARCINOMA ARISING ON AN OLD RADIOTHERAPY SCAR

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Ahu Birol • Erbak Gürgey***

SUMMARY

Pemphigus vulgaris is a chronic autoimmune bullous disease of the skin and mucous membranes. Various factors, including drugs, nutritional factors, physical agents, viruses, and emotional stress are believed to play an important role in those individuals predisposed to this condition. An association between pemphigus vulgaris and basal cell carcinoma is rather unusual. We present the case of a 65 year-old man with pemphigus vulgaris and multiple basal cell carcinoma, which was localized only on his scalp and followed radiotherapy for favus.

Key Words: *Pemphigus vulgaris, Basal cell carcinoma, radiotherapy*

ÖZET

Radyoterapi Sonrası Gelişen Pemfigus Vulgaris ve Multipl Basal Hücreli Karsinoma Vakası

Pemfigus vulgaris, deri ve mukoza tutulumuyla karakterize kronik otoimmün büllöz bir hastalıktır. İlaçlar, nutrisyonel faktörler, fiziksel ajanlar, virüsler ve emosyonel stres gibi çeşitli faktörler hastalığın gelişiminde önemli rol oynar. Pemfigus vulgaris ve bazal hücreli karsinoma birlikteliği oldukça nadir görülür. Burada favus nedeniyle radyoterapi sonrası saçlı deride pemfigus vulgaris ve multipl bazal hücreli karsinoma birlikteliği gösteren 65 yaşında bir erkek olgu sunulmaktadır.

Anahtar Kelimeler: *Pemfigus vulgaris, Bazal hücreli karsinoma, radyoterapi*

Pemphigus vulgaris is a chronic autoimmune bullous disease of the skin and mucosa. Ionizing and ultraviole radiation is thought to play an important role as factors in aggravating or inducing pemphigus (1-3). We present a case of pemphigus vulgaris and multiple basal cell carcinoma arising on an old radiotherapy scar.

CASE REPORT

A 65-year-old man was referred to the Department of Dermatology with a four month history of eroded skin lesions localized on his scalp. Initially the lesion had been small but had progressively enlarged during the last two months. The patient had been treated with radiotherapy for tinea capitis favosa when he was seven years old.

The dermatological examination revealed cicatrical alopecia on the frontal, parietal, and occipital regions. There was an eroded lesion with yellowish, moist, and hemorrhagic crusts measuring 5x7 cm on the vertex (Figure 1). In front of his right ear, there was 0.5 cm hyperpigmented papule. Behind his right ear a 1 cm nodular lesion with telengiectasis were noted. On the right side of his forehead there was a two cm eroded lesion with hyperpigmentation at the edge. Multiple 0.5 cm hyperpigmented papules were also found on the left of his forehead. He did not have any other skin or mucosal lesions. The patient was otherwise healthy; the review of systems was normal, except for a finding of benign prostate hypertrophy. The routine laboratory investigations were normal and included the hematological and the biochemical analyses, a urinalysis, and the erythrocyte sedimentation rate.

Dermatopathologic examination of the biopsy specimen from the eroded lesion on the vertex showed an intraepidermal vesicle in a supra-basal location, typical acantholytic cells, and nodular basal cell epitheliomal islands in the dermis (Figure 2). Direct immunofluorescence studies of the peri-lesional skin revealed IgG and C3 in the intercellular spaces of the epidermis.

