Journal of Ankara Medical School

ISSN 1300–5464

Vol 20, No 3, 1998

Journal of Ankara Medical School

Vol 20, No 3, 1998

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Journal of Ankara Medical School

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Editorial Office:
A.Ü. Tıp Fakültesi Yayın Komisyonu Başkanlığı Sıhhıye-ANKARA

ISNN 1300 - 5464

Typesetting • Design • Print: Öncü Limited, Tel: (0.312) 231 20 26 • Fax: (0.312) 230 73 52

Journal of Ankara Medical School

Published Quarterly by

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CYCLOSPORIN FOR THE TREATMENT OF IDIOPATHIC THROMBOCYTOPENIC PURPURA

Fahir Özkalemkaş* • Rıdvan Ali* • Ahmet Tunalı* • Vildan Özkocaman**** • Tülay Özçelik******

SUMMARY

Cyclosporine has been shown to be effective in refractory Idiopathic Thrombocytopenic Purpura anecdotally. We report here three patients with ITP who were responsive to cyclosporine. We conclude that cyclosporine at doses of 200-400 mg/d is safe and effective in refractory ITP.

Key Words: *Cyclosporine, Idiopathic thrombocytopenic purpura, Autoimmunity*

Idiopathic Thrombocytopenic Purpura (ITP), also referred to as primary immune thrombocytopenic purpura, is defined by low platelet count, normal bone marrow, and the absence of other causes of thrombocytopenia(1). Its pathogenesis related to an antiplatelet antibody, usually of the IgG class, which coats autologous platelets and leads to their phagocytosis and destruction by the mononuclear-macrophage system(2). The proper management of patients with ITP who have not responded to corticosteroids and splenectomy, continues to be a frequently encountered and difficult problem in the practice of haematologist. The principal treatment modalities that can be used in such cases are follows: Cyclophosphamide, Azathioprine, Vinca alkaloids, Danazol, IV IgG, Anti-Rh (D), Vitamin C, Plasma exchange, Colchicine, Immunoadsorption and combination chemotherapy(3). Immunosuppressive treatment with chemotherapeutic drugs as a single agent may be considered in patients with no response prednisone or whom glucocorticoids have side effects. Azathioprine and cyclophosphamide were the first agents with reported success in patients with chronic refractory ITP and have been the most widely used(1). Myelosuppression is the most common side effect of these drugs in the routine practice. Whereas a relatively new and potent immunusuppressive agent, cyclosporine usually does not cause myelosuppression(4) and it has been shown to be effective in refractory ITP anecdotally(5-7). We report here three patients with ITP to whom we administered cyclosporine. In two of them medication was instituted before splenectomy because of various problems.

PATIENTS

Case 1: A 47-year-old woman who was diagnosed as having ITP in June 1993, presented with steroid-resistant relapse in August 1995. Splenectomy was postponed due to the investigation of the aetiology of hypercalcemia detected in her routine blood chemistry. The prednisolon dose was tapered to 20mg/d and Cyclosporine at a dose of 200mg/d (4.7mg/kg/d) was started. The platelet count rose to $100X10^9$/l from $17X10^9$/l on the 17th day. Meanwhile the diagnosis of parathyroid adenoma had been established with parathormone levels, parathyroid scintigraphy, ultrasonography and fine needle aspiration biopsy. Then sple-

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Received: March 4, 1998 Accepted: April 22, 1998

nectomy and parathyroidectomy were performed simultaneously when her platelet count was 66X10⁹/l. The platelet count rose to 853X10⁹/l soon after the operation. She is still in remission without therapy.

Case 2: A 21-year-old man presented with extensive muco-cutaneous hemorrhage and severe thrombocytopenia in October 1995. He was taking prednisolon at a dose of 15mg/d with the diagnosis of ITP for 3 months. 2mg/kg/d prednisolon, IV immune globulin (IVIG), vincristine and platelet transfusions failed to stop mucosal bleedings and the platelet count persisted at around 1X10⁹/l-2X10⁹/l. Splenectomy was avoided because of the risk of peroperatuar bleeding. Therapeutic plasma exchange (TPE) and cyclosporine at a dose of 400mg/d (5.7 mg/kg/d) was started. His platelet count rose to 22X10⁹/l after 4 TPE. We continued the cyclosporine at a dose of 200mg/d. His platelet count was found to be 42X10⁹/l in the 2nd week, and 148X10⁹/l in the 4th week of therapy. We considered the high probability of relapse and adverse effects of long term cyclosporine therapy and decided to perform splenectomy. Thrombocytosis appeared after the operation and he is also still in remission without therapy.

Case 3: A 48-year-old woman who was diagnosed as having ITP in February 1995, was admitted with relapse in August 1995. A remission was achieved by splenectomy, but after 2 months profound thrombocytopenia developed. Steroid, vincristine, IVIG, cyclophosphamide, danazol, colchicine, TPE therapies failed to achieve remission. Cyclosporin was started at a dose of 400mg/d (4.4mg/kg/d) in October 1996. Her platelet count was found to be 52X109/l in the 4th month which was the highest level obtained after relapse. She is still under the cyclosporine treatment and is asymptomatic.

The drug was tolerated without any serious side effect in all patients.

DISCUSSION

The introduction of cyclosporine has provided an entirely new approach to immunusuppression by virtue of its highly selective ability to inhibit activation of T cells. Unlike cytotoxic immunosuppressants, therapeutic concentration of cyclosporine does not cause myelosuppression(8). Cyclosporine was used in severe aplastic anemia(9,10), pure red cell aplasia(11,12) and amegakaryocytic thrombocytopenic purpura(13) successfully. The effectiveness of cyclosporine in each of these cases presumably resulted from its potent immunosuppressive activities. So far, several reports have described successful cyclosporine therapy in other steroid-resistant autoimmune hemopathies: ITP(5-7,14,15), autoimmune haemolytic anemia(4,16,17) and Evans Syndrome(11).

Kelsey et al(6). in 1985 and Velu et al(7). in 1987 reported two patients with refractory ITP treated with Cyclosporine. The doses of the drug were 10 and 6-12 mg/kg respectively in their cases. Brief responses occurred in a few weeks in these patients, but relapses occurred shortly thereafter. Siegel et al(15). reported a preliminary study in which cyclosporine was used in lower doses (2.5-3.3 mg/kg/d). Seven out of 11 cases showed partial and drug-dependent responses in this unpublished study. Recently Emilia at al(14). have dealt with the beneficial effect of cyclosporine in steroid-resistant eight cases of refractory autoimmune haematological disorders, four of them had ITP. They started the therapy at an initial dose of 5 mg/kg/d. All patients were responsive but the majority of surviving patients remain dependent on continued drug administration.

We used the cyclosporine at a dose of 4.4-5.7 mg/kg/d at the beginning of the therapy and the dose was reduced to about 2-3 mg/kg/d after 1-4 weeks according to the clinical response and plasma levels of the drug. Cyclosporin plasma levels at the beginning of the treatment periods ranged from 150-200 ng/ml, after the dose reductions plasma levels of 40-80 ng/ml were present. No significant change in blood pressure has been detected. Blood urea, creatinin, bilirubin, albumin and transaminases have not changed. Probably the reason for this safe course has resulted from relatively low doses of cyclosporine. Although, our second patient who did not have previously undergone splenectomy, showed a good result with cyclosporine, due to the high probability of relapse and potential adverse effects of long term cyclosporine therapy we performed splenectomy. Our third patient's course and the previous literature confirm the partial and drug-dependent results. Also, we confirmed the safety of treatment at an initial dose of 200-400 mg/d of cyclosporine. From this point of view low dose cyclosporine may offer a useful alternative to other immunosuppressive drugs and its side effects compare favourably with those of other drugs commonly used in this situation. We conclude that cyclosporine at a dose of 200-400 mg/d is safe and effective in refractory ITP. We obtained a

good result with cyclosporine prior to splenectomy but we advise that cyclosporin treatment in ITP be restricted to severe and refractory disease because of its potential side effects.

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COLCHICINE THERAPY FOR IDIOPATHIC THROMBOCYTOPENIC PURPURA

Fahir Özkalemkaş* Rıdvan Ali Ahmet Tunalı*** Yusuf Karaslan*****

SUMMARY

Colchicine is a low cost, oral agent which is rarely used in ITP patients and it is still be considered as an unproved therapy. It was given to 18 patients with ITP in doses of 0.5 mg per oral 3 times a day for a minimum of 6 weeks. It was used in 6 post-splenectomic (Sc), 2 both pre- and post-Sc and 10 pre-Sc periods, so efficacy of it was evaluated in 20 therapeutic cycles. The patients were followed for a minimum of 6 months. 3 of pre-Sc and 1 of post-Sc periods exhibited an excellent response. In 6 cycles, platelet count rose to 150000/µl or more but effect was transient or drug-depended. In 4 cycles there was no effect and in other 5 cycles platelet count rose to 50000/µl but below 150000/µl, however, these responses were transient generally. Responses occurred within first 2 to 12 (median:4) weeks of therapy. All patients were treated as outpatients and drug was tolerated well. We conclude that the efficacy of colchicine in treatment of ITP can be comparable with the other therapeutic trials, moreover it has some advantages like being inexpensive, relatively nontoxic and applicable orally.

