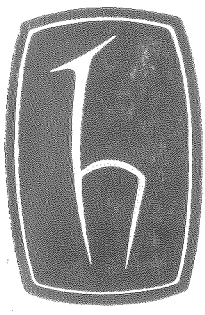

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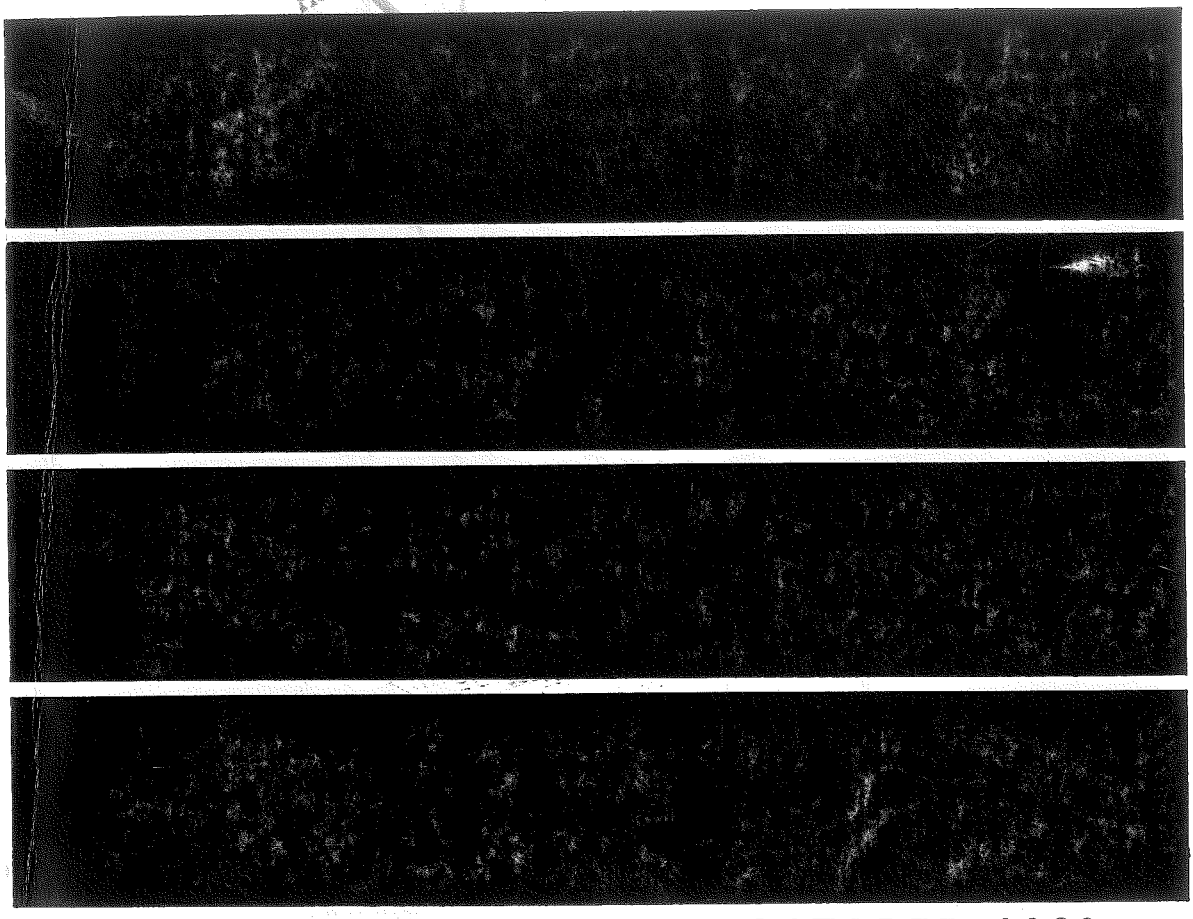

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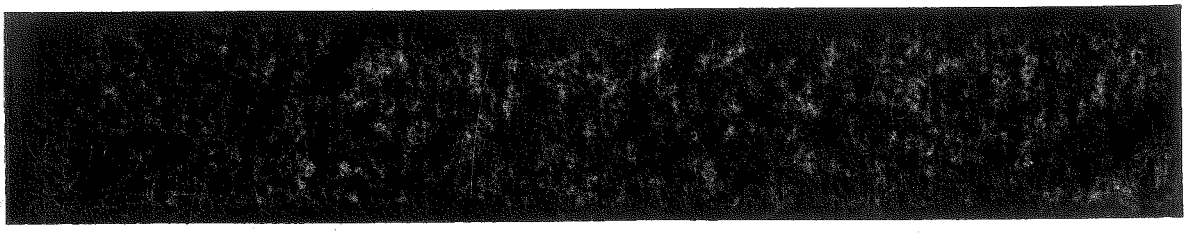

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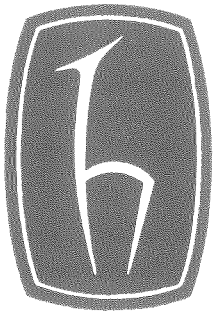

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CONTENTS

Hacettepe Medical Journal
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Familial Mediterranean Fever

A Survey of Clinical Parameters of 50 Patients Compared with the Literature

Lale Tokgözoğlu, M.D.* / Esin Ünlü, M.D.* / Yusuf Bayraktar, M.D. / Burhan Kayhan, M.D.*** / Hasan Telatar, M.D.*****

Summary

Familial Mediterranean Fever (FMF) is a disease characterized by recurrent episodes of fever, abdominal pain, chest pain and joint pain. Its most dreaded complication is the development of amyloidosis. Colchicine treatment seems to prevent these acute attacks and development of amyloidosis. In this study we analysed a few clinical parameters of FMF in 50 patients followed between 1984 and 1988 and compared them with other studies.

Key Words: Periodic disease, amyloidosis, colchicine treatment.

Introduction

Familial Mediterranean Fever, also called Paroxysmal polyserositis, Familial recurrent polyserositis or Episodic fever, is a familial and genetically transmitted disease of unknown origin that occurs predominantly in patients of Sephardic Jewish, Armenian and Turkish ancestry. Many clinical trials conducted so far have been unable to elucidate the etiology and genesis of this disorder although recently the theory of immune regulation disorder received much attention. The disease is manifested by recurrent attacks of fever, abdominal pain, joint pain, pleuretic chest pain and painful erythematous skin lesions lasting for 1 to 3 days. The attacks are accompanied by striking elevations of acute phase reactants.

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The most dreaded complication of FMF is the development of systemic amyloidosis. It is manifested clinically by a nephropathy that passes through proteinuric, nephrotic and uremic stages to death from renal failure. This complication is commonly seen in Jewish and Turkish patients.

In this report we analyse a few clinical parameters of FMF and compare the age of the onset, sex distribution, presenting symptoms, incidence of amyloidosis, and history of surgical intervention of our patients with two other studies from Turkey and with other studies in the literature.

Materials and Methods

This study was carried out in the Hacettepe University Hospital Department of Internal Medicine Division of Gastroenterology. 50 patients with the diagnosis of FMF followed between 1984 and 1988 in the Division of Gastroenterology FMF Outpatient Clinic were chosen for evaluation. All of these patients who had a history of recurrent fever, abdominal pain, chest pain, and joint pain were seen during an acute attack, and the diagnosis was confirmed by a detailed physical examination, radiological findings and elevation of acute phase reactants including plasma fibrinogen level during an attack. Other causes of abdominal pain were ruled out by complete gastrointestinal series and abdominal ultrasonography. All patients had a negative Schwartz-Watson test to rule out Acute Intermittant Porphyria. The diagnosis of amyloidosis was made by rectal or renal biopsy. All patients in this study were started on Colchicine (1.0 to 2.0 mg daily) during 1984 to 1988.

Results

Our patient group consisted of 28 males and 22 females with a mean age of 30 and with an age range of 18-50 (Tables I,II). In 50 percent of the cases the onset of symptoms began in the second decade. A family history was obtained in 9 patients (18 percent) (Table III).

The most frequent symptom was fever in 50 patient (100 percent). This was followed by abdominal pain in 49 patients (98 percent). The other symptoms were joint pain in 25 patients (50 percent), chest pain in 19 patients (38 percent), and skin rash in 3 patients (6 percent) as seen in Table IV. One patient was found to have coexistant Wolf-Parkinson-White syndrome.

Four (8 percent) of our patients gave a history of prior surgical intervention because of abdominal pain (Table V). Three of them had appendectomies and one had an explorative laparatomy.

TABLE I

AGE OF ONSET OF SYMPTOMS IN PATIENTS WITH FMF

Author (s)	Total no. of cases	Ages 0–9	10–19	20–29	30–39	40 +	Unknown
Ozdemir and Sokmen[1]	57	22	18	13	3	1	–
Ozer et al[2]	20	9	6	1	2	–	2
Sohar et al[3]	470	280	121	40	7	–	22
Armenian and Khachdurian[4]	120	64	35	18	3	–	–
Schwabe and Peters[5]	100	50	31	14	4	1	–
Our study	50	10	25	12	2	1	–
Total	817	435	236	98	21	3	24
Percent		53.2	28.8	11.9	2.5	0.3	

TABLE II

SEX RATIO OF PATIENTS WITH FMF

Author (s)	Male	Female	Total	Male/Female ratio
Özdemir and Sokmen[1]	38	19	57	2.0
Özer et al[2]	11	9	20	1.22
Sohar et al[3]	285	185	470	1.54
Armenian and Khachadurian[4]	86	34	120	2.53
Aivasian et al[6]	522	260	782	2.01
Our study	28	22	50	1.16
Total	970	529	1499	1.83

TABLE III

FAMILY HISTORY OF PATIENTS WITH FMF

Author (s)	Total no. of cases	Positive family history No	(%)	Total no of families	Families with more than one member involved No	(%)
Özdemir and Sokmen[1]	57	12	(21)	56	11	(20)
Özer et al[2]	20	8	(40)	–	–	–
Heller et al[7]	74	45	(61)	54	22	(41)
Priest and Nixon[8]	20	5	(25)	19	4	(21)
Siegal[9]	50	10	(20)	42	2	(5)
Schwabe and Peters[5]	100	43	(43)	14	17	(23)
Our study	50	9	(18)	45	5	(11)

TABLE IV

MAJOR SYMPTOMS IN PATIENTS WITH FMF

Author (s)	Total no. of cases	Fever	Abdominal pain	Chest pain	Joint pain	Skin rash
Özdemir and Sokmen[1]	57	57	53	20	25	obs*
Özer et al[2]	20	20	20	10	6	0
Sohar et al[3]	470	NM**	449	197	346	218
Eliakim et al[10]	106	106	106	53	57	14
Schwabe and Peters[5]	100	100	96	87	37	8
Our study	50	50	49	19	25	3

*: observed, **: not mentioned

TABLE V

SURGICAL INTERVENTIONS IN PATIENTS WITH FMF

Author (s)	Total no. of patients	Operated patients No.	Operated patients %
Özdemir and Sokmen[1]	57	18	32
Özer et al[2]	20	1	5
Benhamov et al[11]	24	7	29
Oganesian et al[12]	115	73	63
Armenian and Khachadurian[4]	120	40	33
Schwabe and Peters[5]	100	55	55
Our study	50	4	8

TABLE VI

INCIDENCE OF AMYLOIDOSIS IN FMF BY RACE AND ETHNIC GROUP

Predominant race or ethnic group	Total no. of cases	Amyloidosis No.	Amyloidosis %
Non-Ashkenazi Jews[10-14]	736	202	27
Ashkenazi Jews[15]	50	1	2
Turks[1, 2]	77	47	61
Armenians[6]	1556	228	15
Our study	50	6	12

Forty-seven of the 50 patients had neither proteinuria nor any other evidence of amyloidosis when Colchicine was first prescribed. The remaining three were in serious stages of overt renal failure. Three of the patients developed amyloidosis while still on prescribed Colchicine therapy. Nine patients were taking Colchicine one to ten years before attending our clinic and none of them had amyloidosis. All of our patients in this group were compliant with the therapy. Of the 50 patients 46 (92 percent)

reported complete or partial response of abdominal pain to Colchicine therapy while 4 (8 percent) did not show any responses (Tables VI,VII).

TABLE VII
PREVALANCE OF PROTEINURIA IN COMPLIANT AND NON-COMPLIANT PATIENTS WHO HAD NO PROTEINURIA WHEN COLCHICINE WAS FIRST PRESCRIBED

Patient Group	Total no. of cases	Proteinuria No	Proteinuria %
Compliant patients[16]	906	4	0.44
Non-compliant patients[16]	54	16	29.6
Our compliant patients	47	3	6.3

Discussion

The clinical findings in FMF are of utmost importance since there is no other reliable laboratory method to diagnose the disease. Our findings were generally in accord with the literature.

There seems to be male preponderence in FMF in the literature.[1-6] The male/female ratio in the other series is 1.2 to 2.53; our findings are compatible with a ratio of 1.16. The age of onset in the literature is generally in the first decade. Our patients had a later age of onset with most of them becoming symptomatic in the second decade.

The family history reported is about 40 percent in the literature.[1, 2, 5, 7, 9] Our patients had a much lower incidence (18 percent) of family history, but in some large series there is more than one patient from the same family and each patient is then considered to have a positive family history, thereby leading to false estimates.

The major symptom was fever and abdominal pain as indicated in the literature.[1-3, 5, 10] The incidence of chest pain, joint pain and skin rash was also similar to other series. None of our patients had neurological, endocrine and psychiatric manifestations. None had renal lesions other than amyloidosis. Five had splenomegaly and two had hepatomegaly. Liver function tests, excluding serum proteins, were normal in all of our patient group. The hemoglobin and red cell counts were in normal limits in all of the patients without renal involvement.

Since the introduction of daily Colchicine treatment the clinical course and prognosis of FMF has significantly changed. More than 90 percent of the patients have a complete or partial remission as long as they comply with the Colchicine treatment. In some studies none of the daily Colchicine treated patients developed amyloidosis.[17] In our study 6 patients (12 percent) had amyloidosis. Three patients (6 percent) had

amyloidosis as the initial symptom, and 3 patients (6 percent) developed it while they were on daily Colchicine therapy. These patients were either partial responders (1 patient) or non responders (2 patients) to Colchicine therapy. Only one had a family history.

In other Turkish series the amyloidosis rate is 60 percent, much higher than our results.[1,2] This might be because our study was conducted in a Gastroenterology clinic. In non-Ashkenazi Jews the prevalance was 27 percent and in Ashkenazi Jews it was 2 percent.[10-14]

A study in Israel in which most of the patients were young and most were Sephardic Jews of North African origin, had only 0.44 percent of patients who developed proteinuria while on Colchicine therapy in a 7 year (4-11 years) follow-up,[16] while 6 percent of our patients developed proteinuria during therapy. This may be due to introduction of daily Colchicine treatment at a later age.

We conclude that the clinical manifestations of FMF in this study of 50 patients is in accordance with other series of Mediterranean origin.

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Hacettepe Medical Journal
Volume 22 / No. 4 / October 1989 / pp. 275 - 280

The Association Between Familial Mediterranean Fever and HLA Groups in Turkish Patients

Lale Tokgözoğlu, M.D.* / Esin Ünlü, M.D. / Korkut Özerkan, M.D.*** / Yusuf Bayraktar, M.D.**** / Hasan Telatar, M.D.*****

Summary

Familial Mediterranean Fever (FMF) is a disease of unknown origin seen more frequently in certain ethnic groups. Although a genetic and immunologic etiology is suspected, this has not been proven. HLA antigens have been studied in different ethnic groups without conclusive results. In this study we looked for an association between the four HLA loci in 50 patients with FMF and compared it with a normal population of 236 healthy renal transplant donors. The most prevalent groups of HLA in the normal Turkish population were found to be HLA-A2, HLA-B6, HLA-BW6, HLA-BW35, HLA-CW4 and HLA-DRW.2 We found HLA-DR6 more prevalent ($p < 0.01$) and HLA-DR2, HLA-BW35, and HLA-B6, HLA-BW6 less prevalent ($p < 0.01$) in the patient population. These findings might imply weak association due to linkage disequilibrium but larger population studies are needed for more definitive results.

Key Words: Periodic disease, HLA typing.

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Introduction

Familial Mediterranean Fever (FMF) is a disease of unkown origin occurring predominantly in patients of Jewish, Armenian, Arabic and Turkish ancestry. Since the first description of FMF it has become apparent that the disease is familial and genetically transmitted. There is controversy about the transmission of the gene but most authors believe it to be a recessive trait. The genetic basis and its prevalence in certain ethnic groups may suggest an association with HLA groups.

The exact etiology of FMF has not been elucidated. Several theories have been suggested to explain the pathogenesis: Inborn errors of cathecholamine metabolism[1], circulating immune complexes[2], leukocyte chemotaxis[3] and complement system abnormalities.[4] All have been discounted but no one has given a conclusive or adequate explanation of this entity. Attention has been focused recently on the possibility of disorders in immune regulation and altered T4/T8 ratio. Since the HLA-D region is thought to regulate the immune response, certain HLA-D groups may be important in the pathogenesis or prediction of outcome of these patients.

This study of 50 patients with FMF was made to determine whether there is a preponderence of any HLA group different from the normal population.

Patients and Methods

Fifty patients with a diagnosis of FMF were evaluated at the Hacettepe University Medical Center, Department of Internal Medicine in the Divisions of Gastroenterology and Hematology between 1984 and 1988.

Twenty-eight male and 22 female patients were included in the study with an age range of 18 to 50 years and a mean age of 30. All of these patients who had a history of recurrent fever, abdominal pain and/or pleuritis and arthritis were seen during an acute attack, and the diagnosis was confirmed by a detailed physical examination, radiological findings and the elevation, of acute phase reactants, including plasma fibrinogen levels. Other causes of abdominal pain were ruled out by a complete gastrointestinal series and an abdominal ultrasonography. All of the patients had negative Schwartz-Watson test to rule out Acute Intermittant Porphria. Of the 50 patients 47 had neither proteinuria nor evidence of amyloidosis. Each patient was treated with Colchicine (1.0 to 2.0 mg daily). After starting daily Colchicine treatment 46 patients responded with complete or partial remission of fever and pain. One patient

with partial response and two patients with poor response developed amyloidosis; one of the latter had a family history of Mediterranean fever.

The control group consisted of 236 healthy renal transplant donors. All were completely healthy during the routine work-up as potential renal transplant donors.

The HLA typing was performed by the lymphocyte cytotoxicity method.[5]

Student's t test was performed for statistical analysis.

Results

The results of the HLA typing for HLA-A, HLA-B, HLA-C, and HLA-DR groups are shown in Tables I-IV. These tables show both the normal HLA distribution for the Turkish population and our findings in patients with FMF. The tables show that the most prevalent groups of HLA in the normal Turkish population are HLA-A2, HLA-B6, HLA-BW6, HLA-BW35, HLA-CW4, and HLA-DRW2. HLA-AW32 and HLA-A28 were more prevalent ($p < 0.01$) in the patient group compared to the normal control group ($p < 0.01$).

When the B locus was examined HLA-B6, HLA-BW6 and HLA-BW35, which were the most frequent types in the normal population, could not be demonstrated in most patients with FMF.

HLA-CW2 was more prevalent in the patient group ($p < 0.01$). When the DR locus was examined, HLA-DR6 was significantly higher ($p < 0.01$) and HLA-DR2 lower ($p < 0.01$) than normal controls.

TABLE I

THE HLA-A ANTIGENS IN PATIENTS WITH FMF COMPARED WITH THE NORMAL POPULATION

HLA-A	Controls	Patients
A1	90	16
A2	145	20
A3	62	6
A9	122	18
A11	26	9
A25	2	1
A26	12	6
A28	13	10
AW32	0	14
Total	472	100

TABLE II

THE HLA-B ANTIGENS IN PATIENTS WITH FMF COMPARED WITH THE NORMAL POPULATION

HLA-B	Controls	Patients
B4, BW4	54	6
B5, BW5	49	4
B6, BW6	91	8
B7, BW7	28	5
B8	22	6
B12	18	0
B13	1	0
B14	4	1
B17, BW17	6	5
B18	0	9
B21	3	0
B22	5	4
B27	15	0
BW35	80	3
B40	9	1
BW44	19	6
BW49	10	2
BW50	13	4
BW51	40	17
BW63	5	0
BW73	0	20
Total	472	100

TABLE III

THE HLA-C ANTIGENS IN PATIENTS WITH FMF COMPARED WITH THE NORMAL POPULATION

HLA-C	Controls	Patients
CW2	36	16
CW3	46	6
CW4	116	34
Total	198	34

TABLE IV

THE HLA-DR ANTIGENS IN PATIENTS WITH FMF COMPARED WITH THE NORMAL POPULATION

HLA-DR	Controls	Patients
DRW1	91	18
DRW2	124	10
DRW3	79	11
DRW4	71	12
DRW5	59	8
DRW6	34	16
DRW7	14	9
Total	472	84

Discussion

Certain HLA antigens show an important association with a number of diseases such as rheumatoid arthritis, coeliac disease and Graves' disease which are thought to be of autoimmune origin with a genetic preponderence. Although the exact mechanism is not known, HLA-A and HLA-B groups can influence cytotoxic T cell specifity while HLA-D region is believed to regulate a hyper or hyponormal response to a known exogenous or self antigen.[6] Although the pathogenesis of FMF is unknown, one can speculate that a hypernormal response to an antigen is caused by a defect in immune regulation. This would also explain the familial preponderence.

In Graves' disease a defect in supressor T cells is thought to result in a hypernormal immune response. There are a few reports stating that the T4/T8 ratio is elevated in FMF and this is corrected by Colchicine.[7] This could explain a hypernormal response to an antigen, and be regulated by certain HLA antigens. Previous studies have not found a correlation between HLA antigens and FMF. In one study HLA-DR4 was more prevalent[8] while HLA-DR5 was more prevalent in another.[9] One study reported a HLA-B27 preponderence.

Our studies are not compatible with any of the prior studies. This might be due to the genetic difference of the Turkish population. HLA-A2, HLA-B6, HLA-BW6, HLA-BW35, HLA-CW4 and HLA-DRW2, which were the most prevalent types in the normal Turkish population, could not be found in most of the FMF patients. This difference was especially striking for the B and DR loci. There was an important paucity of HLA-BW35, HLA-B6, HLA-BW6 and HLA-DRW2 genes in the FMF patients ($p < 0.01$). Meanwhile the HLA-DRW6 group was markedly increased ($p < 0.01$) in the patient population relative to the normal controls.