Oral prednisolone at 80 mg/day and azathioprine at 150 mg/day were initiated for the treatment of the

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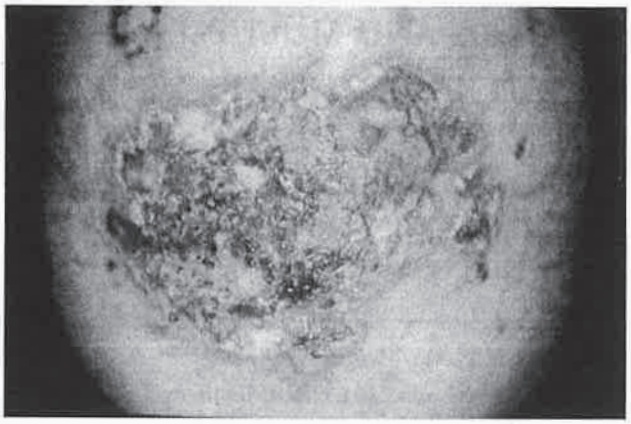

Figure 1: Eczematous and nodular lesions of the scalp

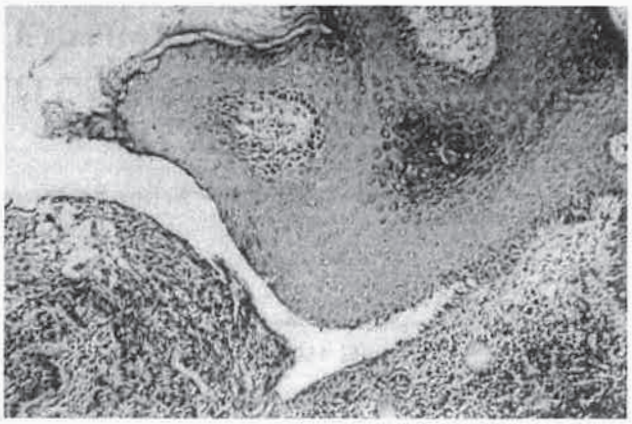

Figure 2: Histopathologic section showing the coexistence of BCC with supra-basal bullae containing acantholytic cells

pemphigus vulgaris. Epithelization was seen within 5 weeks, with a gradual clearing of the lesions and the steroid dose was gradually tapered. The multiple basal cell epitheliomas were totally excised.

DISCUSSION

Pemphigus vulgaris is a chronic bullous disease of worldwide distribution and typical of middle age; it is characterized by thin-walled, relatively flaccid, easily ruptured bullae appearing upon either normal skin or mucous membranes or on erythematous bases. Pemphigus vulgaris may begin in many ways, but the lesions usually appear firstly in the mouth and then most commonly in the groin, face, neck, axillae, or genital areas. Sometimes it may start from the scalp as eczematous lesions, as in our case (1).

Although the cause of pemphigus vulgaris is unknown, a failure in an autoimmune mechanism is clearly the basic instigator. Intercellular antibodies are demonstrable throughout the epidermis or the oral epithelium, and circulating intercellular antibodies are present in the patient's serum. There is an association with various autoimmune diseases such as rheumatoid arthritis, Sjögren's syndrome, myasthenia gravis, lupus erythematous, pernicious anemia, and lymphoreticular disorder (1,2).

Various factors, including drugs such as d-penicillamine captopril, rifampicin, nutritional factors, physical agents, viruses, and emotional stress, may play an important role in those individuals predisposed to developing pemphigus (1,3). Among the physical agents in the environment, ultraviolet light (UV) in sunlight is one of the major factors for the stimulation of the skin. In addition to UV radiation, physical agents such as ionizing radiation and burns have been reported as aggravating or inducing factors in the development of pemphigus (3,4). There have been a few reports of pemphigus vulgaris induced by exposure to sunlight and radiation therapy. It is not known how ionizing radiation may induce pemphigus. It may alter the antigenicity of the epidermal cell surface or expose masked epidermal antigens, and the subsequent impaired immunity that is associated with malignancy may also play a role. (4-6). Some authors suggest that exposure to UVB causes the secretion of IL 6 from keratinocytes, which causes a reduction of the desmosomal connection between cells, and thereby induces the development of pemphigus (2).