Key words: *Colchicine, Idiopathic thrombocytopenic purpura, Treatment*

The rationale for the use of colchicine in idiopathic thrombocytopenic purpura (ITP) stems from its pharmacological property, like vincristine, to bind to tubulin, the subunit protein of microtubules present in the platelet membrane and also in the mononuclear-macrophage system where the antibody-coated platelets are removed and destroyed(1).

Vinca alkaloids must be given intraveously. In addition, neurotoxicity of vincristine and myelotoxicity of vinblastine limit the usage of them in a such benign disorder. Colchicine is a low cost, oral agent which is commonly used in gouty arthritis and familial Mediterranean fever for a long-term therapy without any serious side effect(2). It have been used in only a few patient(3-6) and is still be considered as an unproved therapy.

PATIENTS AND METHODS

Colchicine was given to 18 patients with ITP (mean age:39.3, ranges: 14-75) in doses of 0.5 mg per oral three times a day for a minimum of six weeks. It was used in 6 post-splenectomic (Sc), 2 both pre- and post-Sc and 10 pre-Sc (in patients who refused surgery before other therapeutic options) periods, so efficacy of it was evaluated in 20 therapeutic cycles. The patients were followed for a minimum of six months.

RESULTS

Three of pre-Sc and one of post-Sc periods exhibited an excellent response (number of platelets rose to 150000/µl or more and remain there for at least Three months after discontinuation of treatment). Interestingly one of patients who is resistant to colchicine

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Received: March 4, 1998 Accepted: April 22, 1998

therapy prior surgery developed an excellent respose in exacerbation of post-Sc period. In six cycles, platelet count rose to 150000/μl or more but effect was transient (four cycles) or drug-depended (two cycles). In four cycles there was no effect and in other five cycles platelet count rose to 50000/μl but below 150000/μl, however, these responses was transient generally. Responses occurred within first 2 to 12 (median:4) weeks of therapy. All patients were treated as outpatients and drug was tolerated well. Patient characteristics and results are shown in table I.

DISCUSSION

ITP is a relatively common clinical problem attributable to an antiplatelet antibody, usually of the IgG class, which coats autologous platelets and leads to their phagocytosis and destruction by the mononuclear-macrophage system(1). Therapy is seldom necessary for patients with a platelet count of above 50×10^9/L and a few spontaneous bleeding episodes(7). In adults with severe ITP conventional treatment with corticostreroids and/or splenectomy gives complete response rates of 60-70%(1).

The proper management of patients with ITP who have not responded to corticosteroids and splenectomy, as do those who are considered unsuitable for these modalities (eg. those with preexisting hypertension or hyperglycemia) or who refused the surgery continues to be frequently encountered and difficult problem in the practice of hematologists(8).

Current therapeutic options for patients with refractory ITP include, cyclophosphamide or azathioprine, vinca alkaloids, high dose immunoglobulin G, anti-Rhesus globulin, colchicine, cyclosporine, recombinant interferon-α–2b, etoposide-loaded platelets, plasma perfusion over staphylococcal protein A columns, ascorbate(7), dapson(9)and combined chemotherapy(10) and Danazol(11).

Treatment strategy requires consideration of both long term benefits and long term hazards of each available therapeutic option(12). The risk of treatment particularly important because many patients with chronic ITP are young and in otherwise good health and because the course of chronic ITP is often benign(13). Many agents used in the treatment of refractory ITP have severe toxic effects or are not cost-effective. Whereas colchicine is a low cost, oral agent which, like vinca alkaloids, binds to tubulin and may disrupt the microtubule-dependent event in the mononuclear-macrophage system(1). There is only very limited experience with this agent and it is still be considered experimental therapy for chronic ITP. Melo et al.(5)obtained one complete and five partial responses in their ten cases whilst Strother et al.(6) noted three complete and one partial response among 14 adults. Marwaha's results(4) obtained in nonsplenectomised pediatric patients were comparatively better. Baker et al.(2) reported a good response in a patient who was suffered from steroid-related side effects and reluctant to splenectomy and resistant to danazol therapy.

Both vinca alkaloids and colchicine bind free tubulin dimer to block further microtubule growth(1). Consequent to this inhibition of microtubule dependent events, the macrophages are unable to destroy antibody bound platelets, which therefore remain in circulation. Similarly, the colchicine analogue 2-methoxy-5-(2'.3',+2-trimethoxyphenil)-2,4,6-cycloheptatrien-1-one (MTC) was found to inhibit coccanavalin A- and formyl-methionyl-leucyl-phenylalanine-stimulated human neutrophil degranulation(14). However, Strother et al.(6) could not find a correlation between vincristine and colchicine responsiveness. It is postulated that this may be due to variations in sensitivity of various individuals or an independent mechanism of action for colchicine. The discordant response between two drugs may also be due to the rapid clerance of vincristine given as a bolus(15). Three patients who were responsive to vincristine were also responsive to colchicine. Among the other six patients who were unresponsive to vincristine three of them were responsive to cochicine and the other three patients were unresponsive. Our results suggested the partial correlation of these two drugs. Also Baker's patient(3) exhibited similar correlation.

Synergistic effect of corticosteroids and colchicine has been reported(4-6). We observed the same synergistic effect in some of our cases but our study design was insufficent to make a certain decision about these subject.

Although Strother's report(6) suggest that the increment in platelet count will be seen within two weeks of colchicine treatment, our experience suggests that a longer therapeutic trial may be necessery in some patients.

No serious side effect was reported in all mentioned articles(3-6). Also our experience supports that colchicine is a non-toxic drug.

We conclude that the efficacy of colchicine in treatment of ITP can be comparable with the other therapeutic options, moreover it has some advantages like being inexpensive, relatively nontoxic and applicable orally.

Table 1: Patient characteristics and results

Patient no- Age and Sex	Duation of ITP before starting C	P	C*	C+P*	V	Sx	C**	C+P**	Outcome
1- 67 F	14 y	R, RDR	✱ ➹						pc was n after 3 m cessation the C
10- 35 F	13 y	R, RDR	✱ ➹						pc was n after 2 y cessation the C
14- 14 F	6 m	RDR	✱ ➹						pc was n after 18 m cessation the C
4- 36 F	5 y	R, RDR	✱ ➵						pc was normal in 24th m of the C
6- 26 F	5 y	R, θ	✱ ➴	θ	✱ ➴	✱ ➹			pc was normal in 10th m after Sx
3- 47 F	6 m	θ	❀ ➴	▽ ➵					pc was 50000 with the C+P
18- 47 F	1 y	RDR	○ ➵						pc was 70000 in 9th m with the C
11- 24 F	6 m	θ	▽ ➴	▽ ➴					pc was 30000 with the C+P COTO
9- 65 M	49 y	R, RDR	θ	θ					COTO
13- 64 F	4 m	θ	θ		θ	✱ ➹			pc was n in 3rd m after Sx
12- 14 M	7 y	R, θ	θ		θ	✱ ➴	✱ ➹		pc was n in 12th m after cessation the C
2- 24 F	2 y	R, θ	θ		θ	✱ ➹, N	✱ ➴		pc was n in 4th m of the C+ alternate day P
5- 62 F	6 y	R, RDR			θ	✱ ➹, N	✱ ➹		pc was n in 3th m after cessation the C
15- 49 F	5 y	R, RDR			θ	✱ ➴	✱ ➴		pc was 40000 COTO
8- 15 M	6 m	θ			✱ ➴	✱ ➴	✱ ➴	✱ ➵	pc was n after cessation the P and with only the C
16- 50 F	15 m	θ			▽ ➴	✱ ➴	✱ ➴	θ	COTO
17- 39 F	16 y	θ				✱ ➹ N	❀ ➴		pc was n after cessation the C and with only the P
7- 19 F	3 y	θ			θ	✱ ➴	❀ ➴		pc was 132000 in 4th m with the P

P : Prednisolone therapy
C : Colchicine therapy
V : Vincristine therapy
* : Before splenectomy
Sx : Splenectomy
** : After splenectomy
F : Female
M : Male
y : Years
m : Months
R : Recurrence after initial response
RDR : Recurrence in dose reduction
✱ : Platelet count rose to minimum 150000/mm^3
❀ : Platelet count rose to minimum 100000/mm^3 , maximum 150000/mm^3.
▽ : Platelet count rose to minimum 50000/mm3 , maximum 100000/mm^3 and at least 2 fold according to pretreatment level.
○ : Platelet count rose to minimum 50000/mm^3 , maximum 100000/mm^3 but to below from 2 fold according to pretreatment level
θ : Platelet count rose to minimum 50000/mm^3 and to below from 2 fold according to pretreatment level (unresponsivenes)
➹ : The response was sustained for minimum 3 months after cessation of the therapy
➵ : The response was sustained for only duration the therapy (drug-dependent)
➴ : Platelet count regressed to pretreatment level despite the continuous therapy
pc : Platelet count
n : in normal ranges
COTO: Candidate to other therapeutic options

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REHABILITATION OUTCOMES AFTER FLEXOR TENDON REPAIR IN THE HAND

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Şehim Kutlay* • Aysun Sezer* • Tijen Ergönen* • Süreyya Ergin*

SUMMARY

Following the repair of flexor tendons in the hand, there is difficulty in achieving satisfactory hand function.This puts out the importance of the rehabilitation program after the flexor tendon repair .