The differences between our results and those reported in the literature can be explained in two ways: either our results may be specific for the Turkish population, or there is not a strong association between the known HLA antigens in FMF. There might be a weak correlation due to linkage disequilibrium and typing methods specific for additional D regions may reveal stronger associations.

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The Hemodynamic Effects of Protamine: Intravenous Versus Intra-Aortic Administration

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Summary

The hemodynamic effects of intra-aortic versus intravenous administration of protamine for neutralization of heparin following cardiopulmonary bypass (CPB) were studied in sixteen patients randomly selected into one of two groups. In eight patients protamine was given intravenously and in the other eight it was given into the aorta. Blood specimens were taken and serum histamine levels studied. Changes in the mean arterial pressure were measured. In the group given-protamine intravenously the mean arterial pressure was 82.75 $\pm$ 16 mm Hg which decreased to 56 $\pm$ 8.93 mm Hg 180 seconds after the protamine injection. The change was statistically significant ($p < 0.05$). The serum histamine level before and after protamine administration was 3.1 $\pm$ 0.91 ng/ml and 3.8 $\pm$ 0.67 ng/ml ($p < 0.05$). In the group receiving protamine into the aorta the mean arterial pressure before and after protamine injection was 76.12 $\pm$ 14.76 mm Hg and 71 $\pm$ 20.09 mm Hg ($p > 0.05$). In this group the serum histamine level was 3.17 $\pm$ 1.04 ng/ml and 3.1 $\pm$ 1.2 ng/ml respectively before and after protamine injection ($p > 0.05$). Preliminary studies on protamine attempted to determine whether pro-

tamine induced circulatory changes were produced by effects on peripheral vascular beds or on myocardial performance. In our study protamine-induced circulatory changes were shown to be mediated by endogenously liberated vasoactive peptides such as histamine as has been postulated in other studies.[1-4] The results suggest that protamine administered via the aorta is safer than intravenous administration, especially in patients with poor ventricular function.

Key Words: Protamine, cardiopulmonary bypass, circulatory changes.

Introduction

Systemic hypotension is one of the marked hemodynamic effects of protamine administration for the reversal of the heparin effects following CPB.[1, 2] Preliminary studies suggest that administration of protamine via the aorta or the left atrium is not accompanied by significant changes in blood pressure.[1-3] Other reports state that slow intravenous administration of protamine causes systemic arterial hypotension while its rapid intravenous administration does not.[4-6] Also slow infusion of dilute protamine does not cause systemic hypotension.[4-6]

This study compared the hemodynamic effects of slow intravenous and intra-aortic administration of protamine and the changes in serum histamine levels.

Material and Method

Sixteen patients with different diagnosis who underwent open heart surgery in Gazi University Medical Faculty Hospital between 3.12.1986 and 30.3.1987 were studied. Six were female and ten were male patients with ages ranging between 2.5 and 67 years (mean 41.3 years). Data about the patients are summarized in Table I and II.

Patients in both of the groups were sedated with oral diazepam the night before surgery and with intramuscular diazepam 30 minutes prior to the operation. Atropine sulphate was used for premedication unless a contraindication was present. Ketamine was used in pediatric patients. For the induction of anesthesia, sodium thiopenthal (3-5 mg/kg), pancuronium (0.15 mg/kg) and succinyl cholin (1 mg/kg) were used. Following orotracheal entubation for continuation of anesthesia, N_2O + O_2 (4/2 or 3/3 lt/min) and if needed Ethrane (0.2 % or 0.3 %), pancuronium and for analgesia morphine sulphate were used. Patients were taken to the intensive care unit, and after stabilization of metabolic and hemodynamic criteria they were extubated.

TABLE I

PATIENT DATA

GROUP 1 : INTRAVENOUS PROTAMINE ADMINISTERED GROUP

Patient Nr.	Age	Diagnosis	Operation Performed
1	46	MS	MVR
2	59	CAD	CABG
3	54	CAD	CABG
4	50	CAD + LVA	CABG + Aneurysmectomy
5	52	MS	Comissurotomy
6	44	MS	Comissurotomy
7	17	ASD + PS	ASD Closure + Comissurotomy
8	49	MS	Comissurotomy

TABLE II

PATIENT DATA

GROUP 2 : INTRA-AORTIC PROTAMINE ADMINISTERED GROUP

Patient Nr.	Age	Diagnosis	Operation Performed
1	50	MS	Comissurotomy
2	14	MI	MVR
3	49	AI	AVR
4	47	CAD	CABG
5	67	AS	AVR
6	2.5	ASD + VSD	ASD + VSD Closure
7	17	AI + AS	AVR
8	31	ASD	ASD Closure

MS: mitral stenosis, MVR: mitral valve replacement, CAD: coronary artery disease, CABG: coronary artery bypass grafting, LVA: left ventricular aneurysm, ASD: atrial septal defect, PS: pulmonary stenosis, MI: mitral insufficiency, AI: aortic insufficiency, AS: aortic stenosis, AVR: aortic valve replacement, VSD: ventricular septal defect.

Following the induction of anesthesia the radial artery and subclavian vein of the patients were cannulated and arterial blood pressure and central venous pressure were monitored using an American Optical Gould Statham 5145 type transducer. Electrocardiography, oesophogel and rectal temperatures and urine output were followed. All of the patients were heparinised before CPB. The Activated Clotting Time (ACT) method was used for the control of heparinisation (ACT and Hemochron are trademarks of International Technidyne Corporation). The ACT value before and during the CPB was more than 480 seconds. If needed heparin was added during CPB. After the discontinuation of CPB an ACT value was obtained and the dose of protamine calculated from a dose-response curve. No positive inotropic agents were used after CPB until after protamine administration.

After CPB, mean arterial pressure, heart rate and central venous pressure were noted and blood was taken from the left atrium. To one group of patients calculated dose of protamine was administered through a peripheral vein in 90 seconds. Mean arterial pressure, heart rate and central venous pressure were noted again 180 seconds later. At the same time blood was taken from the left atrium. In the second group of patients all the procedures were repeated that the protamine was administered via the aorta.

Serum histamine levels were measured by a bioassay method in the Gazi University Medical Faculty Pharmacology Department. The changes in serum histamine levels and mean arterial pressure were statistically analyzed by the Hacettepe University Medical Faculty Biostatistics Department using the student-t method.

Results

In the group given protamine intravenously mean arterial pressure before administration of protamine was 82.75 $\pm$ 16 mm Hg and decreased to 56 $\pm$ 8.93 mm Hg 180 seconds after protamine administration. The difference was statistically significant ($p < 0.05$). The serum histamine level was 3.1 $\pm$ 0.91 ng/ml before the protamine injection and increased afterward to 3.8 $\pm$ 0.67 ng/ml. This result was also statistically significant ($p < 0.05$). Detailed results for this group of patients are shown in Table III.

TABLE III
RESULTS OF THE FIRST GROUP

Patient Nr.	Arterial Mean Pressure BPA (mm Hg)	APA	Serum Histamine Level BPA (ng/ml)	APA
1	67	50	1.8	2.4
2	78	62	3.6	3.8
3	120	37	4.4	4.8
4	90	69	4.2	4.4
5	76	56	3.4	4.2
6	66	62	2.8	3.4
7	85	56	2.6	3.8
8	80	56	2.2	3.6
MEAN	82.75 $\pm$ 16	56 $\pm$ 8.93	3.1 $\pm$ 0.91	3.8 $\pm$ 0.67

BPA : before protamine administration
APA : after protamine administration

In the second group given protamine into the aorta, the mean arterial pressure before and 180 seconds after administration of protamine was 76.12 $\pm$ 14.76 mm Hg and 71 $\pm$ 20.09 mm Hg respectively. The

difference was not statistically significant ($p > 0.05$). The serum histamine level was 3.17 ± 1.04 ng/ml before and 3.1 ± 1.2 ng/ml after the protamine administration. The difference was not statistically significant ($p > 0.05$). Detailed results of this group are shown on Table IV.

TABLE IV

RESULTS OF THE SECOND GROUP

Patient Nr.	Arterial Mean Pressure BPA (mm Hg)	APA	Serum Histamine Level BPA (ng/ml)	APA
1	60	68	1.2	1.0
2	69	67	2.4	2.8
3	70	62	3.8	3.0
4	97	105	4.6	4.4
5	89	53	2.6	1.8
6	53	38	3.2	4.0
7	92	85	3.2	3.0
8	79	90	4.4	4.8
MEAN	76.12 ± 14.76	71 ± 20.09	3.17 ± 1.04	3.1 ± 1.2

BPA : before protamine administration
APA : after protamine administration

The graphic illustration of the results of the two groups is shown on Figure 1.

No remarkable changes in heart rate and central venous pressure values occurred following protamine administration in either of the groups.

Discussion

Protamine is routinely used to reverse the effect of heparin following CPB. Systemic hypotension is a remarkable effect of protamine administration.[1-7] Preliminary studies on protamine consisted of different types of investigation. Many studies attempted to determine whether protamine-induced hemodynamic changes are produced by effects on peripheral vascular beds or on myocardial performance.[8, 9] In our study and others protamine-induced circulatory changes have been demonstrated to be mediated by endogenously liberated vasoactive peptides such as histamine.[1-4]

Some authors mention the myocardial depressive effect of protamine.[10] After protamine administration into the aorta we did not find any significant changes in mean arterial pressure which indirectly may reflect the left ventricular function.

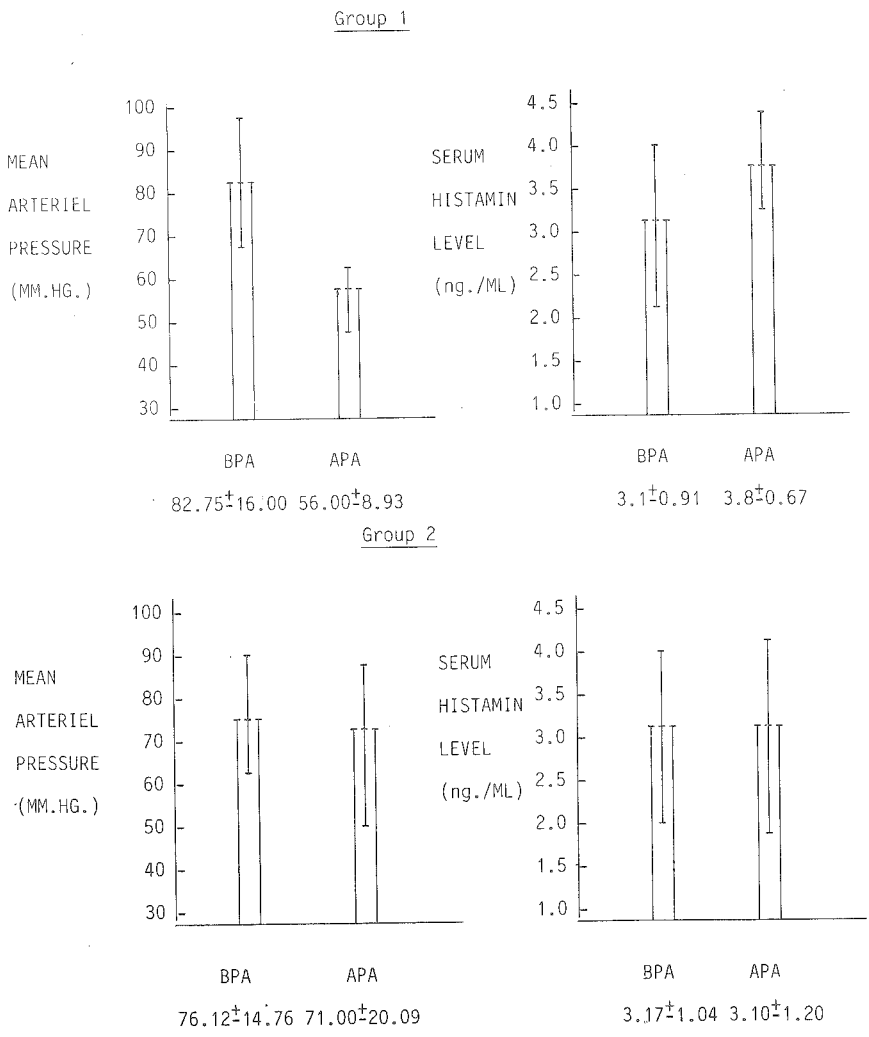

Figure 1

Graphic illustration of the mean arterial pressure and serum histamine level changes in group 1 and group 2.

BPA : Before protamine administration
APA : After protamine administration

A common belief about the effect of intravenous administration of protamine is that it increases the pulmonary arterial pressure and systemic vascular resistance. This effect is considered to be due to the liberation of vasoactive peptides by protamine as it traverses the pulmonary circulation. Such vasoactive peptides have a positive inotropic effect which may compensate the myocardial depressive effect of protamine.

Additionally they have a peripheral arteriolar vasodilator effect which results in systemic hypotension.[1, 3, 4] If protamine is administered intravenously very slowly the induction of vasoactive peptide is slow and systemic hypotension does not occur. If intravenous protamine is given rapidly it passes the pulmonary circulation very fast and vasoactive peptide liberation is lowered.[1-3]

If the protamine is given via the aorta, bypassing the pulmonary circulation there is no release of vasoactive peptide and no significant circulatory changes observed.[2] Also no myocardial depressive effect is seen after intraaortic administration.[2]

During CPB activation of the complement system by both the classical and alternate pathways occurs. This produces anaphylotoxins C_5A and C_3A which are potent inducers of histamine release from mast cells. Formation of protamine-heparin complexes amplifies the effect and the release of vasoactive peptides is increased.[1]

A question is "Why does left side injection of protamine not have the same effect as right side injection?". It is possible that although protamine degranulates the mast cells directly, protamine-heparin complexes do not. However protamine-heparin complexes may be a factor in complement activation. Slow intravenous administration of protamine may thus work by ensuring that all the protamine reaching the lungs is already bound with heparin.

We studied only histamine but other vasoactive peptides also may be responsible for the production of hypotension.

In our study we found that the intravenous administration of protamine induces systemic hypotension which is presumed to be from the liberated vasoactive substances such as histamine as the protamine traverses the pulmonary circulation. Neither ours nor prior studies have produced conclusive evidence for this mechanism, however we conclude that left atrial or intra-aortic administration of protamine is safer than its administration intravenously especially for patients with severely impaired ventricular function.

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The Causes of Pregnancy Following Tubal Sterilization

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Summary

Thirty pregnancies were encountered among 1565 women previously subjected to tubal sterilization, an overall pregnancy rate of 1.9%. One patient had an ectopic pregnancy (0.06 %). Of the 30 pregnancies. 13 occurred after thermal coagulation of the tubes, 8 after fallope ring application, 7 after the Pomeroy procedure and 2 after fimbriectomy. The causes of sterilization failures were evaluated by laporoscopy in 24 patients. The most common cause of pregnancy following tubal sterilization was surgical error.

Key Words: Pregnancy, tubal sterilization.

Introduction

Pregnancy, intrauterine or ectopic can occur after tubal sterilization.[1,2] The major causes of sterilization failures are; true method failures, surgical errors and luteal phase pregnancy.[1,2,3] The literature extensively describes the various failure rates for different tubal sterilization procedures.[1,3] The purpose of this study was to evaluate the reasons for the occurence of pregnancies following tubal sterilization.

Material and Methods

A total of 1565 women in our institution were subjected to tubal sterilization using different methods in a 20 year period from January 1967 to January 1987. Data were obtained from patient files, pathology reports and follow-up forms. Tubal sterilization was performed by

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laparoscopy in 609 (38.9 %), during cesarean section in 541 (34.5 %), with culdotomy in 265 (16.9 %) and with laparotomy (mini/formal) in 150 (9.7 %) patients (Table I).

The Pomeroy procedure and fallope ring application by laparoscopy were the most common techniques employed in 697 (44.5 %), and 416 (26.6 %) patients, respectively. Other techniques used are shown in Table II. The follow-up time for all patients varied from 1 to 3 years. Twenty-four patients who presented with pregnancy following sterilization were evaluated by laparoscopy; 6 patients refused this procedure.

TABLE I
SURGICAL APPROACH AND PREGNANCY RATES (/1000)

Surgical approach	Number of patients Total/Pregnant		Pregnancy rate /1000
Laparoscopy	609	21	34.4
Cesarean section	541	5	9.2
Culdotomy	265	2	7.5
Mini-Formal Laparotomy	150	2	13.3
Total	1565	30	19.2

TABLE II
RELATION OF STERILIZATION TECHNIQUES TO PREGNANCY

Technique	Number of patients Total / Pregnant		Pregnancy rate /1000
Pomeroy	697	7	10.04
Fimbriectomy	241	2	8.29
Fallope ring	416	8	4.81
Tubal cauterization	193	13	67.35
Unknown	18	–	–
Total	1565	30	19.2

One patient had an ectopic pregnancy

Results

The overall pregnancy rate was found to be 19.2/1000 procedures. Of the 30 pregnancies, 13 occurred after tubal cauterization, 8 after tubal ring application. 7 after Pomeroy procedure and 2 after fimbriectomy (Table II).

Surgical errors such as misidentification of the tubes and misplacement of the fallope rings were the most common causes of pregnancy. They accounted for 13 of the 30 patients (43.3 %) (Table III). Luteal phase pregnancy was detected in 7 patients (23.3 %). Recanalization and

tuboperitoneal fistula, were respectively found to be the causes in 13.3 % and 6.7 % of the pregnancies. The cause of failure could not be detected in 4 (13.3 %) patients.

TABLE III
CAUSES OF PREGNANCIES FOLLOWING STERILIZATION

Cause	Fimbriectomy	Coagulation	Ring	Pomeroy	Total	%
Surgical error	1	8	4	–	13	43.3
Luteal phase preg.	–	3	4	–	7	23.3
Recanalization	–	–	–	4	4	13.3
Tuboper. fistula	1	–	–	1	2	6.7
Unknown	–	2	–	2	4	13.3
Total	2	13	7	7	30	100.0

Discussion

Pregnancy following tubal sterilization may occur because of conception before the procedure or method failure. In 1981, Chi et al. reported that the overall pregnancy rates were 6/1000 procedures in 7696 nonpregnant women and were 32.8/1000 procedures in 1703 gravid uterus.[3]

Pregnancy rates following tubal sterilization differ with the method used, surgical approach, operator skill and the type of patient (pregnant versus nonpregnant). Nesser and Hirch have shown that pregnancies following sterilization by bipolar coagulation of the tubes may result from surgical errors (0.5/1000), luteal phase pregnancies (0.6/1000) and true method failure (2.1/1000).[2] In this study of the 13 pregnancies following tubal thermal coagulation 8 (41/1000) were due to surgical error, 3(10.4/1000) were due to luteal phase pregnancies, and 2(10.4/1000) had unknown etiology (Table III).

Studies with the fallope ring show failure rates ranging from 0.1-1.6 %.[4, 5, 6] This figure was found to be 19.2/1000 in our study. Surgical errors, such as misidentification of the tubes and, wrong application of rings and clips currently account for a significant number of failures. Most of these failures can be avoided by use of the correct surgical approach. For doctors who are still undergoing training or are unfamiliar with a new method, endoscopic teaching aids may improve correct application.

Luteal phase pregnancies are estimated to occur in 2-3/1000 interval sterilization procedures.[7, 8, 9] Of the 30 pregnancies, in this study, 7 were

luteal phase pregnancies (4.4/1000). The risk of luteal phase pregnancy can be decreased by performing the procedure before the estimated date of ovulation and using effective contraceptive measures in the month preceding sterilization. Use of pregnancy tests and concurrent D+C appears effective but less reliable in reducing the risk of luteal phase pregnancies.

Ectopic pregnancy following sterilization is an important complication.[10] The ratio of ectopic to intrauterine pregnancies increases with the time elapsed after sterilization.[11, 12, 13] In 23600 sterilization procedures, 15 ectopic pregnancies (0.63/1000) among 179 pregnancies (7.5/1000) were found in a review of the IRFP data, by Chi *et al.*[3] In our study 1 patient with a fallope ring suffered an ectopic pregnancy (0.64/1000). Previous pelvic or abdominal surgery, prior attack of pelvic inflammatory disease and the time following sterilization significantly increase the risk of ectopic pregnancy.[1, 10] Compared to fallope ring the rate of ectopic pregnancy was reported to be higher after diathermy.[2] Overall pregnancy rates are higher in the first year following sterilization then in subsequent years.[1, 3] Of the 30 pregnancies 21 (70 %) occurred in the first year following sterilization in this study.

Conclusions

Pregnancy rates following sterilization differ with the method used, surgical approach, operator skill and the characteristics of the patient undergoing sterilization (pregnant or nonpregnant). Low acceptable failure rates are seen with the Pomeroy tubal ligation and tubal ring application. Overall pregnancy rates are higher in the first year compared to subsequent years.

Surgical errors (misidentification of the tubes or wrong application of clips or rings) currently accounted for 43.3 % of the pregnancies in this study. Luteal phase pregnancy can be avoided by timely scheduling of the procedure and use of contraception the month before.

Ectopic rates are increased with the time after sterilization and should be considered in patients presenting with pregnancy following sterilization.

The high rates of pregnancy following sterilization in this study were caused mainly by surgical errors. The use of the procedure by more senior residents and application of training models for teaching purpose decrease the pregnancy rates to more acceptable levels in this institution.

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Amniotic Fluid Lecithin-Sphingomyelin Ratios in Pregnancies with an Anencephalic Fetus

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Summary

The lecithin/sphingomyelin ratio (L/S) in amniotic fluid of pregnancies with an anencephalic fetus, in which the was known to be aberrant production of fetal pituitary, adrenal and consequently placental hormones was determined. The L/S ratio in amniotic fluid from all pregnancies with an anencephalic fetus was lower than that in amniotic fluid from all pregnancies with a normal fetus at the same stage of gestation. It was concluded that fetal lung maturation as reflected by the L/S ratio is dependent in part upon normal function of the fetal pituitary and adrenal.

Key Words: Amniotic Fluid, L/S.