An association between pemphigus and malignancy is rather unusual (7-9). These malignancies can be thymic or non-thymic in origin. Non-thymic malignancies are seen two times more often than thymic malignancies (7). Previous publications have reported an association between pemphigus vulgaris and malignant proliferations such as lymphomas, Kaposi's sarcoma, thymoma, leukemia and tumors of the ovary, stomach, breast, esophagus, lung and endometrium. It is not clear, however, if the antigenic determinants may act as antigenic stimuli, immunomodulators, or tumor promoters (8,9).

The antigenic structure of pemphigus itself may be responsible for tumor formation, but this has not yet been confirmed. It has been suggested that depressed immune function may alter the immune surveillance

of the skin, which usually acts to destroy potentially malignant mutant cells. Immuno-suppressive therapy in pemphigus may be responsible for the development of malignancy. But malignancies linked to immunosuppression are rather rare in pemphigus. Some authors stress that neoplasm induces autoimmunity, which may lead to pemphigus formation (4,8).

Basal cell carcinoma is the most common malignant tumor of the skin. Although more prevalent with solar exposure and more common in skin types I and II, other factors play a role in the development. In addition to ultraviolet light, arsenic, burns, vaccines, scars, tattoos, trauma, radio dermatitis, and frequent exposure to X rays are also major etiologic factors in the development of basal cell carcinoma. Basal cell carcinoma may also be seen in patients who have had a ringworm infection of the scalp that had been treated by radiotherapy many years previously, as in our case (10). Local immunosupression also occurs in areas of the skin exposed to UVB through the damaging results of ultraviolet light on the Langerhans cells (3).

Radiotherapy is considered to be the predisposing factor for the development of both pemphigus and multiple basal cell carcinoma in our patients who had also been exposed to UV for long periods of time. In this case, we considered that pemphigus and multiple basal cell carcinoma were seen coincidentally. There have been no known case reports of the coexistence of pemphigus vulgaris and multiple basal cell carcinoma arising on an old radiotherapy scar. To our knowledge, our case is the first to appear in the literature.

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TRAUMATIC RUPTURE OF THE DIAPHRAGM: AN OCCULT YET A SERIOUS INJURY

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SUMMARY

Patients in one of the highest surgical risk groups are those treated for thoracic trauma who present with a rupture of the diaphragam. Diaphragm rupture occurs in 5% of those hospitalized as a result of motor vehicle accidents and in 10% of penetrating thoracic traumas. Traumatic ruptures of the diaphragm (TRD) are described in association with 40% of pelvic fractures, 25% of splenic ruptures, 25% of liver lacerations, and 5% of aortic tears. These injuries may dominate the clinical scene, therefore delaying the diagnosis of diaphragm rupture. Because of the high risk of lethal complications, treatment must promptly follow this diagnosis.

In order to illustrate the difficulties in making a diagnosis, we present the case of an 8 year-old boy with TRD as the result of an automobile accident.

Key Words: *Children, diaphragm, rupture, trauma*

ÖZET

Diafragmanın Travmatik Rüptürü

Araç dışı trafik kazası geçiren sekiz yaşında bir erkek çocuğu splenik laserasyon nedeniyle gözlem altına alınmış ve gözlemin ikinci gününde gelişen ani solunum sıkıntısı nedeniyle incelendiğinde travmatik diafram rüptürü saptanmıştır. Cerrahi olarak tedavi edilmiş ve salah ile taburcu edilmiştir. Torasik travmalar içinde yaşamsal önem taşıyanlarından biri olan travmatik diafram rüptürü aynı zamanda gizli bir seyir içinde olabileceği için çoklu vücut travması geçiren çocuk ve erişkinlerde akılda tutulmalıdır.

Anahtar Kelimeler: *Çocuk, diafragma, travma*

Diaphragm rupture in children due to abdominal or thoracic trauma is rare as compared to the occurence in adults. Difficulties in diagnosing this condition should be thoroughly considered because TRD results in high rates of morbidity and mortality (1). Abdominal viscera migrate into the thorax and respiratory problems occur. The obstruction of the intestinal passage or strangulation usually follow. The abdominal viscera may not be detected in the thoracic cavity in a routine x-ray in the first hours or days after the trauma. Thus, the identification of TRD and the difficulties in making a diagnosis will be discussed.