This study reports the results of the rehabilitation program which was applied to 33 patients(68 digits) after flexor tendon repair in the hand.A treatment approach that combines early controlled passive motion and early controlled mobilisation was used.Patients were evaluated regarding the total active motion(TAM), grip strength, finger dexterity and the disability in daily living activities at the 24th week.

TAM results were excellent in 21%, good in 49%, fair in 19% and poor in 11% of the repaired digits in all zones. TAM results for zone 2 injuries were excellent in 5%, good in 70%, fair in 20% and poor in 5%. Grip strength results were good in 67%. TAM and grip strength results were comparable with the previous reports. Hand disability which existed in all patients before the rehabilitation program was found to appear mildly in 76% of the patients.Finger dexterity was rated normal for 61% of the group after the therapy.

We suggest that the evaluation of finger dexterity and hand disability in daily living activities besides finger motion and grip strength, should also be taken into consideration during the rehabilitation phase with flexor tendon repair in the hand.

Key words: *Hand, flexor tendon, rehabilitation*

Hand is very important in achieving our daily living activities. The protection of the hand is difficult, thus it is probably the most injuired part of the body. As the world becomes more industrialized, industriel accidents increase and this causes a rise in the number of hand injuries (1-4). Flexor tendon injuries are common in traumatic hand disorders. Proper postoperative management following the repair of flexor tendon injuries is very important in achieving maximum function of the injuired hand. This study reports the results of the rehabilitation program which was applied to 33 patients following the surgical repair of flexor tendon injuries of the hand.

PATIENTS AND METHODS

Thirty-three patients with 68 digits who had primary or secondary repair of the flexor tendons were included in the postoperative rehabilitation program. Their ages ranged between 12 to 56 (mean: 30.7 ± 13.9). Mean time since the injury was 8.2 ± 3.1 months. 16% of the patients had zone 1, 60% had zone 2, 4% had zone 3, 12% had zone 4 and 24% had zone 5 injuries. 17 patients had also associated injuries including nerve and bone (Table 1).

All patients were operated at the Department of Hand Surgery, University of Ankara. Tendons were operated as primary or secondary repair, using the modified Kessler technique with 3.0 ethibond sutures.

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Received: March 29, 1998 Accepted: April 22, 1998

Table 1. Associated Nerve and Bone injuries

Type of injury	Number of patients
Digital nerve	: 5
Digital nerve and metacarpol fracture	: 2
Median nerve	: 4
Median nerve and metocarpal fracture	: 1
Ulnar nerve	: 1
Ulnar nerve + phalanx fracture + arthrodesis	: 1
Ulnar nerve and arthrodesis	: 1
Median + Ulnar nerve + amputation	: 1
Median nerve and Ulnar nerve	: 1

Postoperative rehabilitation program

A treatment approach that combines early controlled passive motion and early controlled mobilisation were used (5,6). A dorsal thermoplastic splint, holding the wrist in 20° - 30° flexion, metacarpophalangeal(MCP) joints in 70° flexion and interphalangeal(IP) joints in neutral extension was applied on the third postoperative day. This splint could be either dynamic (Kleinert splint) or static. If dynamic splint was used, a rubber band or elastic thread traction were also attached proximal to the wrist crease. The traction should allow the finger to attain full active interphalangeal extension within the splint limits and retain its neutral position into flexion(5,9).

During the first three weeks, passive flexion and active extension exercises for MCP,PIP and DIP joints were done within the limits of splint. Wrist was allowed to be brought to neutral position in the splint at the third week. Active finger flexion was begun at the 3rd or 4th week according to tendon gliding. Tendon gliding exercises were begun at the 4th week. The splint was worn 4 to 6 weeks. Active wrist extension was recommended at the fifth week, initially with the fingers flexed, progressing to wrist extension with the fingers extended over the next two weeks. Strength and endurance exercises were started at the 8th week (5,6,10,11).

Patients were evaluated regarding the range of motion, grip strength, finger dexterity and level of hand disability in daily living activities. The assessments were done by the same author (D.E) at the 6th, 12th and 24th weeks.

Assessment parameters

-Total active motion(TAM): The concept of TAM was introduced and recommended by the American Society for Surgery of the Hand (A.S.S.H) (11). TAM was the sum of the range of flexion at each of the three joints, minus the total extension lag. The total active range recovered in the injured digit was expressed as a percentage of the total active range of the corresponding contralateral digits. This percentage value was then graded as summarised in Table 2.

-Grip strength: American Society of Hand Therapists suggested a standardized arm positioning for the hand. While measuring grip strength, the shoulder was neutrally adducted and neutrally rotated, and the wrist was hold in 30° of dorsiflexion and in 15 ° of ulnar deviation (12,13,14). Dominant hand was measured initially . Measurements were done in both hands with a Jamar dynamometer and assumed that the dominant hand normally had a power of % 100 to % 120 of the nondominant hand. Table 3 shows the grading system (15).

-Finger dexterity: The " Nine Hole Peg test (NHPT)" was used to evaluate the finger dexterity. The NHPT consists of a square board with 9 holes and 9 pegs. Patients were ordered to put the pegs into the holes and then remove them out. The stopwatch was started by the examiner as soon as the test began and stopped when the last peg was taken out (16,17). Normally, test scores were evaluated for both right - hand

Table 2. ASSH grading of active range of motion

Excellent	100*
Good	75 - 90*
Fair	50 - 74*
Poor	<50*

* % of corresponding contralateral digit

Table 3. Grading system of Grip Strength

		DOMİNANT HAND
Good	→	Above % 80 of uninjuired hand
Bad	→	Below % 80
		NONDOMİNANT HAND
Good	→	Above % 60 of uninjuired hand
Bad	→	Below % 60

dominant and left - hand dominant patients. For right-hand dominant patients, their right-hand scores were accepted 1-2 seconds quicker than their left-hand scores. For the left-hand dominant patients, right-hand scores were accepted 1 second slower than left-hand scores.

-Hand disability in daily living activities : This was assessed by a special hand disability index which was formed by the seven items included in Stanford Health Assesment Questionnaire (19). The scores ranged between 0 and 21, 0 showing no hand disability, 21 showing severe hand disability.

TAM, Grip strength and NHPT outcomes were assessed by comparing with the uninjured hand.

RESULTS

TAM results were found to be excellent in 21 %, good in 49%, fair in 19% and poor in 11% of the repaired digits. We made the analysis of TAM evaluation separately for zone 2 injuriesth. TAM results for zone 2 injuries were rated excellent in 5%, good in 70%, fair in 20% and poor in 5% of the repaired digits.

Grip strength results were good in 67% and bad in 33% of the patient group. NHPT results were rated normal for 61% and delayed in 39% of the patients.

Before the rehabilitation program 20% of the patients had severe, 47% had moderate and 33% had mild hand disability. After the rehabilitation program 76% of the group had only mild hand disability. There was no hand disability in 24% of the patients. Hand disability scores were presented in Table 4.

During the rehabilitation program flexor tendon rupture was observed in one patient at the 2nd week.

Table 4. Results of the Hand Disability in daily living activities

	Before Rehabilitation % of patients	After Rehabilitation % of patients
Severe Disability (Score: 15-21)	20	0
Moderate Disability (Score: 8-14)	47	0
Mild Disability (Score: 1 - 7)	33	76
No Disability (Score: 0)	0	24

He was re-operated and continued the therapy. Development of adhesion in one patient caused tenolysis. Reflex sympathetic dystrophy was observed in 8 patients and they underwent medical and physical therapy.

DISCUSSION

Following the repair of flexor tendons in the hand, there is difficulty in achieving satisfactory hand functions. This functional deficit causes disability and dependency in daily living activities (2,3,4). In the past, because of immobilization, long term results of the surgical repair of the tendons were very poor. Patients failed to return their activities and because of this, some of the surgeons began early controlled motion programs. The concept of early motion was designed to minimize the formation of peritendinous scarring and to maximize tendon gliding (20, 21,22). In the early nineteenth century, passive mobilization was described and based on the studies of Duran, Houser, Strickland and Glogovac who reported normal functional return in 80 percent of the cases (8,9,21,22). Duran and Houser claimed that 3 -5 mm of tendon gliding was sufficient to minimize the development of adhesion especially in zone 2 injuries (11,23). The controlled mobilisation program including passive flexion and extension was described by Kleinert and known as Kleinert method (8,20,21,24).

In our study, a rehabilitation program that combines early controlled passive motion and early controlled mobilisation was used after the surgery. Total active motion(TAM), hand grip, finger dexterity and hand disability in daily living activities were measured in order to evaluate the success of the rehabilitation program. Dynamic splints were applied to 16 patients who could not attend the therapy sessions regularly and they made their exercises at home during the first 3 weeks postoperatively. They continued the exercise program at our unit after the third week. Static splints were applied to the other 17 patients and their exercises were done at the therapy unit by the help of the therapist.

Our data showed that TAM results including injuries in all zones, were excellent or good in 70% of the whole patient group after the rehabilitation program. The percentage of poor results were 11%. % 51 of the patients had associated injuries including nerve and the other travmatic lesions. Two papers in the literature, have reported the results of flexor tendon repair including injuries in all zones. In one of them, Edin-

burg presented excellent - good results in 61% and poor results in 19% of his cases. "Poor" rated TAM values were considerably high in his group. However 38% of his patient group had associated injuries (22,25). In the second paper So et al reported ninety-five repaired digits and rated their results as excellent - good in 76% and poor in 1%. Their poor TAM values were quite low compared with both our and Edinburg's series. However they did not have associated injuries besides tendon lesions in their patient group (25).