Introduction

The timetable and identification of the biochemical maturation of the fetal lung is a considerable importance and concern to the obstetrician because functional immaturity of the lung at birth leads to the development of the respiratory distress syndrome. An increasing concentration of lecithin in the amniotic fluid, relative to that of sphingomyelin (the

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lecithin to sphingomyelin, or L/S ratio), constitutes an index of fetal lung maturation.[1] Many substances have been proposed as potentially important in the control of the synthesis and release of pulmonary surfactant.[2] Included among the hormonal factors believed to be important for optimum surfactant synthesis in the fetal lung are products of the fetal pituitary (eg, adrenocorticotropic hormone and prolactin), the fetal adrenals (eg, cortisol and dehyroepiandosterone sulfate), and the plasenta (eg, estrogens derived from the utilization of maternal and fetal adrenal dehydroepiandosterone sulfate).[3-5]

Anencephaly is a malformation characterized by cerebral hemispheres that are either rudimentary or absent and absence of the overlying skull. Most often the pituitary gland is either absent or markedly hipoplastic, and typically, there is extreme diminution in the size of the adrenal glands.[6 7] It is commonly believed that the adrenal hypoplasia is secondary to the absence of the pituitary gland. In anencephalic pregnancy, it is known that the placental hormone production also is diminished.[8]

Thus, for the purpose of evaluating the findings of past and future investigations, it was considered important to determine, indirectly, indexes of lung maturation in anencephalic fetuses. The lecithin to sphingomyelin (L/S) ratio was determined in amniotic fluid obtained from pregnancies in which the fetus was known to be anencephalic, and these data were compared with those obtained in amniotic fluids of pregnancies in which the fetus was normal.

Material and Method

Amniotic fluid specimens were obtained from seven women pregnant with anencephalic fetus by transuterine or transabdominal amniocentesis at the time of delivery. Of the seven fetusus, three were stillborn and the other four died shortly after delivery; the interval between delivery and death was insufficent for hyaline membrane disease to develop.

Gestational age of the newborns was based on menstrual history, ultrasonographic findings, and pediatric assessment. Amniotic fluid was centrifuged at 750 g for ten minutes to sediment debris; resulting supernatant fluid was used for determination of the L/S ratio according to the method of Lake and Goodvin.[10] The L/S ratios in amniotic fluids of pregnancies complicated by fetal anencephaly were compared with those obtained for 138 randomly collected amniotic fluid specimens from normal pregnancies or from pregnancies complicated by maternal hypertension, diabetes mellitus or Rh isoimmunization. All such amniotic fluids were obtained either by transabdominal amniocentesis, by transuterine amniocentesis or at the time of a cesarean section.

Results

The L/S ratios in amniotic fluid of pregnancies complicated by fetal anencephaly are compared with those from a cross section of pregnancies in which the fetus was judged to be normal (Figure 1). The L/S ratio in amniotic fluid surrounding all of the anencephalic fetuses was lower than the L/S ratios in the amniotic fluids of representative pregnancies of similar gestational duration. The highest L/S ratio for anencephalic fetuses was obtained from a pregnancy that terminated with a stillborn anencephalic fetus at 39 weeks gestation. The findings of seven anencephalic newborns are presented in Table I.

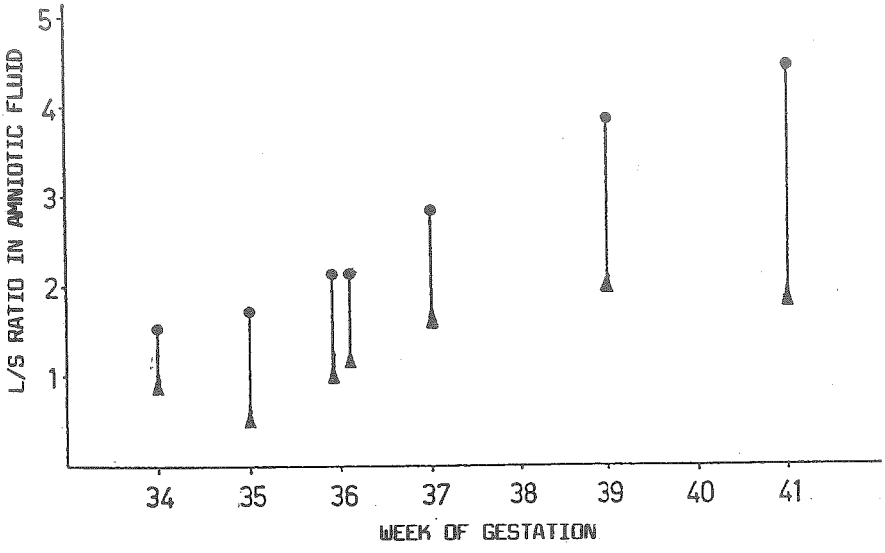

Figure 1

Lecithin/sphingomyelin ratio in amniotic fluid of normal and anencephalic pregnancies. The data for normal pregnancies are presented, N: 14 to 42 per gestational age group (circles); values for the anencephalic pregnancies are presented individually (triangles). Each pair is indicated by vertical line drawn between two values.

TABLE I

PHYSICAL FINDINGS IN ANENCEPHALIC NEWBORNS

Gestational age (wk)	L/S ratio	Sex	Weight (gr)	Delivery method
34	0.9	Female	1350	Vaginal
35	0.5	Female	1440	Vaginal
36	1.0	Male	1680	Vaginal
36	1.2	Female	1550	Cesarean section
37	1.6	Female	2290	Vaginal
39	2.0	Male	2850	Vaginal
41	1.8	Female	3050	Vaginal

Discussion

We found that in all instances the L/S ratio in amniotic fluid of pregnancies with anencephalic fetus at 34 to 41 weeks gestation was appreciably less than in amniotic fluid of pregnancies with a normal fetus at comparable stages of gestation. Our result is supported by other reports.[11-15] Parker et al reported that the reduced L/S ratios were related to the fetal condition rather than to some maternal factors.[12] This was supported by their findings in a twin pregnancy; the L/S ratio for the anencephalic twin was low, but that of the normal twin was high. Based on prior studies such variability in L/S ratios among twin pairs is unexpected.[13] In two other reports where one anencephalic pregnancy was evaluated, both a normal and a low ratio were found.[11, 14]

Hormones synthesized in placenta and in the fetal pituitary and adrenals are believed to serve an important role in the maturation of the fetal lung.[3-5] Thus, the low L/S ratios and maldevelopment of the lung in anencephalic fetuses may be due in part to the known aberrations in the endocrine millieu of such fetuses.[15-20] Whereas prolactin is believed to be important in surfactant production, Parker reported that in the presence of markedly subnormal serum levels of estrogen, normal serum concentrations of prolactin are not sufficent to induce a normal L/S ratio in pregnancies complicated by anencephaly.[12] It also conceivable that lung hypoplasia in many anencephalic newborns and reduced L/S ratio in amniotic fluid could result from decreased thoracic movements in utero. Lung hypoplasia and reduced L/S ratios also occur in fetuses in which there are diaphragmatic hernias.[15-21] Expansion of the lung with amniotic fluid, by virtue of the action of fetal respiratory movements, may be important in lung growth and maturation.[12] If thoracic movements are substantially decreased in anencephalic fetuses, occuring in fetuses with a diaphragmatic hernia, one might expect that even if surfactant was produced in normal quantities in the alveoli of such fetuses, the movement of surfactant into amniotic fluid could be retarded. The presence of surfactant in normal amounts in the lung tissue of anencephalic fetuses is doubtful. Naeye et al found that there are fewer osmiophilic granules, the presumed anatomic progenitors of lamellar bodies that are the storage form of surfactant, in pulmonary type II cells of anencephalic newborns than those are found in lung type II cells of normal newborns.[16]

Nevertheless, it is apparent that in the anencephalic fetus with decreased pituitary and adrenal function and decreased pituitary estrogen production, there is also fetal lung immaturity, hypoplasia and low L/S ratio in the amniotic fluid.

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The Primary Empty Sella Syndrome

Analysis of 12 Patients With Regard to Clinical Characteristics, Radiological Features, and Endocrine Function

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Summary

Twelve cases of the primary empty sella syndrome were analysed with special regard to clinical features, roentgenographic studies, and endocrine function. The findings were compared with those previously reported. A majority of the patients were obese multiparous women with normal pituitary function and normal visual fields. Patients with characteristic features of an empty sella should be followed periodically with pituitary function studies and visual field examinations. If these parameters remain normal during follow-up the patient is likely to have an empty sella.

Key Words: Empty sella syndrome.

Introduction

Te empty sella syndrome, first described by Busch, is an anatomo-radiological entity characterized by an extension of the subarachnoid space into an intrasellar position with subsequent remodelling of the sella turcica and flattening of the pituitary gland. It can be classified as primary and secondary empty sella syndrome.[1]

The term "primary empty sella syndrome" should be used when this anomaly occurs in patients who have not received previous pituitary radiation or pituitary surgery. This condition is related to an anatomic variation, in which the incomplete diaphragma sella apparently allows

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the arachnoid to herniate through the diaphragmatic opening.[2, 3] Primary pituitary pathology, such as pituitary tumors or cysts associated with an enlarged empty sella is also included in the primary empty sella syndrome.

In this syndrome, the sella is radiographically enlarged and communicates with the suprasellar subarachnoid space. An intrasellar mass is absent. The majority of patients are obese multiparous women. An increased incidence of hypertension, pseudotumor cerebri or cerebrospinal fluid rhinorrhea is found.[4] Visual field abnormalities are rare but they can occur.[5, 6] Roentgenographically it presents a diverse picture and can be indistinguishable from a pitutiary tumor. All degrees of sellar deformity may occur, but the most characteristic feature is the symmetrically enlarged sella.[7] It is best evaluated by computed tomography. Most patients with the primary empty sella syndrome have normal pituitary functions[8-10] except patients with pituitary tumors in whom there is usually some abnormality of pituitary hormone secretion.[11, 12] Isolated cases of hypopituitarism with the primary empty sella syndrome have been reported.[12, 13] Posterior pituitary function has been generally very well preserved except for some reported cases of diabetes insipidus.[14] Some studies report a higher frequency of endocrine abnormalities and even hypersecretion of some pituitary hormones, including prolactin[15-18] growth hormon[15, 19, 20], and adrenocorticotropic hormone.[21, 22]

Nontraumatic cerebrospinal fluid rhinorrhea, in association with the primary empty sella syndrome has been reported[12, 20, 21] and increased cerebrospinal fluid pressure[4], pituitary infarction[5, 23] rupture of an intrasellar cyst[24] and atrophy following pregnancy have been suggested as possible causes.

Empty sella due to pituitary surgery or radiation therapy are included in the category of secondary empty sella syndrome.[8] Enlargement of the sella caused by an expanding intrasellar tumor with or without involvement of the optic apparatus, hormonal dysfunction, and visual impairment, are among the features usually commonly present in varying degrees in patients with secondary empty sella syndrome.[3]

In order to compare the frequency of empty sellae with reports in the literature, we reviewed the records of Hacettepe University Hospital, which one of the largest reference hospitals in Turkey. Seventy six cases with the disorder were recorded including those found during diagnostic evaluation of the brain with computed tomography. We present 12 cases who were studied with special regard to clinical features, roentgenographic studies, and endocrine function.

Patients and Methods

During the 10-year period, twelve patients, (10 women, 2 men) with empty sella syndrome have been studied. The diagnosis of empty sella was made by computed tomography in 10 patients and by surgery in two patients. Surgical sella exploration was performed in three cases (two transphenoidal, one transfrontal). All of the patients had primary empty sella syndrome having no previous history of pituitary radiation or pituitary surgery. Roentgenograms of the skull were obtained in all patients, pneumoencephalographic examination in 3 patients, carotid arteriograms in 3 patients, and computed tomography in 11 patients. Corticotropin (ACTH), growth hormone (GH), prolactin (PRL), thyrotropin (TSH), luteinizing hormone (LH), follicle-stimulating hormone (FSH) levels were determined by radioimmunoassay. The central and peripheral visual fields were evaluated with the Goldmann perimeter.

Results

Clinical features: Clinical features of 12 patients are shown in Table I. The mean age of patients was 35 with a range of 20 to 52 years. Seven of the female patients were overweight. Eight women were multiparous and two were nulliparous. The number of pregnancies ranged from two to six. Hypertension was present in three patients. Severe headache was the presenting complaint in six patients, the duration of which was 10 days to 5 years prior to the initial evaluation. Other complaints included galactorhea-amenorhea (in 2 patients) and galactorhea, cerebrospinal fluid rhinorrhea, clinical evidence of acromegaly and Cushing's syndrome in one patient each. No patients had diabetes mellitus or hydrocephalus. A visual field examination revealed left temporal hemianopsia in one patient and bilateral peripheral field constriction in another.

Roentgenographic studies: Skull roentgenograms showed an enlargement of the sella turcica in eight patients. Demineralization of the dorsum sella and erosion of the sella floor were detected in two patients. There was an appearence of deepening and double contour in the sella floor in one patient. The skull roentgenogram was normal in only one patient. Computed tomography revealed empty sella in 10 patients. In one patient computed tomography suggested enlargement of the sella with an intrasellar mass, but operation disclosed an empty sella, in one patient who underwent transfrontal sella exploration, empty sella was diagnosed by the pneumoencephalographic examination, and the diagnosis was confirmed surgically. In the other two patients, pneumoencephalography showed no abnormality. Carotid angiograms were normal in 3 patients.

TABLE I
CLINICAL FEATURES OF THE PATIENTS WITH THE PRIMARY EMPTY SELLA SYNDROME

Case No	Sex	Age (yr)	Height (cm)	Weight (kg)	Blood Pressure (mmHg)
1	Female	31	153	52	100/70
2	Female	42	155	75	210/140
3	Female	36	159	51	135/70
4	Female	37	155	78	170/110
5	Male	18	160	50	110/70
6	Female	31	156	72	110/70
7	Male	35	161	57	170/95
8	Female	32	160	72	120/80
9	Female	39	165	63	100/70
10	Female	52	154	67	120/90
11	Female	35	164	81	115/70
12	Female	35	158	69	120/80

Endocrine function: Endocrine evaluation was available in 10 patients. Five of them had normal values of PRL, ACTH, FSH, LH, TSH, GH, and cortisol. Elevated levels of prolactin were detected in three patients: Two had galactorrhea-amenorrhea and galactorrhea respectively. The third had no galactorhea. Other endocrine function tests were normal. In the patient with clinical evidence of acromegaly, an elevated growth hormone level was found. A transsphenoidal exploration revealed an empty sella and an appearence of a tumoral tissue, but pathologic examination of the material showed normal hypophyseal tissue in the patient with Cushing's syndrome, functional tests of adrenal activity revealed no response to ACTH and absent suppression with dexamethasone at both high and low doses. A transfrontal exploration of the sella demonstrated empty sella, and no tumor was found even by serial sections during surgery. Bilateral adrenalectomy, performed later revealed adrenal hyperplasia.

Discussion

All patients discussed here have primary empty sella syndrome. The incidence of female predominance and other commonly associated findings were similar to those in cases previously reported.[1, 3, 6, 21, 25, 26] Table II shows the comparison of the incidence of clinical features in our cases with those previously reported, by Jordan et al.[4] Multiparity, a common feature of the primary empty sella syndrome, was present in eight of ten women. Headaches were present in eight of our twelve cases. Although, headaches are not uncommon in patients with the primary empty sella syndrome, it is difficult to be certain whether or not they are part of the syndrome.

TABLE II
COMPARISON OF FINDINGS WITH PREVIOUSLY REPORTED CASES OF PRIMARY EMPTY SELLA SYNDROME

Features	Previously Reported		Findings	
	Cases No	Incidence %	Cases No	Incidence %
Female Predominance	205/245	83.7	10/12	83.3
Obesity	127/162	78.4	7/12	58.3
Hypertension	50/154	30.5	3/12	25
Rhinorrhea	24/247	9.7	1/12	8.3

Visual field abnormalities, which are not infrequent in patients with secondary empty sella syndrome[3, 27], are rare in patients with the primary empty sella syndrome.[3, 8, 9] We detected visual field abnormalities in two of our patients, one with bilateral peripheral field constriction and the other with left temporal hemianopsia. Peripheral field constriction and bitemporal hemianopsia or quadrantanopsia with the primary empty sella syndrome have been reported.[5, 6] This suggests that visual field abnormalities can occur in the primary empty sella syndrome.

The most characteristic roentgenographic feature is the symmetrically enlarged sella.[7] All degrees of sellar deformity can occur, and progressive sellar enlargement has also been reported with the primary empty sella syndrome. In 8 of our cases skull roentgenograms revealed an enlargement of the sella turcica. An "empty sella" may exist in a sella which is normal in size, skull roentgenogram was found normal in one of our patients.

Pneumoencephalography, which is an old and reliable method of confirmation of empty sella syndrome, is rarely used now. This procedure was performed in three patients, and air could not be demonstrated intrasellarly in two of them.

When either the primary or secondary empty sella syndrome is suspected the most reliable roentgenographic method of confirmation is computed tomography. In ten of twelve patients the diagnosis of the primary empty sella syndrome was made by computed tomography.

Endocrine testing of five patients demonstrated normal pituitary function. These findings are in agreement with the majority of reports that pituitary functioning is usually normal in patients with primary empty sella syndrome.[8, 9, 10, 11]

Hyperprolactinemia and galactorhea in association with radiographically "empty sella" are known to occur.[28] The determination of blood prolactin concentration is important in the evaluation of patients with enlarged sella. An increased value will be present in approximately

35 per cent of patients with a pituitary tumor.[29, 30] Careful pituitary testing can be of value in distinguishing the patient with a primary empty sella from one with a pituitary tumor. Although we could not detect a tumor in three cases with hyperprolactinemia, the presence of an occult prolactin-secreting microadenoma within the pituitary can not be ruled out.

A rare finding reported in an increasing number of cases is pituitary hormone hypersecretion and primary empty sella syndrome. The first report of pituitary hormone hypersecretion and primary empty sella syndrome was that of a patient with acromegaly due to growth hormone excess.[20] Several cases of growth hormone hypersecretion and primary empty sella syndrome have been reported.[15, 19, 23] All of these patients have had obvious acromegaly and pituitary adenomas, and it appeared that degeneration of an eosinophilic adenoma was responsible for the empty sella in these cases. In our study one case with clinical evidence of acromegaly and elevated growth hormone level, transsphenoidal exploration revealed an empty sella, and a pathologic examination of tumoral tissue failed to show an adenoma.

Several patients have been described with pituitary hyperadrenocorticism associated with an empty sella.[31] In our patient, with Cushing's syndrome we could not detect a pituitary microadenoma by transfrontal exploration; our patient might have no tumor, or transfrontal surgery failed to disclose a microadenoma behind the clinoids.

If all clinical features of the primary empty sella syndrome are considered as a composite, patients are likely to be middleaged, obese, hypertensive and female, and in most patients pituitary function and visual fields are normal. No single feature of the primary empty sella syndrome is specific enough to distinguish it from a pituitary tumor. Pituitary tumors may present in a similar fashion but patients with pituitary tumors tend to have either pituitary hormone abnormalities (hypersecretion or hyposecretion) or visual field defects. Patients with characteristic features of an empty sella should be followed periodically with pituitary function studies and visual field examinations. If the results of these studies remain normal, such patients should be spared the expensive roentgenologic studies but full roentgenologic studies must be performed in patients with atypical clinical features, pituitary function or visual field abnormalities.

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The Results of Surgical Treatment of Craniosynostosis in Older Age Groups

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Summary

Thirty four cases of craniosynostosis in people older than one year of age with intracranial hypertension and various neurological findings are presented. The postoperative results of craniectomy with bilateral fronto-temporo-parietal flaps are evaluated and the advantages of this method discussed.

Key Words: Craniosynostosis, Intracranial hypertension, Fronto-temporo-parietal bone flap.

Introduction

Craniosynostosis has attracted the interest of many pediatricians, ophthalmologists and neurosurgeons since it was defined in 1851. Although the literature on this subject is quite extensive, criteria for diagnosis and indications for surgery are still not definite and methods of operative treatment are open to debate.

Early diagnosis of the condition depends on the proficiency of the obstetrician and pediatrician who first see the infant. Early reports of craniectomy to enlarge the skull were perhaps too enthusiastic. They led to the criticism that the selection of cases was inadequate since no dis-

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tinction was made between the passive fusion of sutures in microcephaly and primary closure with restraint of growth of the brain in craniosynostosis.

Most authors accept the first six months as the ideal age for surgical therapy.[1-6] Unfortunately this can not always be accomplished in developing countries where the surgeon rarely sees a patient before the age of one or two years.

In this paper we report the results of the surgical treatment of craniosynostosis in 34 patients older than one year of age.

Clinical Material

Thirty four patients older than one year of age with craniosynostosis, intracranial hypertension and various neurological findings were treated in the past 15 years. The group consisted of 23 males and 11 females. The age range was from 1.5 to 10 years with a mean age of 4 years. The main presenting complaint was skull deformities but all patients had signs and symptoms of intracranial pressure. Headache and exophthalmos were common complaints. The other findings in order of frequency were papilledema, primary optic atrophy, mental retardation, amaurosis, nystagmus, strabismus and nausea (Table I,II).