CASE REPORT

An 8-year-old boy was admitted after a motor vehicle accident. The primary evaluation and physical examination were performed in the emergency department and revealed abdominal tenderness. The pulse rate and blood pressure were within the normal range. The two plain films of the abdomen and thorax were non-conclusive (Figure 1). A computed tomography (CT) of the abdomen indicated a 5 cm laceration in the upper portion of the spleen.

On the second day of hospitalization in the intensive care unit, respiratory stress with sudden cyanosis

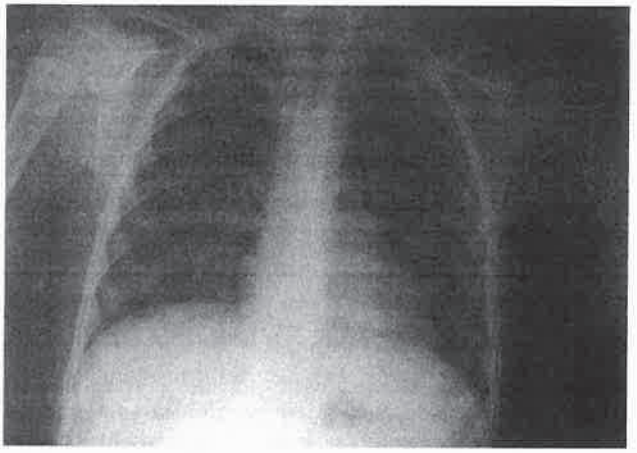

Figure 1: Plain x-ray of the chest on the admission with no pathologic scene

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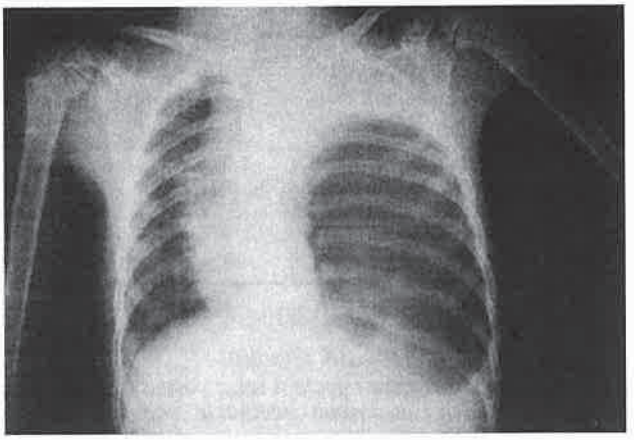

Figure 2: Plain x-ray of the chest with a big coil of air filled structure in the left hemithorax

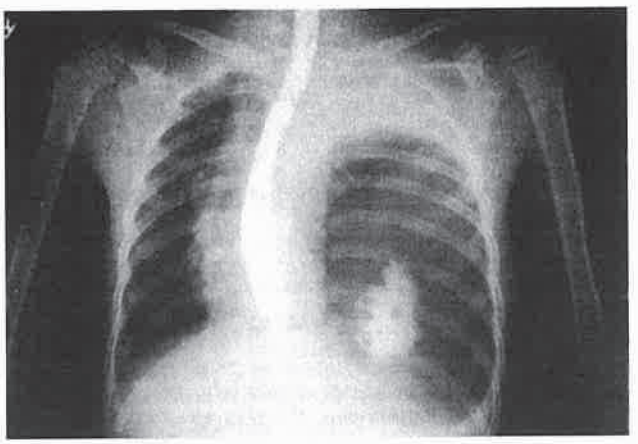

Figure 3: Barium meal thru a nasogastric tube demonstrates gastrointestinal components in the left hemithorax