Most of the studies in the literature report only the results of zone 2 injuries, excluding the other zones as zone 2 is accepted as a critical zone for rehabilitation. Tendon adhesions mostly occur in this zone because of its anatomic positionth. Our zone 2 TAM values were rated 75% excellent/good and 5% poor. 42% of the patients had associated injuries. In Chow's study, excellent or good results were 82% of the patients and none was reported to be poor. Silfverskiöld reported their results as 56%. excellent, 25% good, 14% fair without any poor result but with 5% rupturesth. However in both of these studies the evaluation system was different. They used Strickland's method and they only included the digital nerve injuries as the associated injury (26,27). Karlender, using Lister's clasification method (8) rated excellent/good results in 51% and poor results in 9%. He did not have any associated injuries in his group. Small, who had rated the results of zone 2 injuries according to the TAM system that were used, reported excellent/good results in 77% and poor results in 9% of the cases (11). He also had associated injuries including phalanx fractures and nerve injuries in that group. Small's results are in concordance with our data.

It is obvious from the discussion above that there is a slight discrepancy among the reports presenting the results of range of motion after flexor tendon repair. This discrepancy might be attributed to both the employment of different evaluation systems for the motion of the fingers and associated injuries that affect the results.

Although flexor tendon repair has been an established procedure for a long time, there is no universal method for the evaluation of the results (11). Most of the current methods of evaluation consist of angular measurements of finger joints and TAM is one of the most popular angular measurement system. However the principles of the evaluation of the hand functions should not be limited with measuring range of motion(ROM). Grip strength is another important parameter indicating hand function(28). A few authors have evaluated not only the range of motion but hand grip also for the follow up of the hand rehabilitation program after flexor tendon repair. Boulas and Strickland reported grip strength results as being good in 89% of their patients(29). Our hand grip results were good in 67% of the group. Grip strength of our group seemed to be lower, compared with the former study. This might be due to the fact that grip evaluation systems used in two series were not the same.

Finger dexterity and hand disability in daily living activities should also be taken into consideration for the evaluation of functional outcome after hand injuries. However, the literature concerning traumatic hand injuries does not include these functional hand parameters. In our study, we assessed both finger dexterity and hand disability. Finger dexterity was found to be normal in 61% of the patients after the therapy. At the begining of the rehabilitation program, 20% of the patients had severe , 47% had moderate and 33% had mild disability whereas 76% had only mild disability and 24% no disability at the end of the program.

In this paper we have reported the rehabilitation outcomes after flexor tendon repair of the hand. Our results concerning the range of motion and grip strength of the hand are comparable with the previous reports. We have also presented a decrease in hand disability and an increase in finger dexterity among our patients. As the aim of the rehabilitation process is to decrease disability and to maximise hand functions, we suggest that the evaluation of hand disability and finger dexterity besides assesment of finger motion and grip strength, should also be routinely done during the follow up of these patients.

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EVALUATION OF THE PROTRUSION VALUES OF A HEALTHY POPULATION WITH HERTEL EXOPHTHALMOMETER*

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SUMMARY

The degree of eye protrusion was determined by Hertel Exophthalmometer in 258 randomly selected adults. Ages were between 20 to 84 years with a mean age of 38 years. One hundred and fifty one of the subjects were women and 107 were men. The distance from the orbital rim to the apex of cornea was measured in both eyes. The mean protrusion value for men was 16.05 ± 1.83 mm and for women was 15.42± 1.78 mm and the difference was statistically significant (p<0.05). Upper limit of normal (mean + 2 SD) was found to be 18.98 mm in women and 19.71 mm in men. No difference could be found between right and left eyes of the subjects. It was concluded that measurements higher than these values can be suspected as exophthalmos.

Key Words: *Protrusion, Exophthalmos, Hertel Exophthalmometer*

Exophthalmos is defined as the abnormally forward displacement of the eyes. The degree of protrusion of the eye is an important clinical sign in orbital disease. The upper normal limits of protrusion shows variations between different ethnic groups(1-7). The reasons for these differences in exophthalmometric values can be the variations in the bony orbital structure and globe size in different races. Since the major cause of exophthalmos in adults is Graves' Disease(1), determination of the presence of exophthalmos is very important for the clinician for the diagnosis of existing ophthalmopathy.

We conduct this study to determine the normal ranges of protrusion in a healthy adult population of both sexes.

SUBJECTS AND METHODS

We used Hertel exophthalmometer to determine the degree of protrusion in 258 randomly selected adults. Ages were between 20 and 84 years with a mean age of 38 years. There were 151 women and 107 men in the study group. None of the individuals had history of orbital, thyroid or endocrine disease, chronic obstructive lung disease, myopia (of more than-1 diopters) and none were smoking more than 5 cigarettes per day. Measurements were done by two experienced examiners, each subject evaluated independently by both of them. The distance from lateral orbital rim to the apex of cornea was measured in both eyes of each subject.

We analyzed the data with student's t-test. P values less than 0.05 were considered to be statistically significant. The ranges of normal were determined by the mean ± 2SD since these values involved the 95% of the sample population.

RESULTS

Table 1 shows the values for protrusion of eyes in subjects. The mean protrusion value for men was 16.05 ± 1.83 mm and for women was 15.42± 1.78

* Presented as Oral Presentation in 20th National Endocrinology and Metabolic Diseases Congress , İzmir, 1997

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Received: Fab 10, 1998 Accepted: April 22, 1998

mm and the difference was statistically significant($p<0.05$). The upper limit of normal (mean +2SD) was 18.98 mm for women and 19.71 mm for men. No difference could be found between the left and right eyes according to the sexes. There was also no statistically significant difference between the measurements of two examiners.

None of the subjects had more than 2 mm of asymmetry between eyes.

DISCUSSION

Exophthalmos can be quantitated with an exophthalmometer. The Hertel exophthalmometer measurement is the most accurate way in clinical use today(7), so we used this instrument for the evaluation. With Hertel exophthalmometer both eyes can be measured simultaneously from orbital rim to the apex of the cornea. The malpositioning of the foot plates and prolonged pressure against periorbital tissues while placing the instrument are the major sources of error in measurements (3). These errors can be minimized by recording on the base distance and performing the consecutive measurements on this distance and by the experience of the examiner.

Protrusion values can show variations among populations. Ethnic factors are accepted to have influence on the degree of normal orbital protrusion. Upper normal limits of 18.2-21.7 mm in white race, of 22-24.7 mm in black race and 18 mm in Japanese were reported (2-7). Concerning the great variations among different racial groups, determination of normal upper limits in a given population seems to be very important especially in the diagnosis, treatment and follow-up of ophthalmopathy in patients with Graves' Disease. Our measurements are found to be within the ranges reported for white race.

To our knowledge there were no studies performed with Hertel exophthalmometer in Turkish population. In a study of Pabuşçu et al (9), by using orbital CT, a mean value of 15.39 ± 2.79 mm and an upper limit of 20.97 mm were determined but evaluating all patients by CT for the existence of exophthalmos. Although their and ours results are not so different, in our opinion, CT examination is too expensive and time consuming. Measurement with Hertel exophthalmometer is cheap, easy and not harmful to the patient.

In the present study the mean protrusion value for men was 16.05 mm and for women was 15.42 mm. Statistically significant differences in exophthalmometric measurements in two sexes were also reported by some investigators and our results are in agreement with these (3,6).

The upper normal limit for women was 18.98 mm and for men was 19.71 mm in the present study. So if a woman has a value greater than 19 mm and a man has a value greater than 20 mm can be suspected of having exophthalmos and a search for endocrine disease or other abnormalities may be indicated.

We found a statistically significant difference in the mean protrusion values between men and women. In conclusion sexual differences in protrusion values should be kept in mind while evaluating exophthalmos. We consider the upper normal limit to be 18.98 mm in women and 19.71mm in men and suggest that measurements higher than these values can be regarded as pathologic.

Table 1. Protrusion of the eyes in the study group(values are given in millimeters).

	Female (n: 151)	Male (n:107)	p
Mean (± SD)	15.42 ± 1.78	16.05 ± 1.83	<0.05
Right eye	15.49 ± 1.79 *	16.09 ± 1.84 *	<0.05
Left eye	15.36 ± 1.79 *	16.02 ± 1.84 *	<0.05
Range(mean±2SD)	11.86 - 18.98	12.39 - 19.71	

*There were no statistically significant difference between right and left eyes of the same sex.

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SUCCESS OF SUPRACLAVICULAR LATERAL PARAVASCULAR NERVE BLOCK BASED ON SITE OF TWITCH

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SUMMARY

The supraclavicular lateral paravascular approach (SCLP) to brachial plexus anesthesia has been proposed as an effective, safe alternative to the traditional approaches to brachial plexus anesthesia. Successful regional anesthetic technique utilizing a nerve stimulator (NS) and a sheated needle requires a close proximity of the needle to the nerve.