TABLE I

THE SYMPTOMS IN 34 PATIENTS WITH CRANIOSYNOSTOSIS

Symptoms	Number of patients	%
Cranial deformity	26	76.47
Exophthalmos	18	55.88
Headache	22	64.70
Loss of visual activity	14	41.17
Vomiting	12	35.29
Convulsion	3	8.82
Irritability	2	5.88

TABLE II

SIGNS IN 34 PATIENTS WITH CRANIOSYNOSTOSIS

Signs	Number of patients	%
Exophthalmos	22	64.70
Loss of visual activity	17	50.00
Papilledema	18	52.94
Optic atrophy	14	41.17
Mental retardation	19	55.88
Loss of hearing	1	2.94

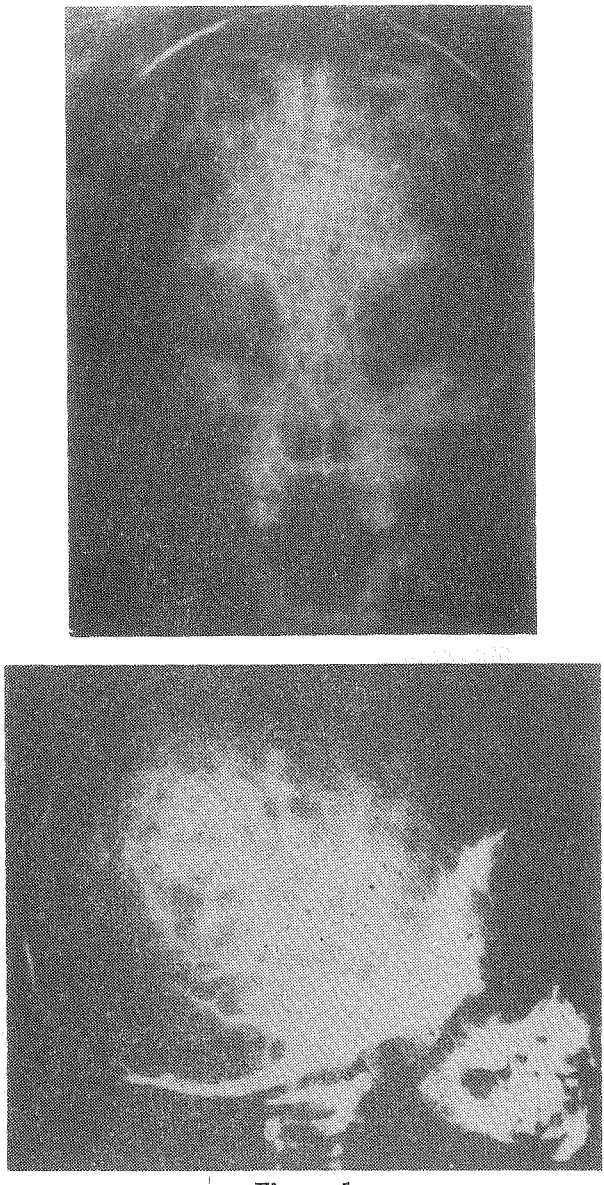

Figure 1
Preoperative skull X-ray of a patient aged 7. a) AP, b) Lateral

The results of IQ tests were below average in 18 cases, above in one, and the others were at a normal level for their age.

Preoperative skull X-rays revealed increased digital markings and synostosis of 2 or 3 sutures. In our series there were 27 cases of oxycephaly, 6 cases of scaphocephaly and one of craniofacial dysostosis of Crouzon. No

other associated congenital anomalies were found. The patients were followed for 1 to 3 years postoperatively.

Head circumferences were measured on the 20th postoperative day, and at the 6th and 12th months. Skull X-rays were repeated at regular intervals to observe the growth of bone at the craniectomy sites (Figures 1,2).

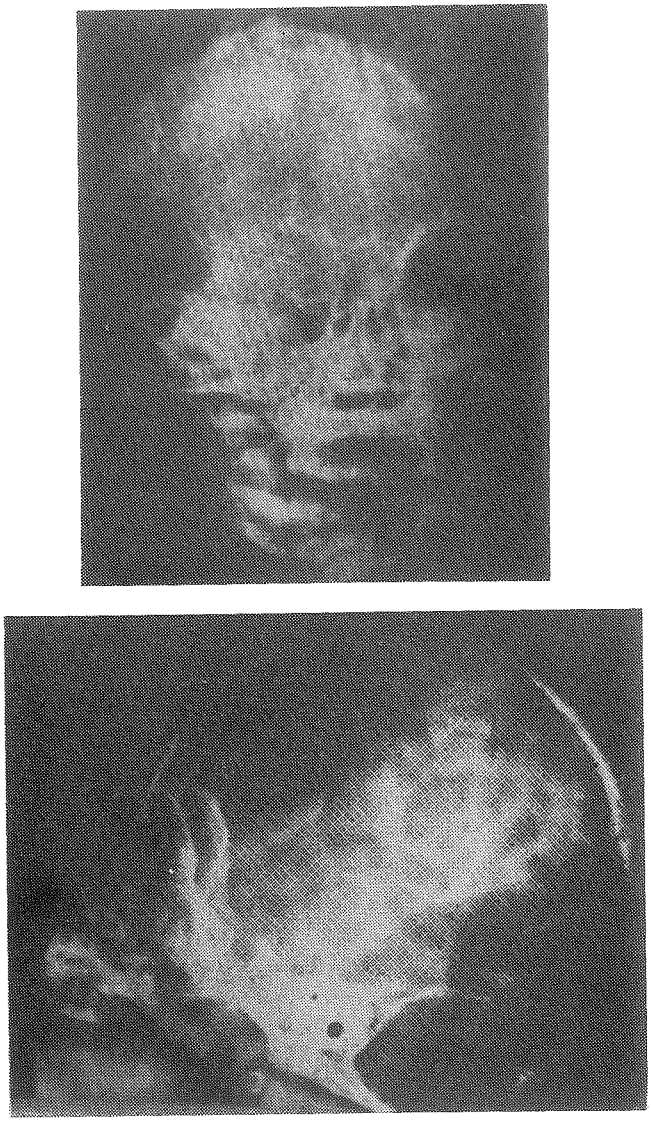

Figure 2
Skull X-ray of the same patient 3 months after the operation. a) AP, b) Lateral

Surgical Method

A coronal skin incision was made extending from a point 1 cm in front of one tragus to the same point on the other side passing nearby the vertex. The skin flaps were reflected over the frontal and occipital areas to expose the skull. Large fronto-temporo-parietal bone flaps were mobilized on both sides by excising a strip of bone 1 cm wide and using the temporalis muscle as a hinge. A bridge of bone was left over the sagittal sinus for protection, but the anterior end was removed at the coronal suture level to form an artificial anterior fortanelle. The cut edges of the bone were covered with "u" shaped strips of polyethylene film fixed to the bone using silk sutures. After careful hemostasis the galea and the skin were closed in separate layers. A drain under the skin flap was left for 24 hours.

Results

Papilledema disappeared completely in 14 of the cases at the end of the first postoperative month. Exophthalmos subsided in 19, but remained unchanged in the other three. Complaints of headache and nausea ceased in all patients. Children, who were previously irritable or agitated became calm after the operation.

Changes in the shape of skulls were interesting: a definite return to normal was noted in 22 patients. In all cases the head circumference showed an increase of 4 to 6 cm within one year. Skull X-rays revealed a decrease in the digital markings. In one case new bone formation was visible between the cut edges six months after the operation but the flaps were still mobile. Three patients had postoperative complications; in two, a hematoma appeared under the skin flap and in one, a cerebrospinal fluid collection which all were managed conservatively

Discussion

There are two indications for surgery in patients with craniosynostosis: cosmetic abnormality and intracranial hypertension.[7] The goal of treatment is correction of the abnormality in cranial shape and/or volume. Craniosynostosis is not a static abnormality; the cosmetic abnormality will usually become significantly worse with growth of the child and it may affect the facial shape.

Unless parents are disturbed about the cosmetic abnormality or there is evidence of intracranial hypertension, there is no indication for surgical treatment.[2]

If not treated surgically, the severity of the deformity often becomes worse from growth of the brain within a vault that has abnormal restrictions on the directions of expansion. The result may be progressive distortion of the cranial vault and adjacent structures such as the orbit, nose, and maxilla.

Surgery to correct the deformities of sutural stenosis can be done at any age[8,9], but the earlier procedure is done, the better the results obtained.[1,3,4,6] It is also best to do the operations "before functional, physiological, and social limitations have developed in the patient."[10]

A linear craniectomy is sufficient in infants with craniosynostosis who are under one year of age and who show no increase in intracranial pressure. When this procedure is performed between the ages of 6 to 12 months, the cranial deformities disappear and the neurological defects are prevented. Linear craniectomies also produced good results in eighteen younger patients, not included in this report.

With increasing age of the child the surgical correction becomes more complex but the increase in complexity is minimal up to 3 to 6 months. Beyond that age, the bones become thicker and more vascular and the extent of the abnormality needing surgical attention becomes greater. Linear craniectomies then may not be sufficient to free the bones of the vault from the base of the skull.

In 1969 Matson[4] published the results of bone flap craniectomies performed in several sessions. He stressed the advantages of these bone flap operations and the favorable results obtained. In later years, advances in neuroanesthesia and surgical techniques made the operation possible as one procedure.

Our cases were operated in one session. Two large bone flaps were turned with a single skin incision. The patients tolerated the procedure well and no surgical shock was observed. This method gives an equal change of decompression to both hemispheres. We found a one session operation easier for both the patient and the family. No chemical means was used to stop bone growth and the polyethylene film was entirely satisfactory in the prevention of synostosis.

We think that one must not hesitate to operate on older cases because the growth of the brain does not stop after one year of age and it is important to relieave the intracranial pressure.

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The Method of Using the Palmaris Longus Tendon As A Ribbon to the Frontal Muscle in Surgical Treatment of Ptosis

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Summary

We applied the ribbon to the frontal muscle using a palmaris longus tendon in 8 patients whose levator function was absent. The palmaris longus tendon as a ribbon is easy to ensure, it doesn't need special instrument, and incisions are small and may be performed under local anaesthesia. The results were satisfactory; thus, in surgical treatment of ptosis the palmaris longus tendon can be an alternative to fascia lata as an organic material.

Key Words: Ptosis, surgery of ptosis.

Introduction

The blepharoptosis is a commonly seen eyelid deformity characterized by a lower position of upper eyelid and being involved so it can't be raised.[1] There is a weakness or paralysis on the muscle of superior levator palpebra, as a lifting force it can't be considered. Since there is a weakness in levator muscle, supratorsal plication becomes less diseases

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and is almost lost. The degree of ptosis is evaluated by measuring the function of the levator muscle. When levator muscle function is found to be less than 4 mm. brow suspension is indicated.[2]

Persisting ptosis in spite of surgical treatment and traumatic ptosis is another indication for using the palmaris longus tendon the ribbon to the frontal muscle.[3]

The method of the ribbon to the frontal muscle has been applied since 1893. Fascia lata was used for the first time by Payr in 1928 for this purpose.[4] Argamaso[5] and Carlson[6] have used sutures which could be arranged during the postoperative period, while Tilled[7] has used a silicon strip, Mustarde[8] used fascia lata, and Morel Fatio has used arrangeable wire sutures.[7]

In this paper, results of the palmaris longus tendon as a ribbon to the frontal muscle is presented.

Material and Method

In the years 1985-1986 ribbon to the frontal muscle using palmaris longus tendon is applied to 8 patients with ptosis who no levator function.

The ages of patients ranged between 4 and 80 years. In two patients etiology of ptosis was trauma (dog bite and traffic accident), while six were congenital. The patients with traumatic ptosis and three of the congenital cases had unilateral pathology.

The tendon of palmaris longus is palpated between flexor carpi ulnaris and flexor carpi radialis tendons in the wrist. By on incision of 0.5 cm, proximally the tendon rehanged up, and remaved as long as 10-12 cm. The band ready, is arranged by splitting into two. Above 3 mm. of the lid margin with ptosis, two incisions are applied (medially, laterally and in the mid position) above the upper border of eyebrow just against those applied on the eyelids (Figure 1). The tendon passed through by Reverdin needle (can be passed through the tarse on the eyelid margin as well) can be drawn-out in the mid incision above the eyebrow and adjusted. Eventually could be sutured by 6-0 prolene. The incisions are also sutured by 6-0 prolene (Figure 2).

Infants are operated under general anaesthesia while in elderly patients local anaesthesia is preferred. All operations are performed an out-patient basis. Sutures were removed on the day and periodical observations were done for one year.

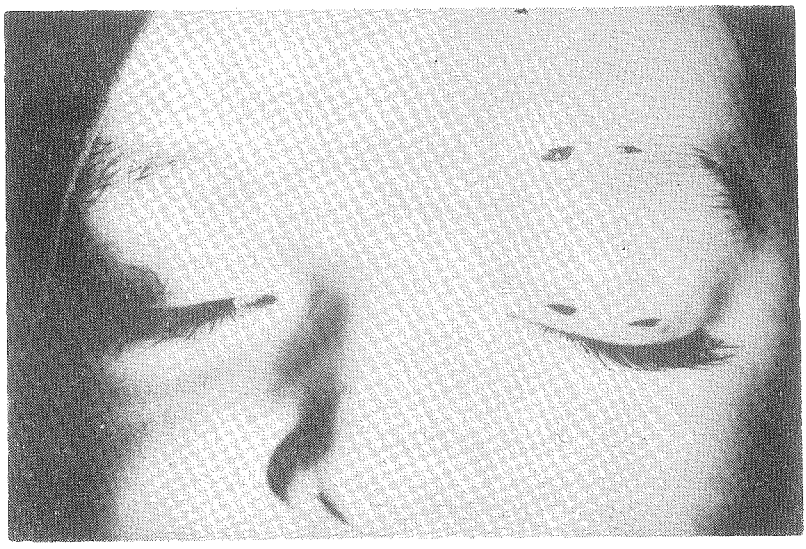


Figure 1
Incisions on the eyelid.

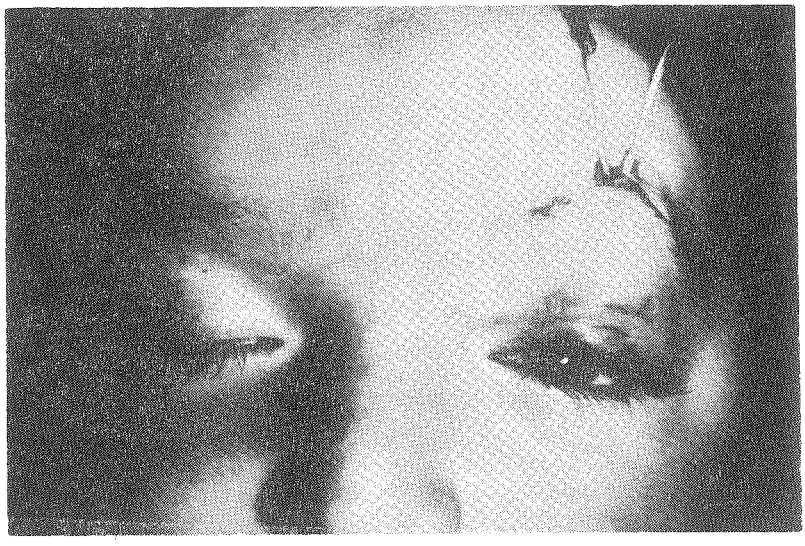
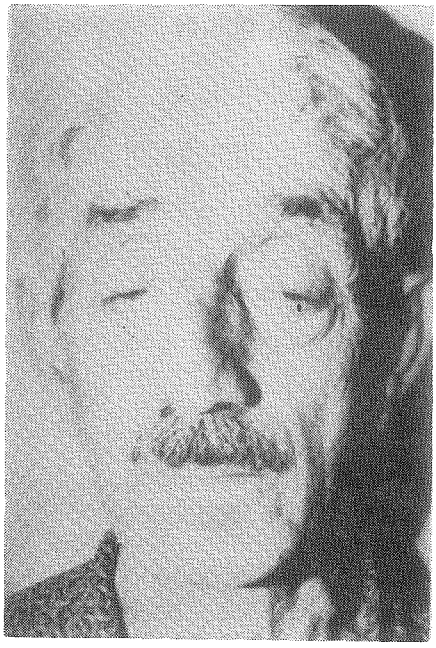


Figure 2
Adjusted tendon and closing the wound.

Results

No complications such as pain, hematoma, infection on the eyelid and donor side of the tendon were detected at the early postoperative period.



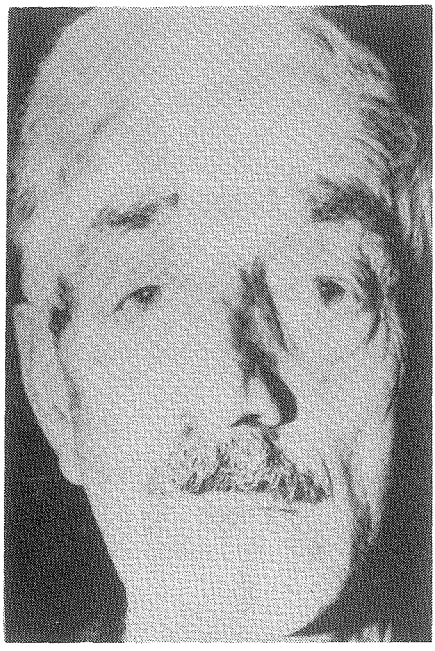


Figure 3 A,B

80 years old male with bilateral congenital pitosis, of which degree has increased continually. First postoperative weekis shown.

All the patients were able to move their eyelids efficiently by using frontol muscles at the postoperative period.

In figures 3,4,5 results of 3 patients are shown.

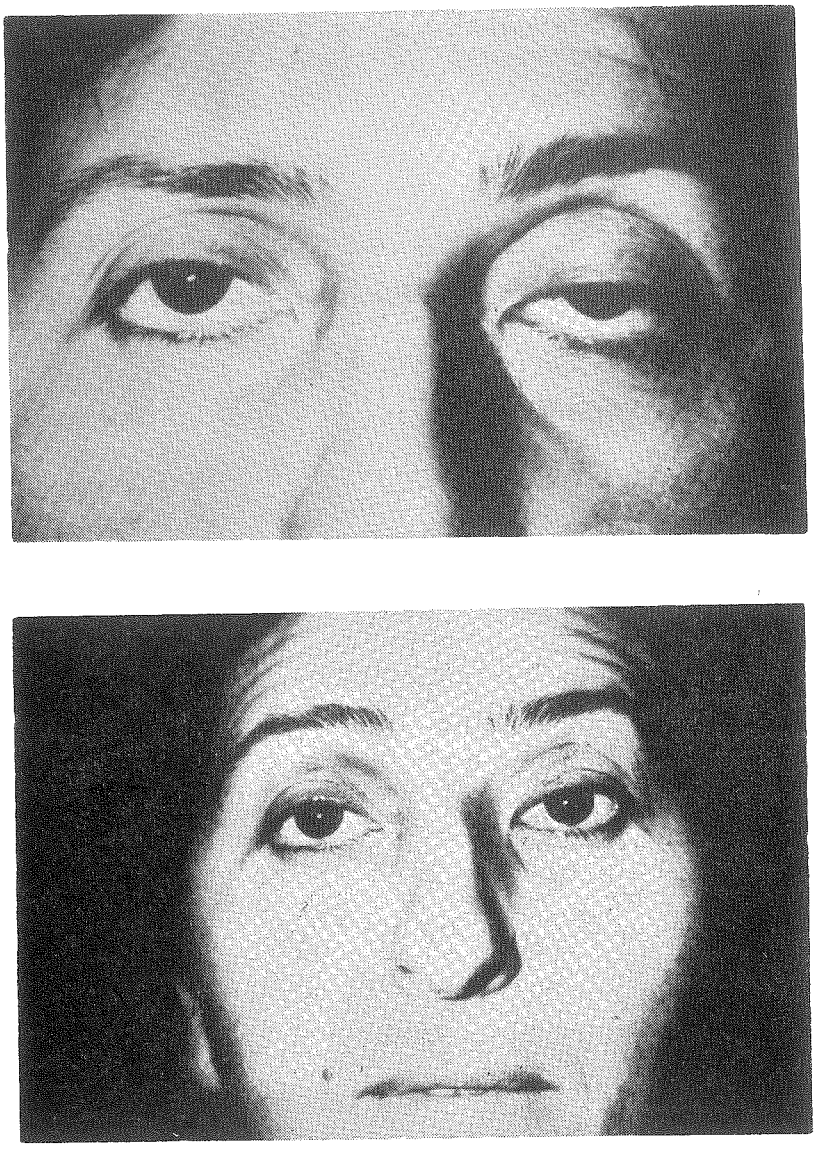


Figure 4 A,B

50 years old female, on the right side the congenital ptosis, and the new formation in the 12th postoperative week.

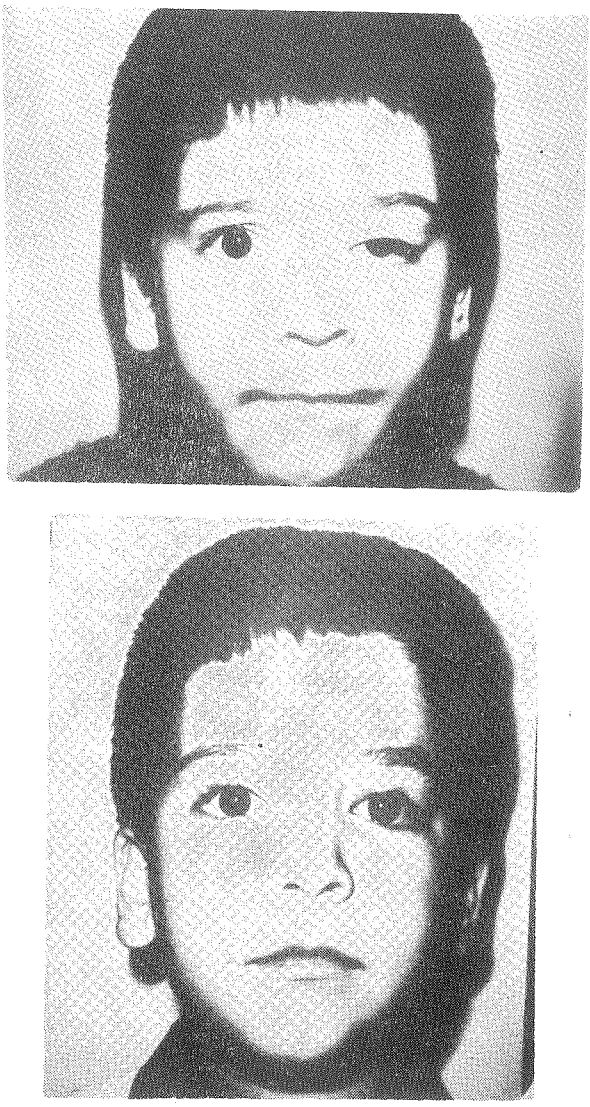


Figure 5 A,B
4 years old male, left unilateral congenital ptosis and new formation in the 12th postoperative week.