occurred. An endo-tracheal tube was placed and the patient was given oxygen. The plain x-ray revealed a large air-filled structure in the left hemithorax (Figure 2). The mediastinum was displaced towards the uneffected side. A barium meal was given thru a nasogastric tube and further confirmed the diagnosis of TRD (Figure 3). Surgery was indicated and the patient was taken to the operating room. A laparotomy revealed that the stomach and a portion of the spleen, as well as the majority of the small intestines, were in thoracic cavity. The diaphragmatic tear was on the central and medial part of the muscle extending more than 10 cm across. The herniated contents were replaced into the abdomen and the defect was repaired with 2/0 silk. A fr 32 chest tube was inserted. The post-operative follow up was uneventful. The patient was discharged on the 12th post-operative day.

DISCUSSION

Blunt trauma caused by motor vehicle accidents and gun shot wounds are the most common causes of TRD in children. There are also reported cases of iatrogenic and spontaneus ruptures (2). Ninety percent of TRDs are encountered on the left side. The presence of the liver on the right, and the weaker tensile strength of the left side, explain the dominance of left sided ruptures in cases of blunt trauma (3,4) . Less than 50% of the cases are associated with rib fractures. The ruptures in blunt traumas may be radial, or circumferential (5). Our case appeared to be radially ruptured. The mechanics of diaphragmatic rupture as a result of trauma is still speculative, but a shearing off of the stretched membrane, the increase in abdominal pressure, and the avulsion of the diaphragm from its attachment points are seen as the primary causes for this condition. (2). The present case is an example of this type of blunt abdominal trauma, and the sudden increase of the abdominal pressure may contribute to the TRD. If there is a delay in diagnosis, the pathophysiological effects of TRD are seen primarily on the circulation and respiratory systems, and gastro-intestinal symptoms follow. The diaphragm's function is clearly impaired, the lungs are compressed, and the venous return to the heart is impaired because of mediastinal displacement. The functional loss of the diaphragm results in a 25-50% decrease in respiratory function (2).

This case also illustrates the rupture of the diaphragm in association with other injuries which dominated the clinical scene. Abdominal pain and the tomographic findings indicated that we should concentrate on the splenic rupture. Such cases of incorrect or delayed diagnosis occur from a few weeks to 40 years from the time of the trauma (6).

The acute phase features of TRDs are abdominal pain, respiratory distress, and cardiac dysfunction. Concurrent injuries, for example, of the head, the pelvis, the abdominal viscera, and the extremities, may contribute to the determination of a false or incomplete diagnosis (2).

The diagnosis of TRD may be delayed until visceral herniation and strangulation occurs. This is associated with a significant mortality and morbidity rate of 40% (7). On the suspicion of TRD, a fluoroscopic eva-

luation of the diaphragm, intra-abdominal installation of radioisotopes, scinti-scanning of the liver and lungs and a spiral CT of the thorax and abdomen may be diagnostic (7). The first choice must be ultrasound imaging, especially for the right-sided TRDs, as a CT may sometimes be unable to demonstrate the defect (7). The most common CT finding of TRD is a sharp discontinuity of the diaphragm (8). Another method suggested for diagnosis is magnetic resonance imaging (MRI)(9). We prefer to rely on plain and radiopaque x-rays, as they provide the easiest and quickest imaging that can be performed.

Patients with a history of blunt trauma and who are admitted with upper gastrointestinal complaints, left shoulder and upper abdominal quadrant pain, dyspnea, orthopnea, decreased breath sounds, obstructive nausea, vomiting, unrelenting abdominal pain, mediastinal shift, and abnormal plain chest x-rays may be surprisingly misdiagnosed and the correct diagnosis may be delayed. When performing an exploratory laparotomy for another trauma, the diaphragm must be thoroughly examined and the possibility of a diagnosis of TRD must be kept in mind, especially when evaluating cases of thoracic-abdominal blunt traumas with concurrent injuries.