The present study is planned to evaluate SCLP blocks performed with a NS by noting whether site of twitch location at a low milliamperage affected success rate. SCLP blocks were performed in 34 patients undergoing minor upper extremity surgical procedures requesting regional anesthesia with a NS. Twitch response in the distribution of the SCLP block was noted and maximized at the lowest mA as possible. No pain or discomfort with surgical incision was considered as successful block. With all twitches obtained at a stimulating current of 0.5 mA or less, an overall success rate of % 88 was achieved. The success rate was increased when twitch response was located distal to the elbow (%96) (forearm, hand, wrist) compared with twitches in the biceps, triceps or elbow (%66). This finding demonstrates a significant increased success rate in distal twitch response ($p<0.01$).

We concluded that if movements of only proximal muscles are observed, in order to obtain a distal twitch at the lowest mA as possible when performing a SCLP, the needle should be further advanced until movements at elbow, forearm or hand are observed.

Key Words: *Anesthetic techniques, Regional - brachial plexus (paravascular), Twitch response*

Regional anesthesia produces fewer systemic side effects than does general anesthesia and provides postoperative pain relief in patients undergoing upper extremity surgical procedures. The brachial plexus may be anesthetized at multiple sites. There are several approaches to brachial plexus anesthesia including interscalene, supraclavicular, subclavian perivascular, infraclavicular and axillary techniques (1-4). To reduce the risk of pneumothorax and enhance the likelihood of successful anesthesia, the traditional supraclavicular approach was modified by Moorthy .et al. and called as supraclavicular lateral paravascular (SCLP) approach (5). The SCLP approach to brachial plexus anesthesia was selected in this current study as this technique has been proposed as an effective, safe and alternative to the classic approaches to brachial plexus anesthesia (5,6).

Successful regional anesthetic technique utilizing a nerve stimulator (NS) and a sheated needle requires a close proximity of the needle to the nerve. The distance between the stimulating needle and the specific nerve being stimulated can be determined with twitch response and twitch location. The elicitation of twitch response in the distribution of one of the trunks of the plexus is the most commonly method to determine correct needle placement within the brachial plexus sheath (7). The location of the elicited motor response is a critical factor in determining the final quality of the block (8). Therefore, the present study was designed to evaluate supraclavicular lateral paravascular block (SLPB) performed with a NS by noting whether site of twitch location at a low milliamperage affected success rate.

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Received: May 6, 1998 Accepted: May 29, 1998

MATERIAL & METHODS

After instutional review board approval and informed constent, 34 adult patients (ASA I, II, III) were studied. Supraclavicular lateral paravascular (SCLP) block was used in patients undergoing minor upper extremity surgical procedures requesting regional anesthesia with a NS. All blocks were performed by anesthesiology residents under supervision by staff anesthesiologists. All patients were unpremedicated and positioned on a trolley in the anesthetic room. No sedation or intravenous analgesia was used.

The SCLP blocks were performed as previously described by Moorthy using a 5cm 22 or 24 gauge Teflon-coated stimulating needle (Stimuplex, B.Braun Melsungen AG, Germany) attached to a nerve stimulator (Stimuplex S; Burron Medical Inc., Bethlehem, Pa.). The nerve stimulator was set at a frequency of 2 Hz and a current of 0.2-0.5 mA. The stimulating needle is advanced to obtain motor activity. Twitch response in the distribution of the SCLP was noted and maximized at the lowest mA as possible. After the motor activity is elicited, the needle is fixed, and, after aspiration, 40 ml of local anesthetic (3mg/kg bupivacaine) is injected. No pain or discomfort with surgical incision was considered as successful block. To determine the significance (at $p<0.05$ level) X^2 test was used whether the site of twitch location affected success rate.

The modified technique (Lateral Paravascular Approach)

Patients receiving the SCLP approach were placed in the supine position with a small sheet rolled under the ipsilateral shoulder. The stimulating needle for a lateral paravascular injection is placed 2 cm superior and posterior to the clavicle, and 1 cm lateral and parallel to the third part of the subclavian artery and the first part of the axillary artery. At this level the upper and middle trunks of the brachial plexus are superior to and lateral to the artery. The needle is advanced inferiorly and laterally toward the axilla and posteriorly until the upper two trunks or their divisions are encountered, as evidenced by movement of the elbow and forearm. The local anesthetic is injected after a negative aspiration once motor activity is elicited (5).

RESULTS

Patients' characteristics and types of surgical procedures could be seen in table 1 and 2. In the group with distal twitch response, 26 of 30 patients were rated as successful and 4 of 30 failed. In the group with proximal twitch response, 4 of 6 patients were rated as successful and 2 of 6 failed. With all twitches obtained at a stimulating current of 0.5 mA or less, an overall success rate of % 88 was achieved. The success rate was increased when twitch response was located distal to the elbow (%96) (forearm, hand, wrist) compared with twitches in the biceps, triceps or elbow (%66). This finding demonstrates a significant increased success rate in distal twitch responses ($p<0.01$) (Table 2). There was no serious complications except one patient whom subclavian artery was punctured before nerve stimulation occured when performing SCLP block among the distal response group. Compression of the artery was adequate for the treatment. This patient was not withdrawn from the study but is considered as not successful.

DISCUSSION

Our overall success rate of %88 with SCLP approach demonstrate the efficacy of this technique. With the combination of a low mA and distal twitch res-

Table 1. Patient characteristics.

Age (years)	
mean	51.5
range	17-65
Weight(kg)	
mean	76.6
range	47-103
Sex	
male	21
female	13

Table 2. Operative procedures in 34 blocks.

Type of surgery	No. of patients
Carpal tunnel release	10
Excision ganglions	7
ORIF hand and finge	5
Dupuytren's contracture excision	3
Nerve decompression	4
Sinovectomy	2
Tendon suture	1
Curettage	2

Table 3. Success of SLPB based on site of twitch.

TWİTCH SİTE	SCLP SUCCESS (patients)	SCLP FAILURE (patients)	SUCCESS RATE (percent)
Distal site	2	2	% 96 *
Proximal site	4	2	% 64
Overall Succes			% 88

* Significant when compared with proximal site ($p<0.01$).

ponse, success rate of SCLP performed with a NS was %96. We believe that the success rate will be increased if it is performed by experienced anesthesiologists,.

With the availability of constant -current, low-output stimulators and insulated needles, the use of nerve stimulators for localization of nerves during regional anesthesia has increased in popularity. The use of a portable nerve stimulator increases the success of regional nerve blocks and provides a precise, safe method of identifying the brachial plexus by the SCLP route (4). Magora et al (9) established that motor stimulation with a current of 0.5mA or less indicates that the needle is close enough to the nerve for reliable block. However, using a nerve stimulator for a brachial plexus block does not guarantee correct needle placement as a needle outside of the sheath may stimulate the motor fibers through the fascia. While the needle is still outside the sheath, proximal twitch response of the musculocutaneous or radial nerve may occur from transmission of current across the sheath (5). Additionally, the needle will be farther from the nerve at the point of stimulation in case of using negative electrode (10).

Our findings suggest that the effectiveness of a brachial plexus block depends on the distribution of the evoked twitch responses. We observed that the stimulation of the middle trunk resulted in the highest incidence of success in blocking the brachial plexus completely as it represents the distal twitch response. The explanation for this higher success rate is that placement of the needle at the location of the middle trunk results in a more central deposition of the local anesthetic agent within the sheath of the plexus (11). As a result, this reduces the likelihood of the anesthetic solution being deposited outside the plexus following an inadvertent movement of the needle tip (8). When the anesthetic solution is placed in the middle of three trunks, it may diffuse more easily from this central location to anesthetize the superior and inferior trunks as well as the middle trunk.

Location of several nerves will increase the chance of entering the brachial sheath (12). In the present study, motor responses elicited by SCLP technique represent stimulation of the trunks of the brachial plexus. However, it is possible for the needle to be outside of the sheath even after successful stimulation. When a nerve stimulator is used in SCLP block, the local anesthetic solution should not be injected until a distal motor response is obtained with a small current (0.1-0.6 mA). This gives a guarantee that most of the local anesthetic is injected inside the neurovascular sheath, the quality of the block depending on the spread of the solution in the sheath (13).

Subclavian artery puncture is a potential complication of SCLP method as well as the traditional techniques of supraclavicular brachial plexus block. Arterial puncture indicates that the needle has been placed medially to the cords of the plexus. Although occasionally resulting in hematoma formation, its occurrence in one case did not cause a sequale. No other complications such as pneumothorax, Horner syndrome and phrenic or recurrent laryngeal nerve block was observed in our study.

If distal twitch response could not be seen, blockade of the medial cord is often incomplete requiring supplementation for adequate surgical anesthesia in that distribution in brachial plexus blockade (14). Therefore, it seems that distal twitch response is essential for successful brachial plexus blockade in SCLP approach. We concluded that if movements of only proximal muscles are observed when performing a SCLP block, distal twitch responses should be sought at the lowest mA as possible by advancing the needle below the clavicle level or redirecting more posteriorly until movements at elbow, forearm or hand are observed.