Discussion

The superiority of the organic materials with in respect to the inorganics has been accepted now. The silk suture which was used by Friedenwall-Guyton has only been used on the infants because when it is used on children it can break out easily.[9] Also the adaptable wire bow of Morel-Fatio might weaken and break out in 4-5 years[7], Tillet's silicon strip

tends to break out easily too. Accordingly as it is a foreign material an infection might develop-for the above reason, organic material is fascia lata strip[10] (BEARD). With this aim we used the palmaris longus tendon in our cases. The reason why we use it is that; It doesn't need any special device, and meanwhile as it is easier to take out if compared to fascia lata. Although the fascia lata is easily taken out without splitter but the larger incission is necessary. A large sheat is taken out to have a straight tape and made available in situ. These patients had the pain of lower extremities postoperatively and there was difficulty in the early ambulation. On the contrary the palmaris longus can be taken in the maximumly 0,5 cm. incission and pain in the postoperative period has not been so important on to donor site. The patients were able to be mobilized at an early post-operative period. No functional loss was observed. Even under local anesthesia removal of palmaris longus tendon is easy and it is easy to get a straight band.

The reason why we chose the palmaris longus tendon in our cases is that although it is not superior to fascia lata, it is easy to get out, can be taken with local anesthesia and as the problem of pain is diminishing on the postoperative donor side, no functional loss is observed. It is minimally scarred, and finally it is strong. From the functional point of view it has no superiority in respect to fascia lata.

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Asherman's Syndrome

A Retrospective Analysis of 43 Patients

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Summary

Forty-three patients diagnosed as Asherman's syndrome were surveyed retrospectively. Ninety-two percent of them had an antecedent pregnancy as a predisposing factor. Currettage after abortion in 74 % and as postpartum curettage in 16 %, preceeded the disease. Ninety-three percent of the patients presented with menstrual disorders and 69 % had infertility. Different therapeautic regimens were applied yielding an overall pregnancy rate of 33 % and term pregnancy rate of 20 %. Uterine perforations occured in 14 % during treatment. One patient developed a placenta accreta as a severe obstetric complication following treatment and required hysterectomy.

Key Words: Asherman's syndrome, management.

Introduction

Intrauterine adhesions (IUA), Asherman's syndrome or traumatic amenorrhea denote a clinical entity with mild to severe fibrosis and obliteration of the uterine cavity. The condition causes menstrual disorders ranging from dysmenorrhea to amenorrhea and infertility. Antecedant trauma, most commonly in the form of curettage can be obtained from the patient's history. Asherman was the first to describe the syndrome and put it into proper perspective, which allowed rational treatment and indicated the result that could be expected.[1] Since then many methods of treatment have been proposed and varying degrees of success reported. This report is a retrospective analysis of 43 cases encountered during a ten year period in the University of Hacettepe Department of Obstetrics and Gynecology.

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Material and Methods

From 1977 to 1987, 43 patients were diagnosed as having IUA. In each patient the diagnosis was made by a positive history and confirmed by a hysterosalpingography. Hysteroscopy was performed as a diagnostic procedure in 6 patients. The mean age of the study group was 27,5 $\pm$ 2,2 and the mean parity was 0,63 $\pm$ 0,11.

In 32 patients (74 %) IUA was ascribed to curettage after abortion, of which 62 % followed induced and 38 % spontaneous abortion and cavity control (Table I).

TABLE I
CAUSES OF IUA IN 43 CASES

Cause	No. of cases	%
Curettage after abortion	32	74.4
Spontaneous	12	
Induced	20	
Postpartum curettage	7	16.3
After evacuation of Mole	1	2.3
Following IUD insertion	2	4.7
Following metroplasty	1	2.3
Total	43	100

* 3 patients had missed abortions

In 7 patients (16 %) IUA was due to postpartum curettage. The procedure was performed immediately after delivery in 4 patients and for late postpartum bleeding in 3 patients. One patient had severe IUA after evacuation of a molar pregnancy at 16 weeks of gestation. No underlying pregnancy was present in 3 patients, (6.9 %) two of whom had used an IUD (Intrauterine device) and 1 followed metroplasty. Of the 43 patients, 40 presented with menstrual disorders ranging from dysmenorrhea to amenorrhea (Table II). Infertility was a complaint in 30 patients (69 %) and 4 patients had a history of recurrent abortions.

TABLE II
SYMPTOMS OF PATIENTS PRESENTING WITH IUA

Symptom	No. of Patients	%
Menstrual abnormality	40	93
Amenorrhea	18	
Hypomenorrhea	20	
Dysmenorrhea	2	
Infertility	30	69.7
Recurrent Abortions	4	9.3

Different modalities of treatment were applied to these patients. Eight patients (18,6 %) had lysis of adhesions with D+C (Dilatation and curettage) without any adjunctive treatment. Eleven patients (25,5 %) were treated with D+C and IUD application, 20 (46,5 %) with D+C+ IUD with estrogens and antibiotics. Estrogen was given in the form of conjugated estrogens (Premarin^{R}) 1.25 mg. orally for 1 month and a tetracycline antibiotic for a period of 10 days. In 3 patients vaginal lysis of adhesions was impossible because of severe cervical stenosis and these patients were subjected to laparotomy and lysis of adhesions by hysterotomy. Two of them had uterine perforations during attempted vaginal hysterotomy. One patient was treated by D+C and Foley catheter application for 7 days (Table III).

TABLE III
TREATMENT EMPLOYED FOR 43 PATIENTS WITH IUA

Mode of Treatment	No. of Patients	%
D + C[1]	8	18.6
D + C + IUD[2]	11	25.5
D+C + IUD + E[3] + AB[4]	20	46.5
Hysterotomy + IUD + E + AB	3	6.9
D + C + Foley cath. + E + AB	1	2.5
Total	43	100

1: Dilatation and curettage, 2: Intrauterine device, 3: Estrogen, 4: Antibiotics.

Results

The results of the different treatment modalities were analysed for the achievement of normal menstrual flow and the ability to conceive a pregnancy in patients with prior infertility.

Early and late complications of treatment were uterine perforations in 6 patients (13,9 %) requiring laparotomy in 3 of them, preterm labor in 2, placenta accreata and hysterectomy in 1 patient (Table IV).

TABLE IV
COMPLICATIONS AS A RESULT OF TREATMENT

Complication		No. of Patients	%
Early			
	Perforation*	6	13.9
	Infection	2	4.6
Late			
	Preterm Labor	2	4.7
	Placenta accreata**	1	2.3
	Placenta previa		2.3

* 3 patients had laparotomy as a result of perforation

** This patient had a hysterectomy

TABLE V

RESULTS OF TREATMENT WITH RESPECT TO FERTILITY

Treatment	No. of Patients	No. desiring pregnancy	No. of pregnancies			Pregnancy Rate	
			Term	Preterm	Abortion	Total	Term
D + C	8	3	–	–	1	33	–
D + C + IUD	11	9	2	–	1	33	22
D + C + IUD + E + AB	20	15	4	2	–	40	26
Hyst + IUD + E + AB	3	2	–	–	–	–	–
D + C + Foley + E + AB	1	1	–	–	–	–	–
Total	43	30	6	2	2	33	20

The results of treatment with respect to fertility is given in TableV. A cumulative pregnancy rate of 40 % with 26 % of them carried to full term was obtained in the group where D+C+IUD were supplemented with estrogen and antibiotics. None of the patients in the hysterotomy group conceived, probably because of the severe involvement of the uterine cavity. In the D+C group three patients presented with infertility and one of them become pregnant, but the pregnancy resulted in an early loss. Results among patients in the D+C+IUD group were similar to these in the D+C+IUD group supplemented with estrogen and antibiotics. The benefit of supplemental estrogen and antibiotics could not be shown in this study probably because of the small numbers of patients in the groups. The one patient treated with a foley catheter failed to become pregnant.

When the results of the treatments were analysed with respect to achieving normal menstruation, it was found that 22 (55 %) of the 40 patients presenting with menstrual disorders had normal menstrual periods after treatment. Of patients presenting with amenorrhea or hypomenorrhea 50 and 55 %, respectively had normal periods after therapy (Table VI).

TABLE VI

RESULTS OF TREATMENT WITH RESPECT TO ACHIEVING NORMAL MENSTRUATION

Menstrual disorder	No. of Patients	Normal menstruation established	%
Amenorrhea	18	9	50
Hypomenorrhea	20	11	55
Dysmenorrhea	2	2	100
Total	40	22	55

Discussion

The exact incidence of IUA has not been determined. A high index of suspicion is required to diagnose the disorder in any given group of women presenting with nonspecific menstrual disorders and infertility. Regarding etiology, postpartum curettage is implicated in 3,7 % of the cases in one report and 21,5 % of cases in another.[2, 3] The most important factor in these patients is the timing of curettage in relation to delivery. Curettage after the first 48 hours and in the second, third and fourth postpartum weeks carries the highest risk of inducing IUA.[4] In a large series reported from Israel the etiologic factor in two-thirds of the cases was curettage after abortion, either induced or spontaneous. Trau-

ma to the endometrium without an antecedent pregnancy is rare and follows myomectomy, metroplasty IUD⁻ insertion, diagnostic curettage or genital tuberculosis. In our patients 92 % had an antecedent pregnancy. In only 8 % of patients pregnancy missing as a predisposing factor. One study reported that a missed abortion followed by curettage carries a high incidence of forming IUA.[5] On our series 3 of 43 patients presented with a missed abortion.

Genital tract tuberculosis involving the endometrium is frequently encountered in Turkey, especially in surveys of infertility. In none of our patients was tuberculosis of the endometrial cavity found upon inspection of the pathologic specimens. Genital tract tuberculosis as a cause of IUA was first reported by Netter et al. in France[6]; Tuberculosis was the cause in 4 % of the cases of IUA in a recently report.[3]

Stilman et al. pointed out the association between Mullerian duct malformations and Asherman's syndrome.[7] They found a strong correlation between Mullerian duct malformation and Asherman's syndrome as predisposing and causative factors. In our series one patient with a bicornuate uterus had severe IUA after metroplasty. It can be suspected that she also had a constitutional factor predisposing to IUA.[8]

The symptoms of IUA always fall into two categories; infertility and menstrual disorders. The classical menstrual disorders are amenorrhea, hypomenorrhea and dysmenorrhea. Among 43 cases in this report, 93 % presented with menstrual disorders, 69.7 % complained of infertility and 9 % had a history of recurrent abortions.

A positive history and a confirmatory fractional hysterosalpingography are usually required to reach a diagnosis. The interpretation of the filling defects on hysterography can constitute a diagnostic problem. Hysteroscopy has greatly enhanced the efficacy of diagnosing IUA.The superiority of hysteroscopy over other methods is confirmed in several reports.[9-12] In six of our patient group hysteroscopy was done as a diagnostic aid.

The treatment of IUA consists of surgical removal of the adhesions and preventing formation of new ones.[3] There is no uniform opinion about how these of goals treatment can be accomplished. Lysis of adhesions can be performed by either the vaginal or abdominal route. The insertion of and IUD following lysis of adhesions has been used by many groups as an efficient way to prevent further adhesions. Others prefer to use a baloon catheter such as a Foley catheter. Prescribing estrogens alone or in combination with progestins to induce endometrial proliferation after surgical treatment is a common practice but its efficacy has been

questioned. In our patients there was no difference in the results with respect to fertility or achieving normal menstruation among those estrogens or only surgical treatment with IUD insertion. Antibiotic administration before, during or after lysis of adhesions is not consistently recommended.[3]

Hysteroscopic resection and lysis of fibrous tissue invading the endometrial cavity has been reported to be superior to other treatment modalities.[14] In a report by March et al. 98 % of the patients achieved normal menstruation and 70 % conceived a pregnancy following hysteroscopic lysis.[11]

Results of treatment are usually given according to fertility and achievment of normal menstrual periods. Among 405 patients surveyed who were treated by lysis of adhesions and IUD insertion the pregnancy rate was 55 %3; in our patients it was 40 % with 26 % term pregnancy. When all the treatment modilities were included, the cumulative pregnancy rate was 33 % and the term pregnancy rate 20 %. Achievment of normal menstruation following treatment in series of 1250 patients was 84 %.[3] In our series was 55 % had normal menstruation after treatment.

Severe obstetric complications can occur in pregnancies following treatment for intruaterine adhesions. In a report by Friedman et al. severe obstetric complications excluding premature labor occurred in 12 % of the cases.[15] Therefore patients treated for Asherman's syndrome should be considered as a high risk obstetric population and should be counseled and managed accordingly.

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Prospective Follow-up of 35 High Risk Pregnancies with the Fetal Biophysical Profile

A Preliminary Report

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Summary

Thirty-five high risk pregnant women attending the perinatology unit of the University of Hacettepe, Faculty of Medicine, Department of Obstetrics and Gynecology were followed prospectively by fetal biophysical profile scoring. A total of 93 tests were performed on 35 women with an average of 2.7 tests/patient. According to the results of the last test performed, 65.7 % were normal, 22.9 % were equivocal and 11.4 % were abnormal. Of the patients with equivocal tests, 75 % reverted to normal on repeat testing in 24 hours. Among the four women with abnormal test results, perinatal mortality was 75 %. The sensitivity and specificity of the profile scoring were 100 % and 96.7 % respectively. The false positivity rate was 16.6 % and the false negativity rate was 0.

Key Words: Fetal biophysical profile, antenatal monitoring, high risk pregnancy.

Introduction

The accurate recognition of an unfavorable intrauterine environment, hence recognition of chronic fetal distress has gained prime importance in antenatal care in order to achive a good outcome of the pregnancy. Recording of the fetal movements by the mother and biophysical tests, such as the contraction stress test and the nonstress test together with

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biochemical monitoring of fetal and placental products has been the mainstay of follow-up in high risk pregnancies. The advent of real time ultrasound imaging now permits simultaneus assessment of a wide range of fetal structures and functional characteristics. Improvement in the perinatal mortality has been reported with the use of a fetal biophysical profile.[1, 2]

A biophysical profile consists of five parameters, of which one is the nonstress test (NST) and the others are ultrasonically recorded fetal breathing movements, fetal tone, fetal movements and the amniotic fluid volume.[3] Some authors suggest that, plasental grading should also be a part of the biophysical profile.[4]

Thirty-five high risk pregnant women were followed prospectively for fetal risk assessement during a period of nine months and the results were evaluated according to the perinatal outcome.

Material and Methods

Thirty-five high risk pregnant women attending the perinatal unit of the University of Hacettepe, Faculty of Medicine, Department of Obstetrics and Gynecology were followed prospectively with the fetal biophysical profile. The mean age of the patient group was 28.40 $\pm$ 3.3 with a range of 21-40 years. All patients had rocognized risk factors and scoring was started at the 30th gestational week and followed until delivery. Biophysical scoring was performed 93 times on the 35 patients with a mean of 2.7 per patient.

The mean gestational age of the study group was 34.70 $\pm$ 1.1 weeks with a range of 30-42 weeks. Distribution of the 35 patients according to the risk factors is given in Table I. Five patient had more than one risk factor. Hypertension was the risk factor in 45.7 % of the study group. Previous stillbirth and suspected intrauterine growth retardation (IUGR) were the indications for scoring in 28.5 and 17.1 % of the patients respectively.

TABLE I
DISTRIBUTION OF PATIENTS WITH RESPECT TO RISK FACTORS

Risk factor	No. of patients*	%
Suspected IUGR	6	17.1
Previous stillbirth	10	28.5
Hypertension	16	45.7
Diabetes	3	8.5
Rh isoimmunization	2	5.7
Previous molar pregnancy	1	2.9

* 5 patients had more than one risk factor

The method used for biophysical scoring has been described previously by Manning *et al.*[3] Four variables (fetal movement, fetal breathing, fetal tone and quanitative amniotic fluid volume) were observed simultaneously during ultrasound examination. The duration of observation was extended until each ultrasound-monitored variable met the normal criteria or 30 minutes had elapsed. A score of 0 was ascribed to each abnormal criterion and a score of 2 to each normal criterion (Table II). A nonstress test was performed after ultrasonic examinations and the results were evaluated according to Rochard *et al.*[5] Decisions on perinatal management were based on the results of the biophysical profile score. A normal score (biophysical profile score $\geqslant 8$) was considered as indicative of a favorable intrauterine environment, hence a nonasphyxiated fetus, and in such cases decisions for obstetric intervention were based on other fetal, maternal or obstetric risk factors. An equivocal test result (fetal biophysical score result =6-7) was considered as an indication for repeat testing in 24 hours, and if the results were equivocal or abnormal, delivery was recomended. A biophysical profile score of 4 or less indicated an asphyxiated fetus and delivery was undertaken regardless of gestational age. Considerations for delivery were made with respect to maternal, fetal and obstetric factors.

The functional capacity of the newborn was assessed according to the standart Apgar score. A single value at 5 minutes was taken into consideration. Perinatal mortality was defined as the death of an infant weighing more than 500 gm and included deaths occurring within 28 days after delivery.

Results

Of 93 tests performed on 35 women (mean = 2.7, range = 1-6), the last test was normal (score$\geqslant$8) in 23 patients, (65.7 %) equivocal (score = 6-7) in 8 patients (22.9%) and abnormal (score$\leqslant$4) in 45 patients (11.4%). Of the 8 tests, that were equivocal, 6 reverted to normal on repeat testing 24 hours later and 2 persisted as abnormal (Table III).

No perinatal deaths occurred in the group with normal test scores and the decision for delivery was made on the basis of obstetric and maternal factors after the establishment of fetal lung maturity.

Of the 8 patients with equivocal test results, 2 (25 %) persisted as equivocal at repeat testing 24 hours later. A decision for delivery was made in these 2 patients and labor was induced. One of the infants died of respiratory distress syndrome (RDS) due to prematurity. The perinatal death rate for the group with equivocal initial test results was 1/8, 12.5 %.

TABLE II

BIOPHYSICAL PROFILE SCORING. TECHNIQUE AND INTERPRETATION

Biophysical variable	Normal (Score= 2)	Abnormal (Score= 0)
1. Fetal breathing movements	⩾ 1 episode for 30 sec in 30 min	Absent or no episode for 30 sec in 30 min
2. Gross body movements	3 discrete body/limb movements in 30 min	<2 episodes of body/limb movements in 30 min
3. Fetal tone	1 episode of active extension with return to flexion of fetal limb(s) or trunk	Either slow extension with return to partial flexion or movement of limb in full extension or absent fetal movement
4. Reactive fetal heart rate	2 episodes of acceleration of ⩾ 15 bpm for 15 sec associated with fetal movement in 20 min	<2 episodes of acceleration of fetal heart rate or acceleration of < 15 bpm in 20 min
5. Quantitative amniotic fluid volume	1 pocket of fluid measuring ⩾1 cm in 2 perpendicular planes	Either no pockets or a pocket <1 cm in 2 perpendicular planes

TABLE III

DISTRIBUTION OF PATIENTS WITH RESPECT TO TEST RESULTS AND FETAL OUTCOME

Test result	No. of patients	%	Fetal outcome Favorable	Dismal
Normal (score $\geqslant$ 8)	23	65.7	23	0
Equivocal (score= 6-7)	8*	22.9	7	1
Abnormal (score $\leqslant$ 5)	4	12.4	1	3
Total	35	100.0	31	4

* Of these 8 patients with equivocal scores 6 reverted to normal within repeat testing in 24 hours.

Four patients had scores of 5 or less. Two infants died in utero 24 and 56 hours after testing. A decision for delivery was not made, because of the extreme prematurity of these two infants. The other two infants were delivered prematurely; one survived and the other succumbed to RDS. The perinatal death rate in this group was 75 %. All of the perinatal deaths occurred in structurally normal fetuses with no congenital anomalies.

The mean Apgar scores at 5 minutes after delivery in patients with normal, equivocal and abnormal scores were 9.3 $\pm$ 0.4, 7.5 $\pm$ 0.3 and 1.5 $\pm$ 0.1 respectively.

The sensitivity and specificity of fetal biophysical scoring in predicting fetal survival were 100 % and 96.7 % respectively, for a good or poor outcome. The false positivity rate was 16.6 % and the false negativity rate 0.

Discussion

It is reported that in the absence of intervention, perinatal mortality rose progressively as the fetal biophysical score (BPS) fell.[3] Perinatal mortality in high risk patients followed by BPS alone was reduced to one-half of the expected.[6] Antapartum determination of BPS has many inacurracies. The false negativity rate for the test is reported to be 0.726/1000 in a recent report by Manning *et al.*[7] In our study the rate was 0, probably due to a small patient population. The false negativity rate for fetal BPS is still less than that reported for NST, which is 3.2/1000.[8-10]

The positive predictive value of BPS can not be determined precisely because intervention is recommended on the basis of an abnormal score.[6] In our series, two infants with abnormal scores were not selected for delivery because of extreme prematurity, and the both died in-utero

24 and 56 hours after testing. Two infants were delivered in spite of prematurity, based on abnormal tests, one survived but the other expired due to RDS.

The concept of fetal biophysical scoring involves evaluation of immediate biophysical activities (fetal breathing, fetal tone, fetal activity, fetal heart rate reactivity) together with the semiquantitative determination of the volume of fluid.[6] The nervous impulses, that initiate fetal biophysical activities arise from different anatomic sites within the brain and the last developed center is the most susceptible to hypoxia.[6] Corsidering the physiology and pathophysiology of fetal biophysical activities as well as erroneous judgements that can result from using the score alone, Vintzileus *et al* proposed that each parameter be considered.[11] If NST is nonreactive, but fetal breathing movements are present and the amniotic fluid volume is adequate, the fetus was considered to be in good condition. Baskett *et al* reported that the fetal biophysical profile varied with the gestational age.[12] The nonstress test, fetal breathing movements, fetal tone and amniotic fluid volume were more likely to be abnormal at 42-44 weeks of gestation than at 37-41 weeks.

In conclusion, biophysical assessment of fetal well being is a valuable tool and should be in the armamenterium of all perinatologists. Independent consideration of the parameters, that constitute the profile holds promise as a method for further improvement of perinatal outcome.

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Electrical Stimulation in the Treatment of Congenital Pseudoarthrosis of the Tibia with Neurofibromatosis

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Summary

This article presents two cases of congenital pseudoarthrosis of the tibia in which the diagnosis of neurofibromatosis was also present. Both of the cases had received various forms of surgical treatment, but the results were unsuccessful. The two patients had type II lesions according to Boyd's and type 3 lesions according to Bassett's classifications; both of these indicated a poor prognosis. The patients were treated in the following manner: atrophic ends of bone were excised, the bones were fixed with intramedullary nailing, and the gaps of bone were filled with spongious bone chips and cortical onlay bone grafts in order to prevent further discrepancy of limb length. Titanium cathode wires were coiled around the onlay bone grafts, then totally invasive electrical stimulation currents were applied. Both patients had clinically and radiologically asserted bone union within three months.