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LEIOMYOSARCOMA OF SPERMATIC CORD

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SUMMARY

Malignant spermatic cord tumors are uncommon. Most of them are sarcomas. 38 years old male was admitted to urology clinic with nontesticular scrotal mass. He underwent right ingiunal exploration. Because of the malign criteria on frozen section radical orchiectomy with extensive dissection of the spermatic cord was performed.

The histopathological diagnosis was leiomyosarcoma.

Key Words: *Spermatic Cord, leiomyosarcoma, cancer, surgery*

ÖZET

Spermatik Kordon Leiomyosarkomu

Spermatik kordonun malign tümörleri seyrektir. Bunların pek çoğu sarkomlardır. 38 yaşında erkek hasta nontestiküler skrotal kitle ile başvurdu. Hastaya sağ inguinal eksplorasyon yapıldı. Frozen section'daki malign kriterler nedeniyle hastaya geniş bir spermatik kordon diseksiyonu ile birlikte radikal orşiektomi uygulandı.

Histopatolojik tanı leiomyosarkom idi.

Anahtar Kelimeler: *Spermatik Kordon, leiomyosarkom, kanser, cerrahi*

Paratesticular intrascrotal tumours are rare. Most of these tumors are benign and arise from the spermatic cord, epididymis and the adjacent tissues.

30 % of spermatic cord tumors are malignant of which 90 % of are sarcomas (1). About 200 cases of spermatic cord sarcomas have been reported in the literature (2). Leiomyosarcoma of spermatic cord is seen primarily in adults and more than 25 cases have been reported (3)

We report a case of spermatic cord leiomyosarcoma.

CASE REPORT

A 38 year- old man presented to Urological Outpatient Clinic with a painless mass in the right side of his scrotum of 6-months duration. There were no associated complaints. He had no history of trauma, surgery or any signs of orchitis.

Physical examination showed a firm, mobile, well circumscribed, painless, mass 5 cm. in diameter. Both testes descended bilaterally and were normal. The mass was distinctly separate from the right testis.

Scrotal ultrasonography revealed a solid mass 3.5x 4x 5 cm. in dimension. It was superior to the testis and below the symphysis pubis. There was no inguinal lymphadenopathy on computed tomography. Abdominal ultrasonography was normal.

Other routine laboratory studies including urinalysis, complete blood counting, renal and liver function tests and chest X- ray were within normal limits.

Right inguinal exploration was performed. The mass was regular, round shaped, encapsulated, originating from the spermatic cord and separate from the testis (Fig 1).

Because of the malign criterias on frozen section, right radical orchiectomy with high ligation of the spermatic cord was done.

Pathology:

Macroscopically, the mass was encapsulated and regular 3.5x4.5x5 cm.in diameter. The cut surcafe was fish- flesh consistency. There were necrotic and hemoragic areas on it.

Microscopically, there were many multinucleited tumour giant cells in the stroma. The nuclei of tumor cells were big, hypercromatic, usually fusiform, polygo-

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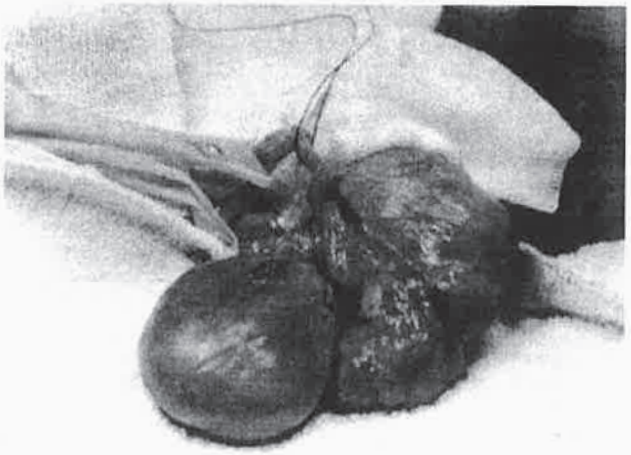

Fig. 1. Gross appearance of tumour measuring 3.5x4.5x5 cm., spermatic cord and tumour introperatively.

nal or ovally. The cell cytoplasm was narrow and pink. In some regions, there were atypical mitotic figures. The tumor cells appeared in crossing bundles or they were in statyform lines. Many capillary sections were seen in the tumoral stroma (Fig 2). The margins of resection were free of tumor. (Hematoxylin-eosin x 100).