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JOURNAL OF ANKARA MEDICAL SCHOOL Vol 20, No 3, 1998 143-148

HEMODYNAMIC ALTERATIONS IN HYSTEROSCOPIC SURGERY DUE TO THE ABSORBTION OF IRRIGATING FLUID

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Tülay Tuncer* • Hakan Şatıroğlu**

SUMMARY

We performed this study on 15 patients to find out the degree of irrigating fluid absorbtion during hysteroscopic surgery and to determine the biochemical changes ,the alterations in hemodynamia and blood gases because of quick fluid absorbtion. Hemodynamia, blood gases and the biochemical values were studied in preoperative (as control values),peroperative and postoperative period. The mean amount of irrigating fluid used was 9763.32 ml and the amount of fluid absorbed was detected as 2853.33 ml. There was a significant increase in PCWP,CVP and PAP in the 10. min. ($p<0.05$) and in the 20., 30., 40. min. ($p<0.01$) after the surgery started compared to preoperative values. Although an increase was observed in 10.and 20. min., a significant decrease was detected in 30. and 40. min. ($p<0.01$) in Cardiac Index (CI) during the surgical procedure compared to preoperative values. In the same period, the decrease in pulmoner shunt fraction, PaO2 and O2SAT were significant. Besides, a significant decrease was observed in the levels of Hct, Na and K in 10. min. ($p<0.05$) and in 20. and 30.min. after the starting of the surgical procedure ($p<0.01$) compared to preoperative values.

As a result in patients underwent hysteroscopic surgery, there was an excessive fluid absorbtion due to the pressure of the irrigating fluid used, to the time of the surgical procedure and to the magnitude of operation area. Because of quick fluid absorbtion, the hemodynamic and biochemical alterations can create serious problems in these patients. The pressure of the irrigating fluid should be lowered to a minimum level allowing a good visualition of the operative field in patients undergoing hysteroscopic surgery and the hemodynamic and biochemical alterations should be monitorized during the surgical procedure..

Key Words: *Fluid balance :irrigation fluid absorbtion, hysterescopic surgery , gynaecological, hemodynamia, biochemical changes*

Endometrial ablation is a recently developed technique for management of menorrhagia, submucous myom, uterin septal defect (USD) or disfunctional uterin bleeding. Laser, radiofrequency electromagnetic energy, electrocoagulation or electro-rezectoskope are used for this procedure (1-4). Although patients with dysfunctional uterine bleeding account for about %20 of hysterectomies, endometrial ablation has been effective in abolishing or reducing bleeding in %70 to % 90 of such cases. Submucous myoms, endometrial adhesions, polips and USDs are treated with this procedure surgically (5-7). An irrigating solution is infused continuously into the uterin cavity to wash away operative debris, facilitate surgical visualization and maintain optimum surgical conditions in uterine cavity during the operation. Sorbitol, Glisin, %0.9 NaCl and Mannitol are used as irrigation solutions (4-10). The irrigating solutions are used with a determined pressure to allow a good visualization of the operative field during the surgical procedure. By the effect of the surgery, a large quantity of irrigation solution is absorbed through the ruptured sites of the a. and v. uterina. Related to the magnitude of surgical area, to the pressure of irrigating solution and to the operation time; hypervolemia, cardiogenic or non-cardiogenic lung oedema, dilutional hyponatremia, hyponatremic encephalopathy and tromboemboli could develop in these patients (1-5, 7-9).

The aim of our study is; in women undergoing endometrial ablation, with the use of %5 Mannitol as an irrigating solution to investigate the relationship between the operation period, the absorbed fluid and

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Received: April 27, 1998 Accepted: April 29, 1998

the complications occured by measuring the hemodynamic, blood gases and serum Na, K, Htc values during the surgical procedure.

Materials and Methods

The ethic comittee of AÜTF approved the protocol and all patients gave written informed consent. 15 patients ASA physical status I or II scheduled for endometrial ablation were studied in AÜTF Gynecology & Obstetrics Unit. All patients were premedicated with 10 mg Diazem + 0.5 Atropin i.m. 1 hour before the operation. After admisson to the operation room, iv cannulas were inserted to the patients and % 0.9 NaCl infusions were started. Provided that the collateral circulation was adequate with modified Allen test, arterial pressure monitorization was maintained with inserting a (18G) tephlon catheter into the left radial artery. After the patients were placed in appropriate position, a three lumen thermodilution catheter was introduced through internal juguler vein to the pulmoner artery under local anesthesia.

During the surgical procedure, ECG with three derivation, heart rate, systolic & mean arterial pressures, CVP and PA pressures were followed continously with Nihon Kohden monitor with two pressure channels. 5mg/kg Thiopental was used for induction of anesthesia and 0.5 mg/kg tracrium was used for muscle relaxation. After endotracheal entubation, %1.5 MAC Halothan +%50 O_2 + %50 N_2O was used for the maintenance of anesthesia.

As an irrigation solution;

%5 Mannitol was used with pressure bag by providing the Intrauterin Pressure (IUP) as 120 -130 mmHg (Figure 1). The liquid leaked through the tuba uterina to peritoneal cavity during the operation was aspirated with laparoscopy at the end of the surgery.The resultant absorbed liquid was calculated.

Cardiovasculer hemodynamic measurements, blood gases, Na, K, Hct values were studied;

- in preoperative period(as control values)
- in 5 min. after the induction of anesthesia
- in 10.,20.,30.,40. minutes after the operation.
- in 30. and 120. minutes postoperatively.

Hemodynamic measurements;

-Heart Rate (HR)

-Systolic, diastolic and mean arterial pressures

-Central Venous Pressure (CVP)

-Systolic, diastolic and mean pulmoner arterial pressures

-Pulmoner Capillary Wedge Pressure (PCWP)

-Cardiac Output (CO)

With using the parameters above, Cardiac Index (CI), Stroke Volume Index (SVI), Pulmoner Vasculer Resistance (PVR), Systemic Vasculer Resistance (SVR), Right Ventricule Stroke Volume Index (RVSVI), Left Ventricule Stroke Volume Index (LVSVI) were calculated with standard formulas.

Arterial Blood Gases;

- Arterial O_2 Pressure (PO_2)
- Arterial CO_2 Pressure (PCO_2)
- Arterial O_2 Saturation (SaO_2)

Mix Venous Blood Gases;

- Mix Venous O_2 Pressure (PvO_2)
- Mix Venous CO_2 Pressure ($PvCO_2$)
- Mix Venous O_2 Saturation ($SavO_2$)

In preoperative and postoperative period 30. and 120. min. FiO_2 was taken as 0.21 and intraoperatively as 0.5 for the measurement of pulmoner shunt fraction. Because of a possible hypervolemia or dilutional hyponatremia , patients were observed clinically in addition to the hemodynamic measurements and labarotory results intraoperatively and postoperatively. As soon as the complications were seen, the procedure was discontinued immediately and the medical therapy was started.

All the results were given as mean ± standard error in this study. "Paired - t test" was used for the evaluation of statistical analysis. Level of significance was defined as $p<0.05$ and $p<0.01$.

RESULTS

Patient charecteristics such as; age, weight, height, body surface areas and type of the surgery could be seen in table 1. Eight patients for submucous myom, two patients for Uterin Septal Defect and five patients for endometrial ablation were underwent to operation. No patients were given medical therapy except three patients with submucous myoms whom they were given Danazol therapy.

The mean amount of irrigating fluid used was 9763.32 ml and the amount of fluid absorbed was detected as 2853.33 ml .

Table 1. Demographic data

Patients (n)	15
Age (year)	38.73±5.37
Weight (kg)	66±12.76
Height (cm)	161.2+4.52
Type of surgery	
Submucous myom	8
Uterine septal defet	2
Endometrial ablation	5

Mean values ± SD

HR and MAP alterations; 5 min. after tracheal intubation, a significant increase in heart rate and MAP was observed compared to preoperative period ($p<0.05$). While there was a significant decrease in heart rate after the operation started compared to control values ($p<0.05$), a significant difference was not detected in MAP values (Fig 1) (Table2).

There was a significant increase in PCWP,CVP and PAP in the 10. min. ($p<0.05$) and in the 20., 30., 40. min.($p<0.01$) after the surgery started compared to preoperative values.While the significant increase in CVP and PCWP continued ($p<0.05$) in 30. and 120.min. during postoperative period, PAP values were similar to preoperative values (Fig 2) (Table2).

No difference was observed in CO and CI values between preoperative period and just after endotracheal entubation while an increase which was not statistically significant in CO and CI values was seen 10 min. after the surgery started. There was a significant decrease in CO and CI values in the 20. min ($p<0.05$) and in 30.and 40.min.($p<0.01$) after the surgery started compared to postoperative 30. and 120.min. values (Fig 3) (Table 2).

A significant decrease was not detected in SVR and PVR between the preoperative period and the other periods (Table 2). There were no significant differences in serum Na, K, Hct levels between preoperative period and five min. after endotracheal entubation. A significant decrease was observed in serum Na, K, Hct levels ($p<0.01$) during peroperative and postoperative period when it was compared to control measurements (Fig 4, 5) (Table 3).

In the first hour during postoperative period, two patients showed such symptoms;headache, emesis and disorientation. At that moment, their Na levels was detected 107 and 112 mEq/L respectively. Patients' Na deficits were completed in 8 hours' time with NaCl %3 solution and two of them were discharged on postoperative 3. day without sequale.