Key Words: Neurofibromatosis, congenital pseudoarthrosis of the tibia, Bone growth stimulator.

Introduction

Congenital pseudarthrosis of the tibia is a rarely encountered disease with an incidence rate of approximately 1 per 250.000 live births.[1,2] There is no doubt that this disease is related to neurofibromatosis.[2-7] Stigmata of neurofibromatosis, including skin and osseous lesions is reported in 20 to 80 per cent of patients in a large series with the disorder.[1, 8, 9]

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The surgical treatment of congenital pseudoarthrosis of the tibia frequently offers a challenge to the surgeon. The operative results are often less than successful; many of the cases require several surgical procedures and a significant number of cases ultimately require amputation of the limb.[9] Many authors believe that the rate of union for patients with congenital pseudoarthrosis of the tibia treated surgically exhibits no significant difference, regardless of whether or not a diagnosis of neurofibromatosis is established.[7, 10, 11] On the contrary, others suggest that the presence of neurofibromatosis is associated with a poor prognosis.[9, 12]

Morrissy and associates reported the overall rate of successful union to be 45 per cent; Sofield and Andersen reported the success rate to be 53.2 per cent and 69.6 per cent, respectively.[9, 13, 14]

Recent studies have evaluated the use of external pulsating electromagnetic fields (PEMF) and internally implanted constant direct current in the treatment of established congenital pseudoarthrosis of the tibia and the results seem to be promising.[15-17] Surgeons using PEMF produced by external coils alone or in combination with bone grafting have reported success rates of about 70 per cent, regardless of the type of congenital pseudoarthrosis of the tibia. In lesions with a poor prognosis, surgery in combination with PEMF can produce bone union in about 30 per cent of the cases.[17] This technique required a considerable amount of cooperation from the child since the coil had to be worn for at least 12 hours each day.

Paterson pioneered the application of the totally invasive technique of electrical stimulation for the treatment of congenital pseudoarthrosis of the tibia. In a series of 27 patients Peterson and Simonis achieved a success rate of 70 per cent, using bone grafting and intramedullary nailing in combination with a totally implantable electrical bone growth stimulator.[11]

The aim of this article is to review the few reports on this subject and to add two new cases.

Materials and Methods

A diagnosis of neurofibromatosis has been considered positive according to the criteria established by Fienman and Yakavacs when a patient had more than five café-au-lait spots over an area 0.5 centimeters in diameter.[2]

There have been several attempts to classify congenital pseudoarthrosis of the tibia.[7, 9, 12, 18] This author has used Boyd's (Table I) and

Bassett's classifications, the latter being of more prognostic value. According to Bassett's classifications, type 1 lesions are those in which bowing of the tibia is accompanied by significant sclerosis of the medullary canal at the apex of the lesion and usually a simple transverse fracture line. Gaps in these patients are limited to 5 milimeters or less and hyperthrophic or oligotrophic features of repair are present. Type 2 lesions include all cases in which a cystic or lytic lesion is present in the medullary space, with or without bowing. These individuals generally have a gap of less than 5 milimeters. Type 3 lesions are characterized by a significant gap and atrophic spindled bone ends.

The surgical technique and the application of the bone growth stimulator has been fully described by Paterson.[10, 11]

TABLE I
BOYD'S CLASSIFICATION OF CONGENITAL PSEUDOARTHROSIS

Type I	Those born with anterior bowing and a defect in the tibia (rare)
Type II	Those born with anterior bowing and an hourglass constriction. Spontaneous fracture occurs usually before two years of age. This type is often associated with neurofibromatosis.
Type III	Those developing in a bone cyst, often at the junction of the upper and lower third of the tibia. Anterior bowing may precede or follow a fracture.
Type IV	Those originating in a sclerotic segment of tibia without any narrowing or fracture; the medllary canal is partially or completely obliterated. This type progresses to a stress-type fracture which fails to unite.
Type V	Those who also have a dysplastic fibula; these children develop pseudoarthrosis later.
Type VI	Those with an interosseous neurofibroma or schwannoma (very rare)

Case Reports

Case 1: (S.Y. Protocol no: 845408) This patient was a 3 months old baby girl who presented with a deformed right leg. Radiographic studies revealed the diagnosis of congenital pseudoarthrosis of the tibia. A below-the-knee plastic brace was prescribed to protect her leg. After the application of the brace she was not followed-up at our hospital until she was 11 years old. Six operations had been performed at different institutions when she was admitted to Hacettepe Hospital she was using an ischial-weight bearing caliper, and had a limb length discrepancy of 7 centimeters. A diagnosis of neurofibromatosis was considered according to the criteria of Fienman and Yakovac.[2] The clinical examination and radiograms were consistent with Boyd's type II and Bassett's type 3 pseudoarthrosis of the tibia (Figure 1). Surgery was performed on the patient using cancellous and cortical bone grafts, intramedullary nailing, and a bone growth stimulator (Osteostim-2000 BGS). The titanium cathode wire was coiled around the dual onlay grafts at the defective site (Figure 2).

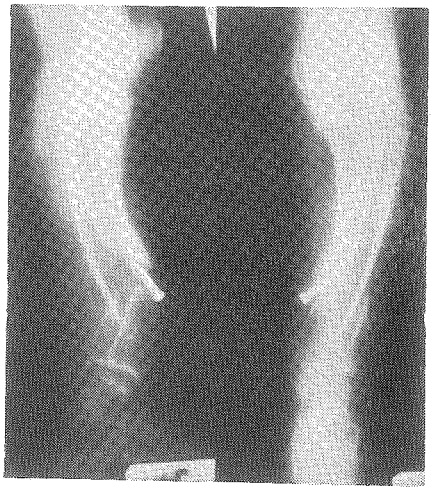

Figure 1

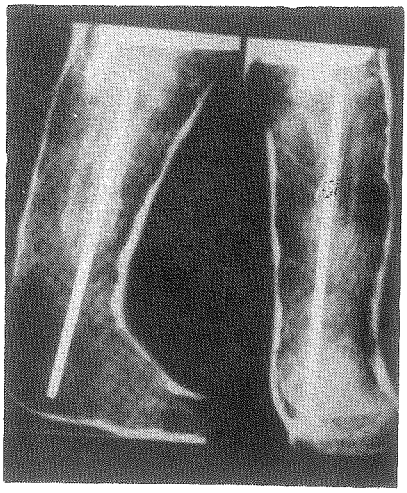

Figure 2

The limb was immobilized by a full length plaster cast from the groin to the toes. The pathologic specimen was reported as neurofibromatosis at the site of nonunion. Pathological examination of the tissue from the pseudoarthrosis site revealed densely cellular fibrous tissue. Alternating with this tissue were myxoid areas with smaller fusiform cells with pylenotic nuclei (Figure 3). Occasional structures resembling Verocayis bodies were present in this tissue. Immunoperoxidase stain for S-100 protein disclosed scattered cells displaying this marker for marker peripheral nerve cells within these areas (Figure 4). Histologic and immunohistochemical studies were interpreted as evidence for the presence of neurofibromatous tissue in the area of pseudoarthrosis. At the end of 3 months postoperatively both clinical and radiologic unions were obtained. The stimulator was left in place for a year and then removed. The patient's leg has continued to be protected with the aid of an ischial-weight bearing caliper. She is now 13 1/2 years old and the union is sound (Figure 5).

Case 2: (S.C. 1648179). This patient was a boy born with a deformation of his left leg; his left tibia was anterolaterally bowed. When he was 6 months old, a below the knee plastic brace was applied to protect his leg (Figure 6). At 3 years of age a clearly defined pseudoarthrosis of his left tibia was confirmed with radiological findings (Figure 7). Large and numerous café-au-lait spots were observed on his body. He was treated surgically with an intramedullary rod and cancellous bone grafting; his leg was immobilized in a long leg hip spica for 3 months. In spite of this treatment the tibia failed to unite and developed a well defined

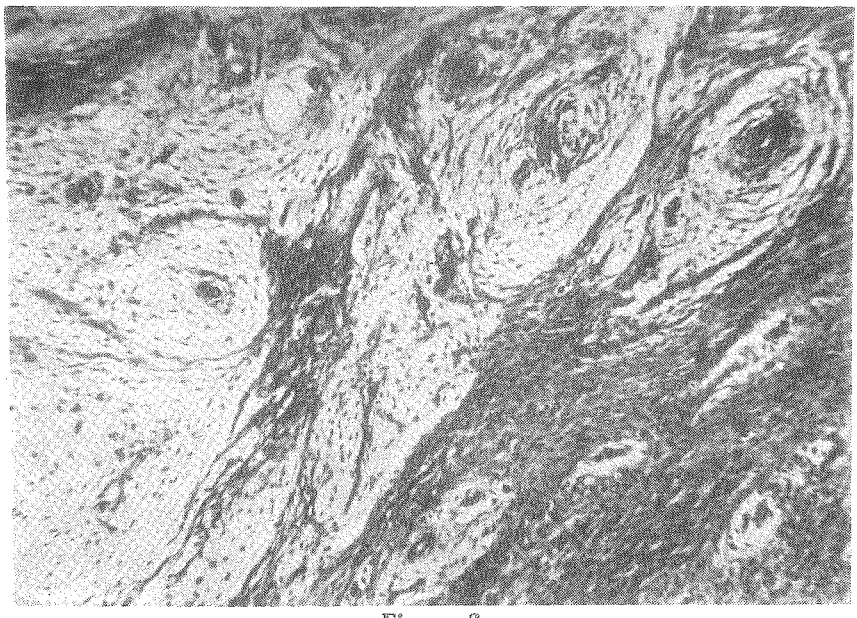

Figure 3

Histologic section of the pseudoarthrosis site showing dense cellular fibrous tissue on the right, alternating with loose myxoid neurofibromatous tissue on the left. H+Ex150

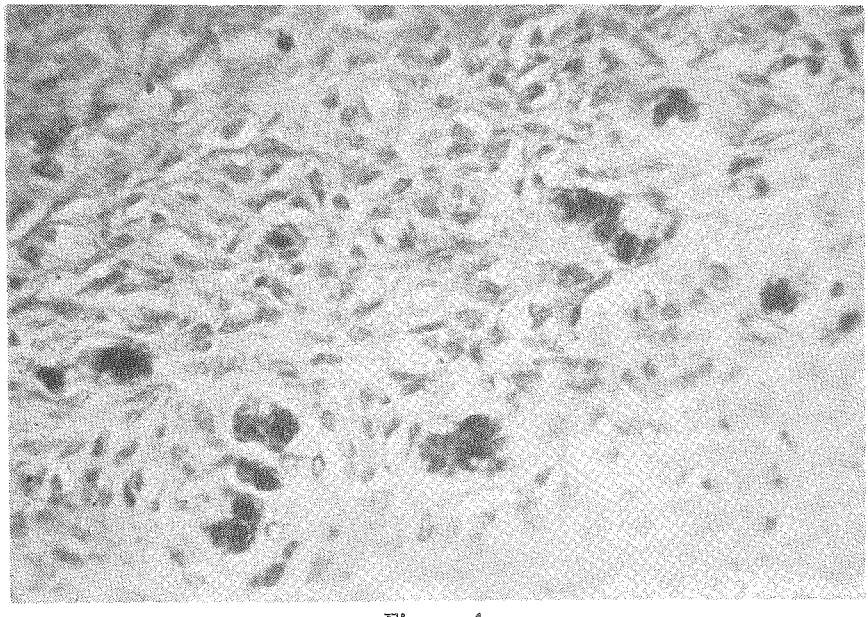

Figure 4

Immunohistochemical staining for S-100 protein. Scattered positive cells are present in the densely-cellular fibrous area. Immunoperoxidase x 400.

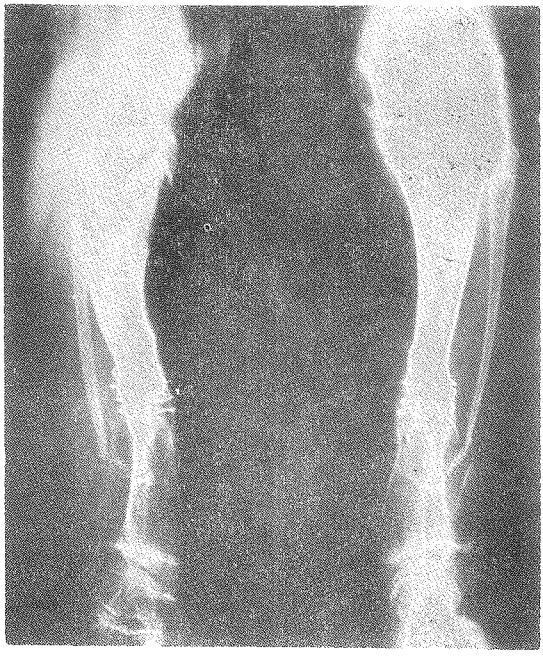

Figure 5

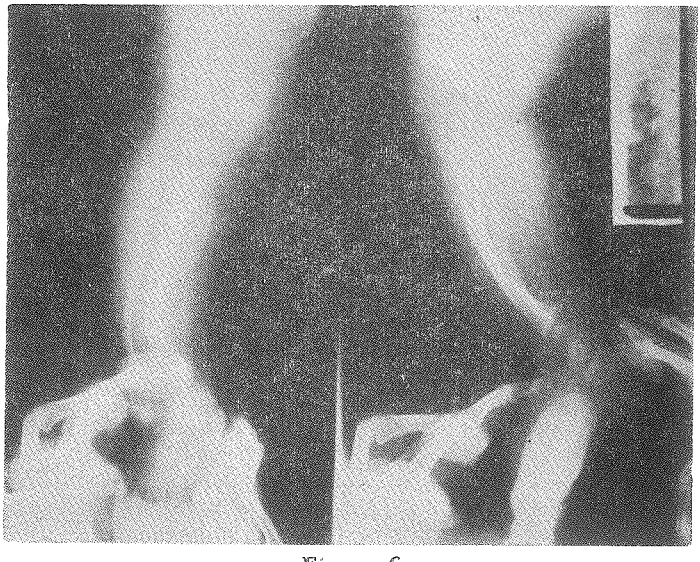

Figure 6

pseudoarthrosis which was again confirmed clinically and radiologically. The pseudoarthrosis was in the form of Boyd's type II, and Bassett's type 3 (Figures 8,9).

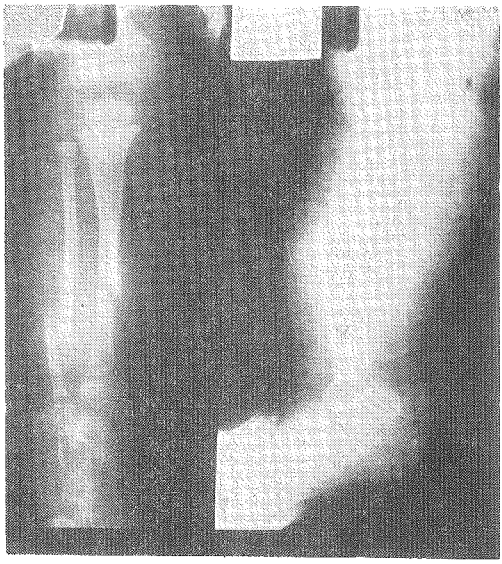

Figure 7

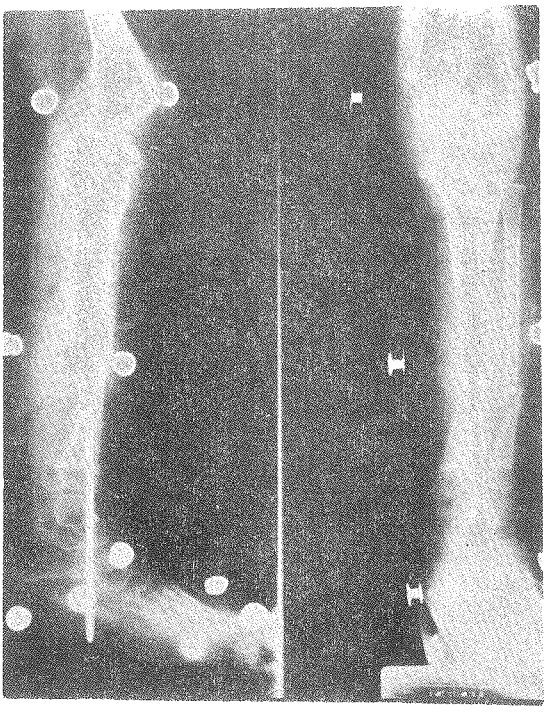

Figure 8

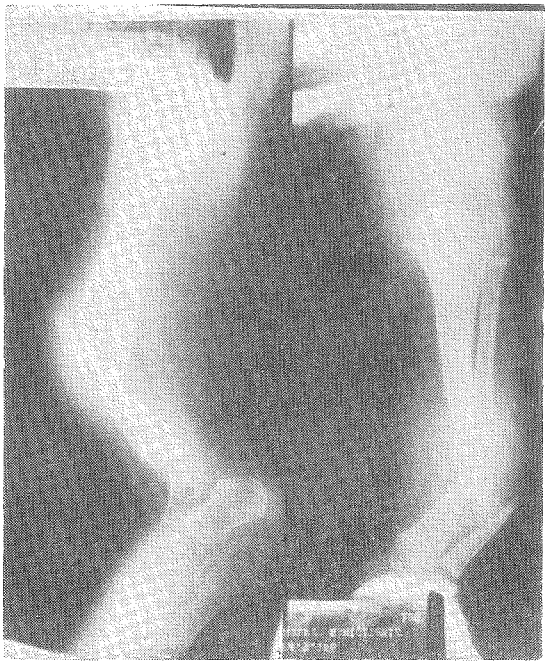

Figure 9

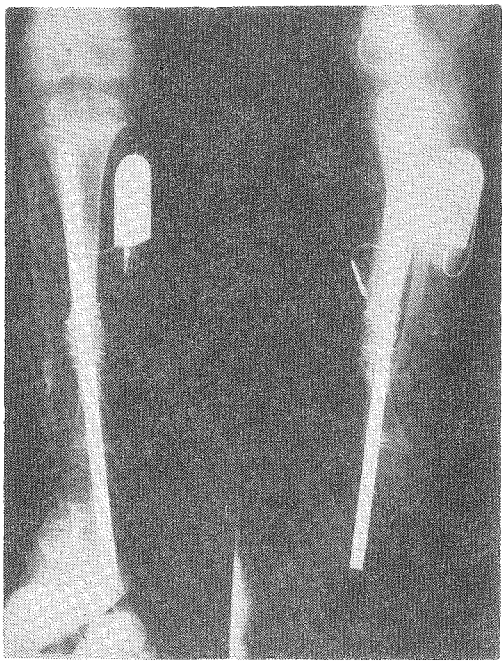

Figure 10

A year later the same type of bone growth stimuator mentioned in the previous case was applied to the site of pseudoarthrosis with a renewed intramedullary nail and bone grafting. Three months after this operation there was an abundant formation of callus. Although the radiological union was found to be satisfactory, the limb is still being protected in an ischial-weight bearing caliper (Figure 10).

Discussion

Congenital pseudoarthrosis of the tibia is a rare disease, but the difficulties arising in its surgical management cause it to stand out in the minds of most orthopedic surgeons who have occasionally treated this condition.[17]

It is not easy to analyse the significance of the many factors that may affect the prognosis this relatively uncommon condition. The prognosis is poor when both the tibia and the fibula are involved, when the pseudoarthrosis is very mobile or when there is atrophic bone with pointed ends, displacement and angulation. Also, when the lesion is more distal the outcome is worse.[9, 13, 17] The two cases presented in this article had identical fractures as described above and both were expected to have a poor prognosis. Boyd and Andersen believe that Boyd's type II pseudoarthrosis is the most common form and tends to have the poorest prognosis[5, 6 12]; Sutcliffe demonstrated that Bassett's type 3 lesions responded poorly to PEMF treatment compared to Bassett's type 1 and type 2 lesions.[16] When Bassett's and Sutcliffe's series are combined, the rate of failure in type 3 lesions is found to be 21.6 per cent.[16, 18] The two cases presented in this article had Boyd's type II and Bassett's type 3 lesions and were treated successfully. The time necessary to achieve union was three months. In Bassett's series the mean time for union was 9.9 months and 14.2 months for functional union.[8] In Suthcliffe's series the duration of treatment in cases treated with coils alone was 7.7 months. Cases in which coil therapy and surgical treatment were applied simultaneously the union took 6 months. The mean time in obtaining a union is likely to be about 9 months.[16, 17] In Paterson's series the time ranged from 3 to 18 months, with an average of 7.2 months after the insertion of the battery.

There are a few reports dealing with treatment of congenital pseudoarthrosis of the tibia utilizing the following technique: resection of the atrophic ends of bone, apposition of the freshly formed distal and proximal ends of bone with an intramedullary nail, opening a slot through the bone and then placing the spiral titanium cathode within this groove. The main disadvantage of this technique is further impairment of limb

length caused by resection of the atrophic bone ends. To overcome this problem we have modified the above technique by placing cancellous bone chips around the intramedullary nail and closing the gap with onlay cortical bone grafts; we coiled the cathode wire around the onlay bone grafts. We were able to avoid causing further discrepancy between the limbs and have not encountered any problem arising from the modified technique.

Surgeons should consider implanting a bone growth stimulator in the treatment of cases of pseudoarthrosis of the tibia with a poor prognosis.

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Fibromuscular Dysplasia of the Basilar and Vertebral Arteries

In a Case Associated with an Arteriovenous Malformation

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Summary

A case of fibromuscular dysplasia (FMD) of basilar and bilateral vertebral arteries associated with a cerebellar arteriovenous malformation is presented. FMD is a disease of unknown etiology, commonly affecting women and involving small and medium sized arteries. The involvement of vertebral and basilar arteries has rarely been reported. Although an aneurysm has been demonstrated frequently in cases of FMD, arteriovenous malformation as an associated finding of FMD is uncommon.