COMMENT

Nontesticular tumours of the scrotum are rare. 90 % of these tumours arise from the spermatic cord of which 30 % are malignant (1,2).

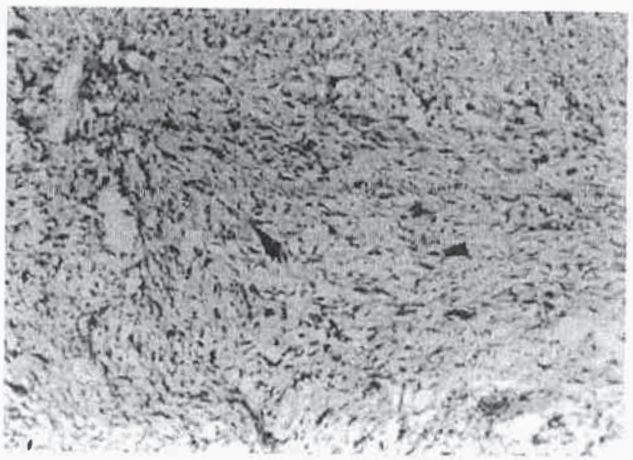

Fig. 2. Microscopic appearance of tumoral tissue. The tumour cells with large polygonal or fusiform hypercomatic nuclei and narrow cytoplasm. In tumoral stroma, there are some giant tumour cells.

Rhabdomyosarcomas generally are seen in men under the age of twenty. Other paratesticular tumours (leiomyosarcomas, fibrosarcomas, seminoma and metastases) generally occur in men over forty years of age (4, 5)

The origin of extratesticular sarcomas is uncertain but undifferentiated mesenchymal cells from blood vessels, cremasteric muscle, vas deferens and dartos muscle are possible sources (6, 7)

Spermatic cord sarcomas are firm to rubbery in consistency, nontender and usually irregular. They do not transmit light. These tumors usually arise from the lower part of spermatic cord or adjacent to the testes (8, 9, 10). In our case, the tumor was nontender, but regular. The mass was originated from the lower part of spermatic cord superior to the testis.

The clinical diagnosis of spermatic cord tumors remains difficult. The differantial diagnosis includes inguinal hernia, hydrocele, spermatocele, hematocele, testicular tumors,chronic epididymo-orchitis, tuberculosis and benign and malignant tumors of epididymis and paratesticular tissues(2,10, 11).

More than 25 leiomyosarcoma of the spermatic cord cases have been reported (3)

All authors agree that the standart therapy of spermatic cord and epididymal leiomyosarcomas is radical orchiectomy with high ligation of the cord (3, 8).

Grey et al recommend retroperitoneal lymph node dissection for leiomyosarcomas if there was evidence of retroperitoneal lymph node involvement on computed tomograpy but no evidence of distant metastases (9). Radiation theraphy and chemotherapy has been reported to have limited success (11,12).

In our case, there was no evidence of lymph node involvement on computed tomography and no evidence of distant metastases, thus only radical orchiectomy with high dissection of spermatic cord was done.

Spermatic cord leiomyosarcomas show a strong tendency for local reccurence. Distant metastases have been reported most commonly in the liver and lungs (8). Metastases occur by hematogeneous and lymphatic routes (12). The tendency for local recurrens does not necessarily imply a poor prognosis. However when distant metastases develop, the prognosis becomes extremely poor (1)

Although most of the extratesticular scrotal masses are benign, malignity must be kept in mind. Frozen section should be applied during scrotal exploration.

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