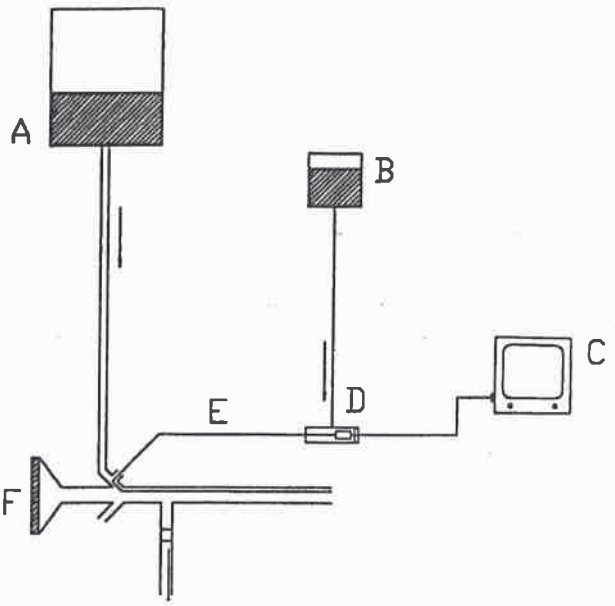

Fig. 1: İntrauterine pressure monitoring
A: Irrigation solution (%5 mannitol), pressure bağ.
B: %0.9 NaCl+2500 U heparine C: Nihon Kohden Monitor
C: Transducer E: Epidural catheter (16 G) F: Endoscope

Alterations in arterial and mixed venous gases: The statistical analysis of arterial and mix venous blood gases and the pulmoner shunt fraction were studied in preoperative period and postoperative period ($FiO_2 = 0.21$) and in the periods when patients were under general anesthesia ($FiO_2 = 0.5$). There were no significant differences in $PaCO_2$, PvO_2, $PvCO_2$ and SvO_2 values during preoperative and postoperative period. A significant decrease was observed in PaO_2 and SaO_2 values in the 40. min after the operation started compared to values in 5 min. after endotracheal entubation ($p<0.05$) (Table 3). The increase in pulmoner shunt fraction in postop 120. min. was statistically significant compared to preoperative period

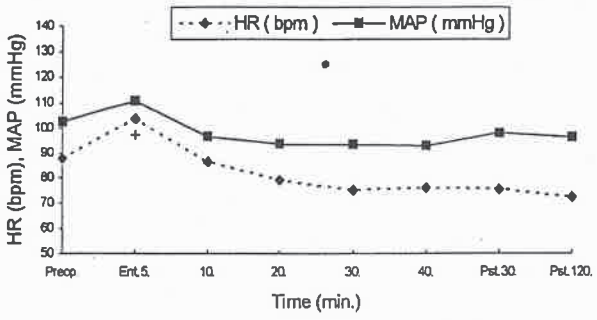

Fig. 2: Mean arterial pressure and Heart rate changes.
* $p<0.05$ the preoperative measurement.

Table 2. Hemodynamic Data

	Preop.	Ent.5 min.	10 min.	20 min.	30 min.	40 min.	Pst.30 min.	Pst.120 min.
HR (bpm)	87.93±5.5	103.6±4.34*	86.4±3.72	79.06±3.43	75.02±3.3	75.93±3.31	75.4±2.36	72.22±2.06
MAP (mmHg)	102.53±3.76	110.6±3.46	96.53±2.79	93.6±2.17	93.46±2.75	92.86±2.15	97.93±5.13	96.4±4.2
CVP (mmHg)	8.73±0.43	9.4±0.16	11.6±0.57*	14.2±0.53**	15.33±0.65**	14.46±0.74**	13.13±0.74	12.6±0.82
PCWP (mmHg)	10.86±0.58	12.4±0.87	17±0.73*	20.87±0.76**	23.87±0.95**	24.3±1.31**	20.2±1.57**	17.13±1.15*
PAP (mmHg)	16.6±1.17	18.93±1.11	23.87±1.23*	26.27±1.25**	28.2±1.26**	27.06±0.092**	23±1.82**	20.07±1.57*
CO (L/min.)	6.63±0.18	6.55±0.18	6.87±0.23	5.69±0.24*	4.93±0.15**	4.80±1.3**	5.37±0.19**	5.74±0.12**
CI (L*min.m^2)	3.94±0.13	3.88±0.11	3.97±0.13	3.34±0.12*	2.93±0.09**	2.86±0.11	3.18±0.12**	3.41±0.13**
SVI (ml*m^2)	46.74±2.8	37.97±1.2	39.48±1.9	38.18±3.36	39.76±1.8	38.74±2.2	42.18±1.91	47.31±1.79
RVSVI (g-m beat.m2)	10.5±0.98	9.75±0.48	13±1.13	14.46±1.07*	14.98±0.81*	13.62±0.65*	11.68±0.097	11.02±0.89
LVSWI (g-m beat.m2)	55.75±3.16	50.86±2.54	33.18±1.13**	34.46±1.07**	37.63±2.16**	36.24±2.36**	43.82±2.18*	49.85±1.76
PVR (dynes*s*cm^2	65.93±8.68	84.66±11.17	91.61±2.34	80.73±11.52	74.61±5.81	44.8±6.91	53.93+/-8.20	49.86±7.30
SVR (dynes*s*cm^2)	1174.65±9.91	1247.45±10.11	1241.33±8.16	1258.69±4.46	1285.36±4.31	1322.15±5.76	1262.9+/-79.5	1163.5±59.9

Values are mean (SE)
HR: Heart rate; MAP: Mean arterial pressure; CVP: Central venous pressure; PAP: Mean pulmonary artery pressure; CO: Cardiac output; CI: Cardiac index; SVI: Stroke work index; RVSWI: Right ventricular stroke work index; LVSWI: Left ventricular stroke work index; PVR: Pulmonary vascular resistance; SVR: Systemic vascular resistance
* P<0.05 versus the preoperative measurement, ** p<0.01 versus the preoperative measurement.

(p<0.05). Besides, there was a significant increase in pulmoner shunt fraction in 30. and 40. min. after the surgery started, compared to values 5 min. after endotracheal entubation (Table 3).

In one patient operated for myomectomy a lung oedema table characterized by bloody sput and widely crepitan rales in the bottom of lungs was developed 15 min. after the surgical procedure. PCWP and SaO_2 were detected 28 and 84 mmHg respectively.The patient was immediately reentubated, ventilated positif pressure and administered 40 mg Furosemid intravenously.The irrigating solution used to the patient was 12.300 ml and the absorbed fluid was 3200 ml. 1200 ml urine output was observed during the 1. hour of the treatment. As soon as the symptoms of lung oedema disappeared the patient was extubated and transferred to ICU. She was discharged without sequale three days later.

DISCUSSION

Endoscopic intrauterin surgery is a new technique used for the treatment of submucous myom, USD, polip, endometrial adhesion and disfunctional bleeding. The irrigating solution is used with a constant pressure to enlarge uterin cavity, maintain visibility and wash away operative excessive tissue (1 - 3,5,7). The most important complication of Endometrial Laser Ablation (ELA) and transservical resection is the absorbtion of

Table 3. Laboratory data

	Preop.	Ent.5 min.	10 min.	20 min.	30 min.	40 min.	Pst.30 min.	Pst.120 min.
Na (mEq/L)	142.16±0.82	141.63±0.94	136.52±0.91	131.47±1.1*	128.09±1.3**	122.56±1.79**	128.62±1.45**	131.74±0.87
K (mEq/L)	3.87±0.12	3.80±0.02	3.34±0.14*	3.32±0.13**	3.18±0.12**	3.16±0.12**	3.27±0.22**	3.35±0.11*
Hct. (%)	40.05±0.85	39.35±0.95	35.38±1.07**	32.09±1.29**	30.36±1.11**	30.13±1.11**	32.43±0.86**	34.18±0.81**
PaO_2mmHg	86.22.3	169.2±7.11	172.26±9.82	172.6±10.8	161.6±8.8	143.53±11.5	90.6±4.8	91.6±1.65
$PaCO_2$mml lg	37.0±0.8	35.2±1.38	33.8±1.57	36±1.33	36.46±1.04	40.2±1.58	41.6±0.81	41.73±0.89
SaO_2 (%)	94.33±2.2	99.13±0.27	99.2±0.2	98.2±0.64	98.3±0.52	97.6±0.51#	93.86±0.84	94.7±0.59
PvO_2mmHg	50.4±2.2	52.4±1.67	54.06±1.92	52.6±1.49	52.26±1.78	53.8±3.08	46.6±1.77	47.53±1.56
$PvCO_2$mmHg	36.81±1.52	37.81±1.5	36.75±1.52	37.31±1.84	36.89±1.46	40.61±2.49	40.05±1.59	41.37±1.34
SvO_2(%)	77.4±1.2	81.13±1.24	81.13±1.43	79.8±0.81	79.73±1.3	78.13±1.1	73.8±1.23	74.53±1.19
Qs/Qt (shunt)%	11.77±2.9	8.26±1.54	8.56±1.7	12.09±3.24	13.46±2.78	13.25±2.55#	18.11±2.8##	12.85±1.9