Key Words: Fibromuscular Dysplasia (FMD), Basilar Artery, Vertebral Arteries, Arteriovenous Malformation.

Introduction

Fibromuscular dysplasia (FMD) is an uncommon nonatheromatous and noninflamatory angiopathy of unknown cause.[1] Primarly, it affects small and medium sized arteries.[2] According to Mettinger's review, FMD has been recognized in the renal, celiac, splenic, hepatic, iliac and vertebral arteries.[3] Involvement of the basilar artery was rarely reported in the older literature.[4-6] The most common associated finding with FMD is aneurysm[1, 3] but arteriovenous malformation (AVM)[7-9] or arteriovenous fistula are sometimes present.[3]

In this case report, we present a female patient who has FMD of bilateral vertebral arteries which also involved the basilar artery with a cerebellar AVM.

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Case Report

A 24-year-old right handed woman was referred to the Hacettepe University Hospitals in August 1986 with a persistent occipital headache. Five days prior to admission she had a sudden severe headache followed by nausea and projectile vomiting.

On initial evaluation, she had neck stiffness and positive Kernig and Brudzinski signs. General physical examination was unremarkable. During hospitalization, complete blood cell count, erythrocyte sedimentation rate, blood glucose, BUN, urinalysis, skull x-rays, CT scan of brain and ECG were all normal. Lumbar puncture revealed xanthocromia and opening pressure of 130 mm H_2O. The CSF protein was 60 mg/100 ml. The first tube contained 120 RBCs per cubic millimeter, and the third tube showed 180 RBCs.

Bilateral carotid and vertebral angiograms were done by the transfemoral route which showed a bilateral "string of beads" sign of the vertebral arteries, stenosis and irregularity of the basilar artery (Figures 1-3). There was an AVM in the left cerebellar hemisphere, filling from the posterior inferior cerebellar artery (Figure 4). Subsequently, she was operated upon and the AVM was confirmed histologically.

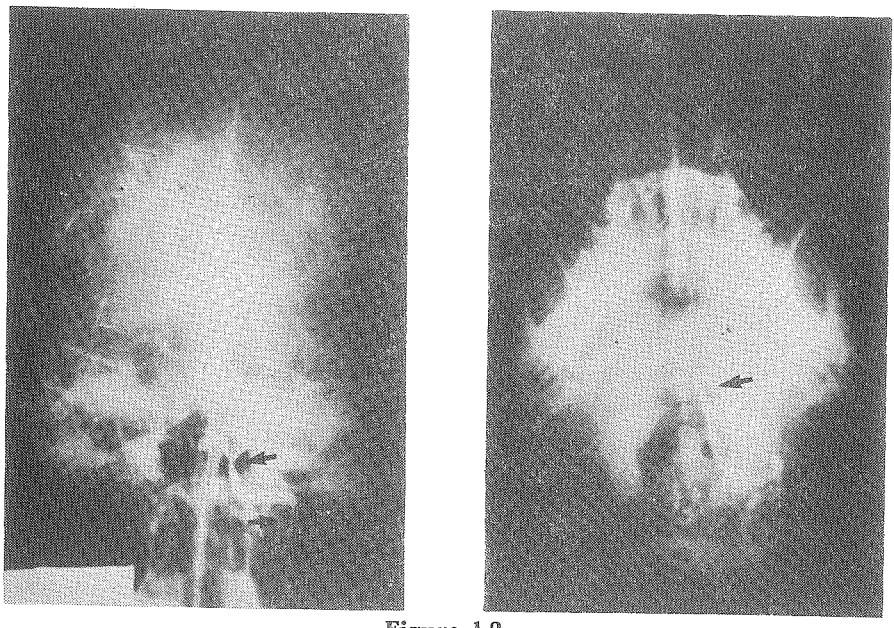

Figure 1,2
Left vertebral arteriography, demonstrating the typical "string of beads" sign of FMD of vertebral arteries which involved the proximal part of the basilar artery.

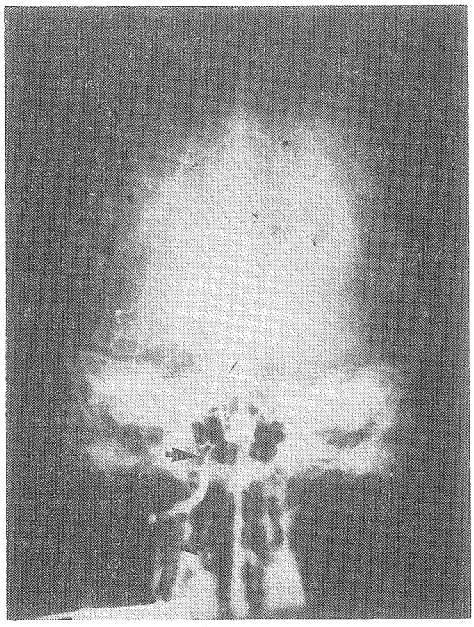

Figure 3
Right vertebral arteriography, showing the "string of beads" sign and unifocal stenosis of the right vertebral artery.

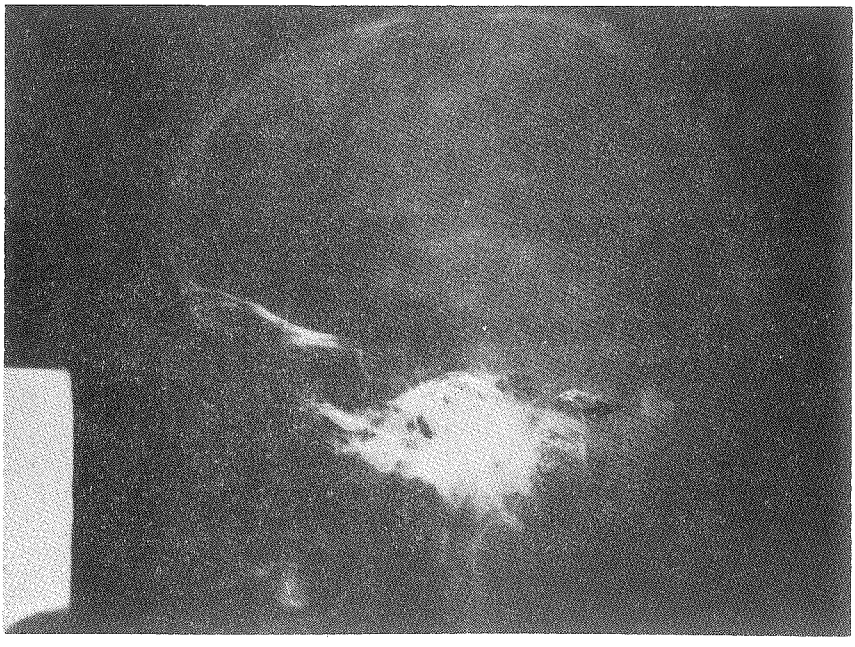

Figure 4
Lateral view of left vertebral arteriography, showing the left cerebellar AVM.

Discussion

Fibromuscular dysplasia (FMD) involving various arteries has been described in a large number of patients since 1938 with a particular predilection for the renal arteries followed in order of frequency by carotid, vertebral and iliac arteries. To our knowledge, basilar artery involvement has been previously shown in 3 cases.[4-6]

The most common angiographic pattern of FMD is the "string of beads" appearance which is accepted by several authors as pathognomonic for FMD. Osborn and Anderson reported that a second much less common angiographic pattern, is unifocal or multifocal tubular stenosis.[10] A third roentgenologic type of FMD has been termed atypical FMD with diverticular outpouching.

Patients with FMD of cranial arteries may present with neurologic symptoms, including transient cerebral ischemia, amourosis fugax, completed stroke, vertebrobasilar insufficiency or subarachnoid hemorrhage from associated intracranial aneurysm or AVM. The incidence of intracranial aneurysm in patients with FMD varies from 22 to 51 percent.[3] However, intracranial AVM has been reported previously in only two patients.[3, 8]

Although the origin of FMD is obscure, it has been suggested that mechanical, genetic, metabolic, hormonal, ischemic or immunologic factors may be responsible for its development. The association with intracranial aneurysm and arteriovenous fistula or AVM supports the possibility that FMD represents a generalized arteriopathy.

In our patient a bilateral "string of beads" sign was shown in the vertebral arteries and involved the basilar artery in association with a left cerebellar AVM. This appears to be the fourth case of basilar artery involvement of FMD and the third case of FMD associated with intracranial AVM in the literature.

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Neck Stiffness And Papilledema in Guillain-Barre Syndrome

Case Report and Review of the Literature

Rana Karabudak, M.D.* / Tülay Kansu, M.D. / Turgut Zileli, M.D.****

Summary

A patient who had papilledema and neck-stiffness associated withGuillain-Barré syndrome is reported. The results of clinical observation, lumbar puncture, computed axial tomography and radiolabelled isotope cisternography are presented. The data suggest that increased CSF protein and defective CSF absorption play important roles in the pathogenesis of papilledema.

Key Words: Papilledema, increased intracranial pressure, neck-stiffnes, Guillain-Barré syndrome.

Introduction

Papilledema and increased intracranial pressure are rare but well recognized complications of the Guillain-Barré syndrome (GBS). They are present in about 4 % of cases in adults[1], and 4 %-6 % in children.[2-5] Papilledema in GBS was first reported by Gilpin *et al.* in 1936.[6] Since then a number of cases have been reported.[7, 8] In this paper a case of GBS with papilledema and marked neck-stiffnes is presented and discussed.

Case Report

A 19 year old girl was admitted to the hospital in September 1987 with a one-week history of weakness in all extremities following an upper

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respiratory tract infection. On examination she was unable to sit or stand and had generalized weakness with severe muscle tenderness. She was areflexic and had facial diplegia. There was marked neck-stiffness. Ophthalmoscopic examination revealed a slight elevation of the disc with blurred margins suggesting early papilledema.

At the end of the first week in the hospital, the weakness was more pronounced and she could not move her arms and legs; her speech became slurred and difficulty in swallowing and coughing developed. During the third week of the illness papilledema with haemorrhages developed, but gross visual acuity was normal. The results of the following clinical laboratory investigations were normal or negative: complete blood count, urinalysis, blood urea nitrogen and electrolytes, blood sugar levels, liver function tests, X-rays of the skull, chest, cervical and thoracolumbar spine. In an electrocardiogram there was a juvenile pattern. Arterial blood gases were within normal limits. Tests for collagen disease. porphiria, antinuclear antibody, anti DNA and the sedimentation rate were normal throughout the illness. Cultures of the throat, urine and feces were normal. Brucella agglutination test was negative (For CSF pressure and biochemical values see Table I).

During the hospital course marked lid lag was observed and attributed to thyroid ophthalmopathy. Results of thyroid function tests were: Free T_3 5.50 pmol/L (3-8.50 pmol/L), free T_4 18-70 (9-25 pmol/L) T uptake 0.83 (0.72-1.24). TSH 34 uUnit/ml (0.30-4). Scintography of the thyroid showed diffuse hyperplasia; the ultrasonography of the thyroid revealed no parencyhmal pathology.

On needle electromyography of the right anterior tibial and extensor digitorum brevis muscles, fibrillation potentials, positive sharp waves at rest and a reduced interference pattern were elicited. The motor and sensory conduction velocity measurements showed marked reduction.

Slight ventricular dilatation was demonstrated in a cerebral CT scan and isotope cisternography with the intrathecal injection of 1 mC of DTPA (diethylene triamine pentaacetic acid) was carried out. Scintiscans were taken at 3,6,24 and 48 hours and a reduction in the rate of absorption of CSF from the subarachnoid space was demonstrated.

Guillian-Barré syndrome was diagnosed and prednisolone 100 mg daily was started. Ten weeks after admission, the patient began to improve and in the next 2 months she had a rapid recovery with resolution of the neck-stiffness. Her strength improved to grade 2-3/5 in the arms and 3-4/5 in the legs. The papilledema was subsequently observed to regress slowly in association with the clinical improvement. The CSF pressure

TABLE I

CSF PRESSURE AND BIOCHEMICAL ANALYSES THROUGHOUT THE ILLNESS

DATE	PRESURE (mm/H_2O)	COLOR Bright	PROTEIN (mg %)	GLUCOSE (mg %)	CHLORIDE (mg %)	CELL COUNT	CYTOLOGY
28/09/87	240	Colorless	283	64	110	–	N.
01/10/87	240	”	440	80	124	2x11MN	
05/10/87	240	”	600	71	121	–	
09/10/87	190	”					
12/10/87	300	”	609	89	119	–	
20/10/87	300	”	800	80	118	–	
23/10/87	300	”	546	84	113	–	
26/10/87	300	”	450	79	122	–	
28/10/87	300	”	868	80	139	1x11MN	
30/10/87	300	”	560	77	119	–	
02/11/87	300	”	854	82	124	–	
03/11/87	300	”	714	81	128	–	
06/11/87	300	”	510	63	122	–	
16/11/87	320	”	616	78	123	–	
18/11/87	240	”	539	78	123	–	
20/11/87	240	”	476	82	124	–	
24/11/87	290	”	518	78	122	–	
27/11/87	240	”	434	80	122	–	
01/12/87	295	”	350	82	120	–	
08/12/87	300	”	273	79	121	–	
11/12/87	300	”	260	42	123	–	
15/12/87	265	”	210	83	121	–	
18/12/87	165	”	105	92	121	–	
23/12/87	168	”	170	75	125	–	
29/12/87	175	”	145	62	120	–	
05/01/88	200	”	130	72	132	–	
08/01/88	145	”	155	77	120	–	
12/01/88	140	”	140	66	127	–	
16/01/88	170	”	105	67	124	–	
19/01/88	190	”	80	80	130	–	
22/01/88	170	”	33	66	128	–	

and protein levels gradually decreased after the second month, returning to normal values at the end of the fourth month of the illness. On the final CSF examination one month after discharge, the pressure was 150 mm of water and the protein level was 33 mg/100 ml. By this time the patient was walking without any support and her reflexes had returned, but the optic discs were still mildly elevated.

Comment and Discussion

This patient fulfilled the criteria for the diagnosis of GBS; the interesting and significant features were the marked neck-stiffness and the papilledema. Although textbooks do not mention neck-stiffness as a symptom of GBS Löffel *et al.* in 1977 mentioned it as an unusual symptom associated with GBS.[9] They analyzed 123 cases with respect to clinical symptoms and signs giving particular emphasis to unusual findings, prognosis and follow-up. In the 123 cases, 14 patients had neck-stiffness at the beginning. They found no correlation with the CSF cell count, protein levels or pressure. Also Dyck, Lambert, Thomas and Bunge stated that some patients complaining of diffuse headache at the onset of the illness and stiff neck of uncertain cause were detected in approximately 10 % cases.[10]

In 77 cases of GBS admitted to the Hacettepe University Hospitals in the last 5 years, this patient was the only one presenting with a stiff neck. We observed that when CSF protein levels decreased to normal values neck-stiffness ceased; however there was no definite correlation between the CSF pressure, cell count and course of the neck-stiffness.

Another unusual feature of this patient was the development of lid-lag during the hospital course. Although it has been reported as a rare finding in GBS[11], her lid-lag was thought to be related to thyroid dysfunction.

Papilledema, which in this patient was associated with a severe clinical course, and remitted with clinical improvement and decreasing protein levels, was not found in any of the other patients observed.

Theories about the pathogenesis of papilledema in GBS can be divided into two main groups:[19]

1) Increased CSF protein levels and incerased intracranial pressure, and

2) Increase in the brain substance due to cerebral edema.[12-19]

In 1952 Denny-Brown described autopsy findings of deposition of amorphous material in the aracnoid villi suggesting that the papilledema

was a consequence of abnormal protein interfering with the absorption of CSF.[12] Supporting the protein obstruction theory, Gardner *et al.* in 1954 demonstrated that the addition of autologous serum protein reduced the rate of absorption of Ringer's solution from the subararchnoid space in a dog.[13]

In 1980 Reid and Diaper measured ventricular volume from CT scans of a patient with GBS and found reduction of ventricular volume with resolution of papilledema.[14] They postulated that an immunological disturbance with activation of the classical and alternative complement pathways may have caused impaired CSF absorption at the arachnoid villi or alternatively, increased production of CSF at the choroid plexus in GBS with papilledema.

On the other hand against the protein obstruction theory, in 1964 Hayreh could not produce papilledema and an increase in CSF pressure in monkeys by injecting isologous serum fibrinogen into the intrathecal space.[15]

Joynt proposed that cerebral edema is responsible for the papilledema. His studies on biopsy specimen showed intracelluler edema in the cortex resembling the gross and microscopic features encountered in pseudotumor cerebri cases.[16]

In later reports ventricular dilatation has been demonstrated in GBS complicated by papilledema, in 1981, using radiolobelled isotope cisternography, Davidson, Jellinek and Behan found normal CSF absorption and concluded that cerebral edema is responsible for increased intracranial pressure in this syndrome.[17]

Thus in several reports approaches to the cause of papilledema are paradoxical. In our case the patient fulfilled the criteria for the diagnosis of GBS.[20] The occurrence of papilledema was a complication of the disease and the detailed visual testing and VER examinations were entirely normal so the question of optic neuritis was ruled out. We believe that any explanation for the increased CSF pressure and papilledema must consider the rate of high protein levels in CSF and the defective CSF absorption. With the high CSF protein levels and impaired CSF absorption demonstrated by radiolobelled isotope cisternography, the present case supports the first theory. We also emphasize that frequent lumbar punctures and fundoscopy of the patients with GBS are indicated, and papilledema should lead to appropriate investigations such as CSF flow studies and ventricular size monitoring with serial cerebral CT scans.

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Fournier's Gangrene of the Male Genitalia

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Summary

Three cases of Fournier's gangrene (necrotizing subcutaneous infection of the male genitalia) have been reported. The gangrene of the genital skin developed quickly in all patients. No predisposing factors were found. Although the mortality rates are high in this syndrome, successful results in our cases were obtained with the treatment of broad spectrum antibiotics, debridement and grafting.

Key Words: Gangrene, Male genitalia, Fournier's.

Introduction

The syndrome described by Fournier, a French venereologist in 1883, is known as Fournier's syndrome or gangrene, spontaneous fulminating gangrene and essential or idiopathic gangrene. It is a necrotizing subcutaneous infection of the male genitalia.[1]

Case Reports

Case 1: A 42-year-old male was admitted to our clinic complaining of "a growing wound" on his penis and "a discharge with repulsive odour". The history revealed that the process had begun with an abrupt pain, swelling and redness of the penis. On examination the whole skin of the penis was gangrenous and sloughed, but the patient had no fever. Blood and urine cultures were negative; B.hem.streptococci and proteus were isolated from the wound.

Case 2: A 60-year-old male applied to our clinic because of a wound involving both the penis and scrotal region. Pain and blackness had occurred ten days before admittance and the skin of the region had begun

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to slough a few days later. On examination, he had fever of 39°C and a wound involving the penis and scrotum with redness of the skin reaching the umbilicus. Blood and urine cultures were negative. Pseudomonas aeruginosa+E.coli were isolated from the wound (Figure 1).

Case 3: A 50-year-old man was admitted with swelling and a purple colored lesion on the penis. He was hospitalized and broad spectrum antibiotics were started with the question of Fournier's gangrene. In spite of antibiotics, a gangrene developed and sloughing of the penile and scrotal skin occurred quickly. Blood and urine cultures were negative, but Staphylococcus aureus+Candida were isolated from the wound (Figure 2).

Discussion

Fournier's syndrome is a type of gangrene of the male genitalia with an abrupt onset and an explosive course. In a healthy male it begins with pain or itching on the penis or scrotum followed by swelling and redness of the genitalia involving the penis or the scrotum or both. The swelling may enlarge to huge proportions. Crepitus may be felt on palpation and systemic effects of the infection such as fever, nausea, vomiting, prostration or chilling may be present. Gangrene of the penile and scrotal skin develops gradually. A diminution in pain may be felt with the development of gangrene due to destruction of sensory nerves. The skin, subcutaneous tissues and fascia begin to slough, and there is a discharge with repulsive odour. As a rule, the testes are intact.[1, 2]

Although Fournier reported that this gangrene had been seen in young adults, it can occur at any age. A case in an 8 year old boy was reported[3], but usual age is 40-51.[2] Predisposing conditions such as diabetes mellitus, local traumas, surgical procedures, urethral strictures, perianal diseases or implantation of penile prosthesis may be present.[2, 4] Aerobic gram-negative rods, gram positive cocci and anaerobic bacteria (especially Bacteroides fragilis) may be isolated from pus or necrotic tissues. Blood cultures are usually negative.[2]

Once the diagnosis is established, broad spectrum antibiotics, preferably in combination against both aerobic and anaerobic bacteria, must be started. Appropriate wound care with dressings and repeated debridements is performed, and it is important to seek and treat predisposing conditions if they are present. When the process is under control, split-thickness skin grafting is used to cover the wound.[1, 2]

With this treatment modality (antibiotic, wound care and grafting) excellent results were obtained in our three cases.

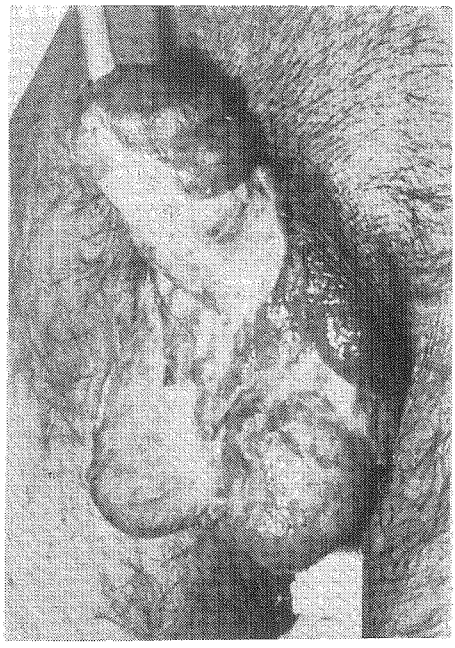

Figure 1
A 60 year-old-male. Loss of the penil and scrotal skin.

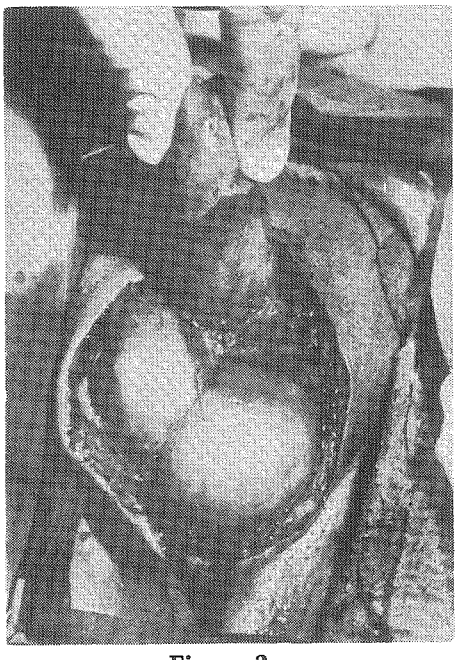

Figure 2
A 50 year-old-male. The appearance of the genital region (after debridement).

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Hacettepe Medical Journal
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Sinus Pericranii

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Summary

A case of sinus pericranii which has a tiny bone defect in the right frontal region, is presented.

Key Words: Sinus pericranii.

Introduction

Sinus pericranii is an abnormal communication between the intracranial and extracranial venous systems through a tiny bone defect. It may be located beneath or in the periosteum of the cranial bones, mostly in frontal bones, and may be congenital or acquired. In this article a case of sinus pericranii is presented.

Case Report

A twenty-one year-old male was admitted to the hospital because of a soft, painless mass in the right frontal region. The mass became more noticeable with coughing, increasing intrathoracic pressure and positioning head down.

This complaint had begun after striking his head on a wall. He fainted with a short period of unconsciousness but had no other problems at that time. Later he became aware of a tiny cavity in the right frontal region just at the point where he struck his head. One year later, a gradually increasing swelling became manifest when he lowered his head or when lying down. There had been no pain.

After the intrathoracic pressure was increased by coughing, grunting or lying down, a soft tissue swelling approximately 5 cm. in diameter was

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seen in the right frontal region. This swelling had a clearly defined boundary and was soft and fluctuant. There was no discolorization of the skin overlying the lesion. It was fixed, although the overlying skin moved freely. With the patient erect or with pressure on the swelling, it disappeared completely. Needle aspiration of this mass demonstrated venous blood but did not alter the size.

Plain skull films showed a thin and irregular area with a soft tissue swelling in the right frontal bone. Direct injection of contrast media into the mass showed prolonged retention and a connection with the intracranial veins (Figure 1,2). The lesion appeared multiloculated. CT scans of the head demonstrated the bone defect in the frontal region (Figure 3). No evidence of calcification was observed within the adjacent soft tissue (Figure 4). The mass was vascular in character.

In surgical intervention a semicircular skin flap was made in the right frontal region. The vascular mass was located beneath the periosteum and caused an erosion in the neighbouring bone. The mass was totally extirpated from the normal periosteum. Macroscopically it was a

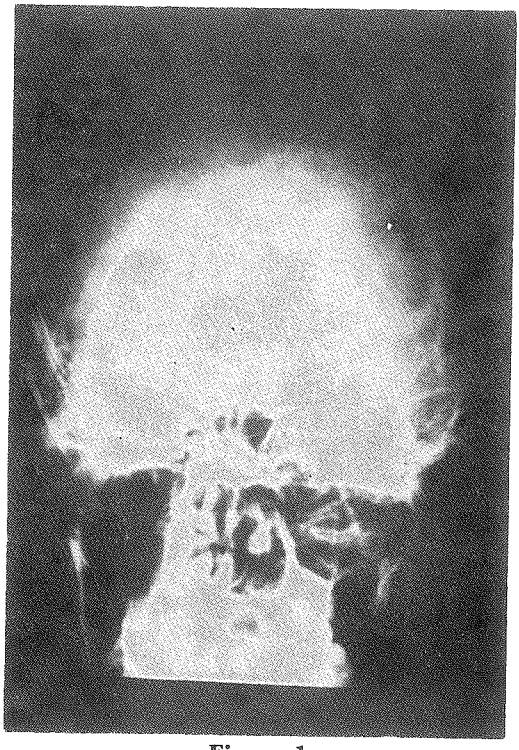

Figure 1
Prolonged retention of contrast medium in the mass is seen after direct injection.

spongy tissue which contained venous blood. Microscopic examination showed irregular sinuses lined by endothelium and small vessels in the spaces between the sinuses.

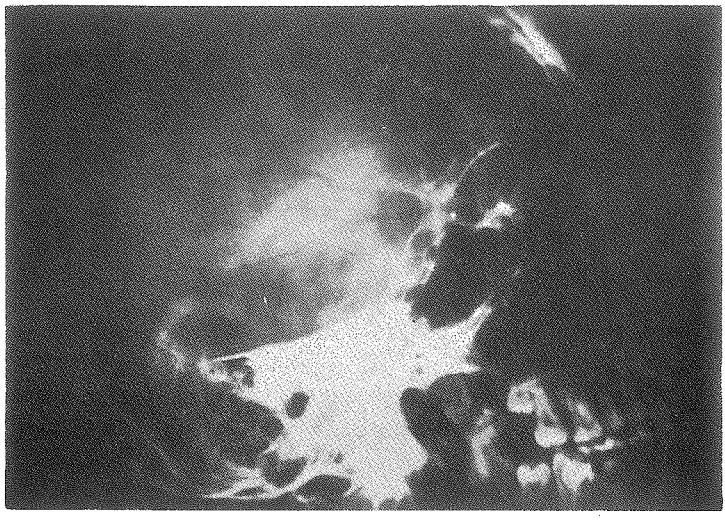

Figure 2
Connection with the intracranial veins is clearly demonstrated by direct injection of the contrast medium into the mass.

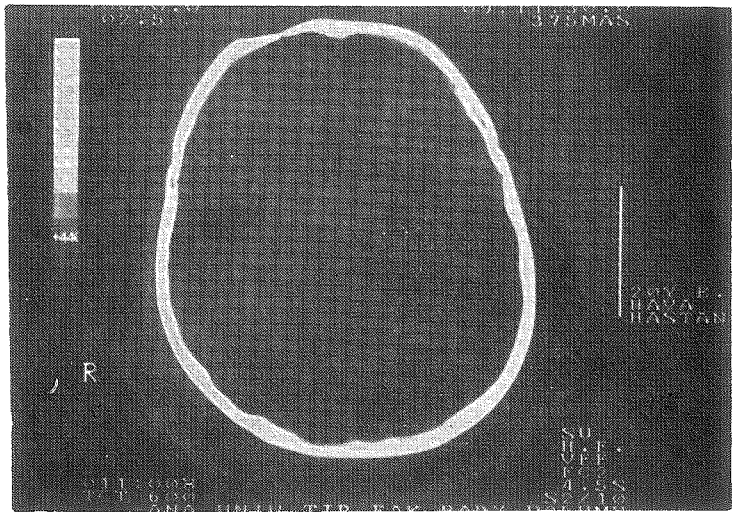

Figure 3
There is a tiny bone defect in the right frontal region. The outer tabula also is thinned. This is the same level as shown in Fig. 4 but in bone windowing.

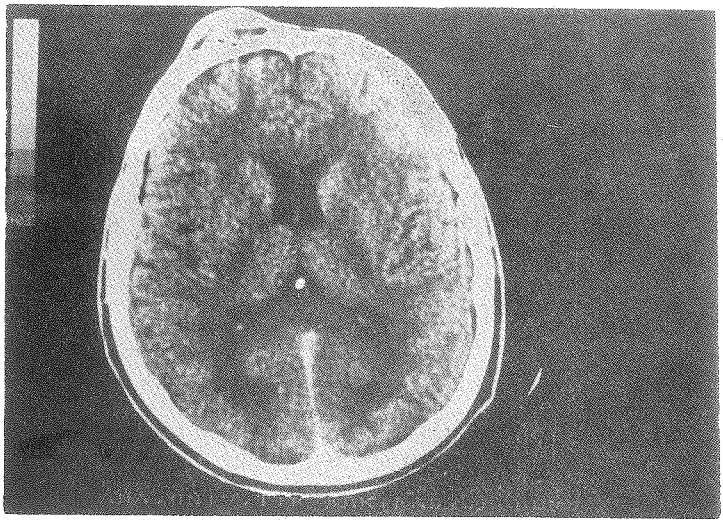

Figure 4
There is a soft tissue mass just under the scalp of the right frontal region.

Discussion

Sinus pericranii is a collection of nonmuscular venous blood vessels or venous hemangioma adhering tightly to the outer surface of the skull bone and communicating directly with intracranial venous sinuses by way of diploic veins of various sizes.[1-4] Venous blood comes from the intracranial venous sinuses and drains into the same sinuses or rarely into the extracranial venous channels.[1-4]

Many etiologies such as head trauma, congenital abnormalities or spontaneous origin (by following the chronic disease of the skull vault) have been proposed.[1, 2]

Patients are usually asymptomatic and present with cosmetic concerns. There is no difference in symptoms between cases of congenital, spontaneous or traumatic origin. Headache, nausea and vertigo have been reported.[1] Sinus pericranii is a soft fluctuant swelling that appears with the patient's head down or when he raises his intrathoracic pressure by coughing or grunting.[1, 3] The swelling disappears by applying pressure on the mass. It is often progressive. Boney changes below the swelling are found in almost all of the cases. These changes are possibly due to the traumatic depression or to the resorption of bone from continued pressure. It is located beneath or in the periosteum. The frontal region is most frequently involved.[1, 3, 4]

Congenital cases have walls of vascular origin; traumatic cases have no walls at first, but a capsule is formed later.[1]

The diagnosis of sinus pericranii can be made from the appearance and disappearance of the swelling with changes of head position, increased intracranial or intrathoracic pressure and by aspiration of venous blood from the mass. Plain skull films and CT scans are helpful and cerebral arteriograms demonstrating the abnormal communications diagnostic of the condition.[2, 4, 5] Skull films after direct injection of contrast media into the mass also can be diagnostic.

The differential diagnosis includes cavernous hemangiomas, angiomas, other A-V malformations, A-V fistula, sebaceous and dermoid cysts, abscesses, meningoceles, and encephalocels.[2, 5] Venous cavernoma of the scalp, located in the subcutaneous spaces does not adhere to the skull bone. It neither communicates directly to the intracranial venous sinuses nor does it disappear with pressure. Venous cavernoma also receives blood supply from extracranial vessels and drains to the extracranial channels.[1-3]

The therapy is complete extirpation of the mass and reinforcement of the underlying bone.[1] Massive bleeding or traumatic air emboli are encountered as complications of surgical intervention.[1]

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The Status of Current Teaching Program in Obstetrics and Gynecology and Strategies For Solving Problems*

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Summary

In Turkey over the past decade, the capacities of medical schools have been strained in meeting the educational needs of increasing numbers of medical students. Large class size have acutely affected departments of OB & GYN which have traditionally been operating with small faculties that have significant responsibilities for clinical medicine, research and teaching. As yet there is no increase in the number of hospital beds and teaching facilities and full-time teaching faculty have decreased in number as opposed to part-time staff.

Increased class size and several other factors which influence the motivations of the faculty, have resulted in the dilution of teaching effectiveness. Faculty tend to teach in the more formal and structured instructional time mainly in the class rooms. In accord with this trend, in the evaluation of student performance, heaviest emphasis is placed upon students' remembering knowledge basically in the lecture notes.

The current educational programme is the traditional one which shows the student what the facts are and then leaves it to the student to apply his acquired knowledge and skills in practice.

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The author suggests the reformulation of some of the objectives. Teaching aids such as plastic pelvic mannequin and even better, the professional simulated patient programs, to teach pelvic examination could be of help. Multidisciplinary work of an integrated type, collaboration with regional community hospitals and others have been discussed as potential solutions to the progressive impairment of medical education.

Key Words: Medical education, Teaching Obstetrics and Gynecology, Affiliation with community hospitals, Class size and teaching, Professional simulated patient.

In this report, the current status of teaching of Obstetrics and Gynecology in Turkish University Medical Schools, will be examined. The statements expressed in this presentation are mostly based on the author's experience as an individual who has lived in the medical education system, first as a medical student and resident between 1966-1977 at Hacettepe University Medical School, as a clinical fellow and instructor in the United States between 1977 and 1981, as a member of teaching staff at Hacettepe and currently at Gazi University Medical Schools. The author will also attempt to propose solutions to some of the problems of Obstetrics and Gynecology education, to improve the teaching and learning milieu.

Over the past decade, the capacities of medical schools have been strained in meeting the educational needs of increasing numbers of medical students. Various factors have caused a difficult educational situation. *The large number of medical students, the small number of medical teachers, the scarcity of research and teaching facilities have led to a lower level of achievement of the students attending our medical schools.*

Growing enrollments have acutely affected departments of Ob/Gyn because they have traditionally operated with small faculties that have significant responsibilities for clinical medicine, research and teaching. In the clinical departments like Ob/Gyn, the increased numbers of students may result in the dilution of teaching effectiveness unless more faculty members, beds and patients are also added. It is only with surveys to assess the medical student teaching resources, that is, the number of full time faculty members and the ratio of faculty to students and the number of residents, beds, surgical and obstetrical procedures and curriculum hours, correct planning decisions can be made for the teaching activities in reproductive medicine and such increases in student number can be rationalized.

Obstetrics and Gynecology provides a unique and very important educational experience that should be required for all students. Once agreeing on the basic

importance of undergraduate Ob/Gyn education, the following question should be answered; How well are students prepared for entry into the Ob/Gyn clerkship?

Since it is the objective of medical education to produce a clinician in medicine, faculties need to look at how teaching in "preclinical" or "basic science" years of medical education contributes to the overall objective of producing an effective, efficient and humane clinician *During the preclinical years,* far away from the clinical environment, *medical students must passively memorize astronomical amounts of facts presented in the contexts of the sciences basic to medicine-not in the contexts of medicine-in order that they can successfully recall these details on multiple-choice tests that,* according to several studies, *usually require only the lowest order of cognitive skills or the recall of an isolated fact, concept, list or definition.*[1]

The students are for the most part spoon-fed, passive learners in these years and are dependant on the teachers to provide information in lectures and reading assigments, and students never learn to acquire effective or efficient self directed educational skills. *The recognition of these problems* associated with the preclinical years have *caused many medical schools* including the ones in Turkey-Hacettepe University being the leader-*to incorporate problem based; self directed learning of basic science information into their curriculum.* As yet there are too many lectures. The teaching is overcrowded with too many details and it is still subject-and teacher-oriented. As a result, *most products of Turkish Medical Education will enter their clinical years with essentially no capabilities for self-monitoring or self-assessment and little ability to dig out high quality, contemporary information from the clinical or basic sciences on their own.* The burden of learning then must fall in the clerkship years. Now then, the second question to be answered is where do the gynecologists fail or have problems in the clinical education of medical students?

It has been shown that the *students using a problem-solving approach are better physicians and have better retention of information* than comparable students in the traditional educational system.[1-5] Then we have to switch to a system with more emphasis on problem solving and standardized measurements of clinical skills. One must go to the bedside not to the class room, to learn medicine. One must keep the teaching and patient care team small.

The majority of clerkship teaching occurs on hospital inpatient floors in Turkey. This *hospital system, highly organized according to specialties and subspecialties is efficient and works well for the hospital and its staff. Students fit easily into such a system provided the number of students is limited.* As class

size has increased, many medical schools have been unable to accomodate all their students in the medical center. This problem is present at both Hacettepe and Gazi Medical schools. Both schools have therefore, taken advantage of affiliations with community hospitals in order to conduct clinical clerkship in other settings.

This system carries major disadvantages in Turkey. Firstly such community hospitals do not have real affiliation with the university medical centers. *Community hospitals, in the present status are mainly responsible from patient care, not from education.* Therefore, by necessity students are given almost no responsibility.

The leadership of community hospitals and the staff, all of whom have private offices, may be less committed to education and may not even have any experience in teaching students. Furthermore, community hospitals may have weaker residency programs than those in medical centers. The members of the community hospital staff do not have any privilege of evaluating medical students. As s result, their understanding of educational goals may be a problem.

As a solution, adequate number of faculty members from the medical center should be assigned at the community hospitals who will primarily be responsible from the medical education of the students. A formal affiliation system should be constructed between universities and Ministry of Health and Social assistance Community hospitals.

In recent years, advances in diagnosis and treatment have led to effective patient care out of the hospital. The present climate of *prospective payment* displaces even more patients from the hospital to less expensive ambulatory settings. The recently *increased cost of patient care at the university hospitals* also *have displaced large number of patients to the community hospitals.* As admission criteria become more strict, university hospitals will have not only more complex patients but also fewer patients. These changes have a profound effect on the education of students in clinical clerkship.[6, 7]

In the ambulatory care environment, the physician sees the vast majority of medical problems. *Many of these illnesses are never seen in hospitalized patients.* It is pedagogically sound for beginning clinical students to be introduced to patients with simpler, common types of illnesses. The introduction of medical students into limited outpatient clinic space especially when they are given responsibility to interact with patients, takes considerable time and additional room. *From the patients' point of view, in a gynecology outpatient set up, it is inconvenient and embarrasing to spend extra time to be seen by a medical student.* Medical schools must recognize the

cost of ambulatory teaching, both with regard to the physicians' time and the additional space required for teaching. Teaching the most difficult skills to teach to medical students, *physical examination of the breasts and pelvis, with classic lectures slides conveys far less information,* than actually performing the examination. *The use of clinic patients for teaching students the pelvic exam, raises a number of ethical and logistical questions.*[8] Although one learns most thorough practical experience, with the current large number of students it is not feasible and also advisable to expose patients too often to totally inexperienced medical students. The so-called "paper patients" are a great help in arriving at diagnostic thinking, but the personal medical approach demands a lot more.[9]

The use of simulated or programmed patients seems to be highly valued by all of the students as an educational method.[10-16] Such surrogate patients learn to perceive proper and complete palpation of the breast, abdomen and internal pelvic organs and provide immediate feedback about what is being felt and whether the examination is being properly performed. In an ideal set up, following didactic instruction, a film on pelvic exam, small group instruction on a "Gynny" plastic model, students would be assigned to "simulated patient" training modality. Problems involved in the use of surrogate patient program include obtaining administrative approval and a supplementary budget to employ the "gynecology teaching associates".

Evaluation of the medical student is a major issue. Between postgraduate teaching, clinical practice and research demands, clinical faculty members seem to have less and less time for undergraduate teaching. The easy way out of this dilemma in clinical evaluation is to give the students multiple choice written examinations. *Multiple choice tests will rarely come into the emergency room or clinic for the students to answer.* If it does not bother medical faculties, it should be of concern to the public which will be the eventual subject of the graduated students' ministrations.

The general complaint among teaching staff has been the increasing number of medical students. As yet we, being the complaining faculty are unwilling to give negative evaluations. *Medical faculty tend to consider the borderline or failing performances successful.* This may be partly because we feel guilty of not giving adequate training during clinical clerkship.

Unwillingness of faculty members to record negative evaluations about students and failure by appropriate persons to act on negative evaluations received about students are the usual trends in the Turkish medical schools. On the other hand, the practice of asking inadequate students to repeat a clerkship experience is insensitive to the individual student's particular problems and in

many cases does not improve performance. Worse, the passing on of a questionable or marginal student to the next clerkship often leads to the graduation of students who are clinically incompetent.

Faculty members whether in full time or part time status are the primary providers of medical teaching. The system in Turkey is quite unique. Part-time teaching staff, whose private offices are located not in the university campus, but far from the hospital, leave the medical center at noon. They can participate the teaching activities only during the first half of the day. They are not privileged to examine, to admit and to treat their private patients at the medical center. Therefore they have to go to the private hospitals to give Obstetrics and Gynecology patient care. Ambulatory care could only be provided at their private offices. Continuing teaching medical students and residents and taking care of the patients at the university hospital in the afternoons and also night calls are full time staff's responsibilities. It is my personal opinion that under present stipulations, *part time faculty members have less committment to and interest in teaching. They have to combine this committment and interest with a busy private clinical practice outside the medical center.*

A system which enables all of the teaching staff to provide patient care including the private patients', for example after 4.00 p.m., in the university medical center, using all of the facilities 24 hours a day and 7 days of the week, would let more medical students to be trained by the specialists both at the out-patient and in-patient environment. *Let us wellcome the private patients into our educational milieu.* Let us avoid excessive focus on details, national guidelines and long lists of goals and objectives.

As economic constraint on full time faculties increases with more limited government funding, medical school full time faculty members increasingly are expected to see more patients. Education will only achieve a significant role in a faculty member's life, when it is appropriately rewarded.[17] Somebody in the system should have the power to change incentive systems to reward clinical educators with release time and financial remuneration.

In contrast to the present status in the medical schools, *residents should be the role models for medical students' clinical education.*[18] They are always on the floors and are close in age to students. Residents see a different aspect of the student than do the faculty members who are present for only limited periods in more formal sessions. Efforts should be directed at teaching Ob-Gyn residents how to teach. Residents who teach, learn twice, and thus residents who teach benefit not only the students but also themselves. Residents, like members of the faculty should be awarded for their teaching.

In conclusion, the organization of undergraduate medical education in Turkey is passing through a crisis. Although the responsibilities for teaching Obstetrics and Gynecology have significantly increased during the past decade, especially in terms of student numbers and curriculum content, the resources (like personnel, space and material) to accomplish the teaching have not increased. The part time teaching staff have been pushed away, in the present status, from the medical education system and have, wrightly, lost their interest in and committment to teaching. Among whole team of medical staff, there is a noticable loss of motivation to teaching medicine, for various reasons.

It appears safe to conclude that if the number of the medical students can not be decreased, the class size may have no impact on undergraduate performance in Obstetrics and Gynecology as long as a) the medical school has community hospitals that help train students under university supervision b) student feedback from these community hospital programs is regularly solicited and evaluated and c) the community hospital physicians who teach the students in community settings are made to feel a part of the university faculty.

What is clear is that clinical faculties can not continue to neglect the progressive impairment of medical students' clinical education. Medical school deans, departmental chairmen and faculties must make a major commitment to sustain and improve clinical teaching. Although increasing size of classes and financial constraints and heavy demands on faculties to contribute to their own salaries will make such commitment difficult, each medical school must seek unique solutions that are compatible with its environment.

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Hacettepe Medical Journal, Volume 22, 1989
AUTHOR INDEX

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SUBJECT INDEX

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