Values are mean (SE)
Hct=Hematocrit, PaO_2=Arterial oxygen pressure, $PaCO_2$=Arterial carbon dioxide pressure, SaO_2=Arterial oxygen saturation, PvO_2=Mix venous oxygen pressure, PvCO2=Mix venous carbon dioxide pressure, SvO_2=Mix venous oxygen saturation, Qs/Qt=Right - to - left shunt
* p<0.05 versus the preoperative measurement. ** p<0.01 versus the preoperative measurement.
# p<0.05 versus (FiO_2 = 0.50). ## p<0.01 versus the preoperative measurement (FiO_2=0.21)

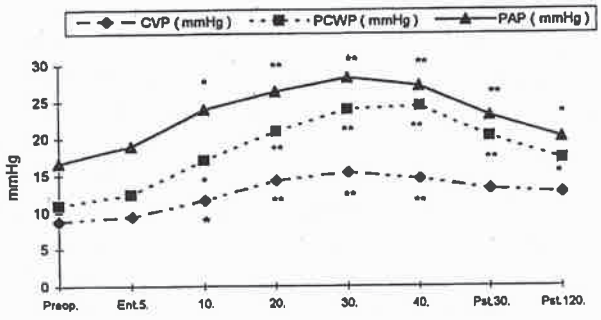

Fig. 3: Central venous pressure (CVP), Mean pulmonary artery pressure (PAP) and Pulmonary capillary wedge pressure (PCWP)
* p<0.05 versus the preoperative measurement,
** p<0.01 versus the preoperative measurement

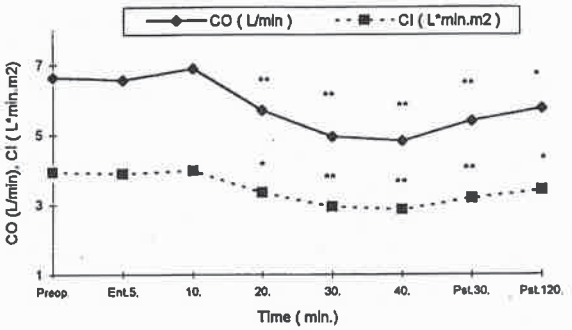

Fig. 4: Cardiac output (CO) and Cardiac Indekx (CI)
* p<0.05 versus the preoperative measurement,
** p<0.01 versus the preoperative measurement

irrigating solution into systemic circulation. Due to the excessive fluid, pulmoner edema, metabolic abnormalities, even death may occur(2-4,11-14). %1.5 Glisin, Sorbitol, Hyscon (70 Dextran), %0.9 NaCl and %5 Mannitol are used as irrigating solutions. Specific complications may develop related to the type of the irrigating solution used. Hyscon; an irrigating solution with a high moleculer weight is used widely in hysterescopic surgery (11,14). With the use of a large quantity of hyskon solution, complications such as; ARDS, pulmoner oedema, coagulopathy and anaphylactic reactions could be seen. The incidence of anaphylaxy was reported as 1/10.000 (2,14). With the use of % 1.5 Glisin solution, the most observed complications are dilutional hyponatremia, ammonia encephalopathy and pulmoner oedema.

The opened veins in the operation field and the leakege of fluid to peritoneal cavity via tuba uterina are the main reasons of fluid absorbtion during hysterescopic surgery (1 - 3, 5). The uterin wall is thick and the leimyoms are uncapsuled in fertile women.The pressure of irrigating solution used is higher than the normal pressure in veins.In addition to this; in fertile woman during menstruel cyclus endometrium is enlarged in the phase of proliferation and secretion and vascularization is increased.

Different kind of methods were studied to minimize the fluid absorbtion during hysteroscopic surgery such as; hyperdilatation of the cervix, decrease the level of the irrigation fluid bottle, use high density fluids. However, none of them was found to be successful (5). When the high density fluids were used, the absorbed high density fluid drew much more liquid into intravasculer compartment (2,3,5,11). It was pointed out that in patients undergoing hysteroscopic surgery, the vascularization of the endometrial tissue could be decreased by the use GnRH agonists. In our study, there was only three patients given antiestrogen therapy in preoperative period.

F.Hasham et al. (5) reported that the absorbtion of irrigating fluid might be decreased by lowering the IUP to a minumum level allowing a good surgical visualization. Investigators found out that the fluid absorbtion was minimum in patients undergoing hyste-

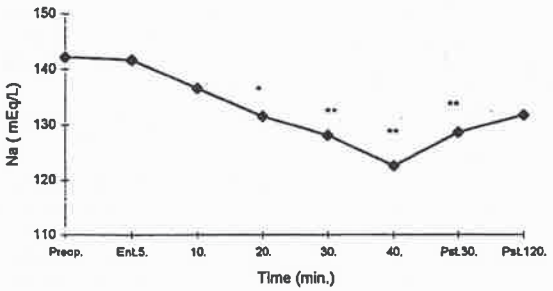

Fig. 5: Serum sodium (Na+) levels
* p<0.05 versus the preoperative measurement,
** p<0.01 versus the preoperative measurement

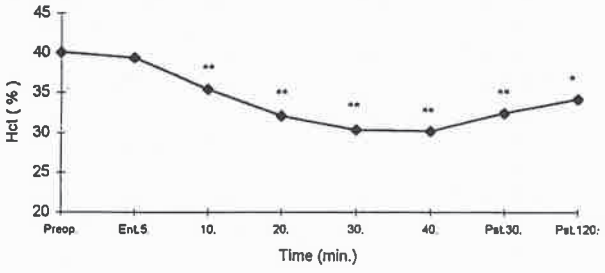

Fig. 6: Hematocrit (Hct %)
* p<0.05 versus the preoperative measurement,
** p<0.01 versus the preoperative measurement

roscopy when IUP was maintained with a pressure of 70 mmHg, but when the pressure was increased to 136mmHg, a mean of 1830 ml fluid absorbtion was detected.

In our study %5 Mannitol was used as irrigation solution.%5 Mannitol is an isotonic solution and is not metabolized in the body and doesn't cause hypoosmalarity (8). The IUP was maintained between 150 - 180 mmHg during the surgical procedure.The resultant of irrigation of endometrium with high pressure fluid is the absorbtion of fluid into intravasculer compartment.At the same time the leakege of fluid to peritoneal cavity via tuba uterina passes to systemic circulation. As a result of this, acute increase in intravasculer fluid occurs. The increase in volume causes hemodilution. Hyponatremia, hypopotasemia,decrease in Htc and hypoproteinemia occur as a result of hemodilution. Another result of acute hypervolemia is the disappearence of sympathic tonus and decrease in myocardial contractions (15). Myocardial contractions decrease due to anesthetic agents used during surgical procedure. Bradycardy occurs because of acute hiponatremia. Sympathic tonus disappears because of acute hypervolemia. Capillary vasodilatation occurs as a result of the direct toxic effects of mannitol. The common results of these factors above cause a decrease in CO and CI (1,15).

Another important effect of acute hypervolemia is an increase in end diastolic volume and pressure (15). As a result of this CVP, PAP and PCWP increase. Although the difference was not significant, there was an increase in CO in our cases parallel to the increase in CVP, PAP and PCWP in 10. and 20. min after the surgery started compared to control values. A decrease in CO in 30. and 40. min after the surgery started was observed. Pulmoner oedema occurs because of the decrease in CO, the direct toxic effects of the irrigation solution to pulmoner vascular system and the decrease in plasma oncotic pressure (4,11). A decrease was observed in PaO_2 and SaO_2 values because of pulmoner oedema. The decrease in SaO_2 in 20. min after the operation started was significant in our cases. Besides there was an increase in pulmoner shunt fraction at the same period.

Although our study was held in ASA I and II group patients who had no cardiac pathology, an lung oedema was seen in one patient. There is an excessive fluid absorbtion in patients undergoing hysterescopic surgery due to the pressure of irrigating solution used, to the time of procedure and to the magnitude of surgical field.

Haemodynamic and biochemical alterations occur according to the quantity of the fluid absorbed and cause serious problems. We believe that it is vital to follow the hemodynamic measurements especially in patients with cardiac pathology if they are going to be operated with hysteroscopic procedure.

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SIGNIFICANCE OF SERUM FSH LEVELS AND TESTICULAR MORPHOLOGY IN INFERTILE MALES

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SUMMARY

Objectives: *To determine the relationship between plasma levels of FSH with testicular spermatogenic pattern.*

Methods: Testicular biopsies were obtained from 99 infertile men. Biopsies were performed either in order to distinguish type of azoospermia (obstructive/non-obstructive) or because of severely subnormal semen variables. Serum FSH was measured by immunoassay (normal range is less than 7 mIU/ml).

Results: *Statistical significance were detected among patients with sertoli cell only syndrome and normal spermatogenesis, hypospermatogenesis and maturation arrest ($p<0.01$, $p<0.01$, $p<0.05$ respectively). We did not observe statistical significance with regard to normal spermatogenesis and both with hypospermatogenesis and maturation arrest.*

Conclusion: *Our study revealed that elevation of serum FSH correlates with only the appearance of sertoli cell only syndrome. We think that, azoospermic or severely oligoasthenoteratozoospermic patients with highly elevated plasma FSH levels (three times normal) could be protected from separate testicular biopsy. The reason is, since these patients are not suitable for conventional treatments if they are willing to undergo an IVF program sperm will often be present, no matter what the testicular histology, to use for assisted reproductive techniques particularly ICSI.*

Key Words: *Testicular morphology, FSH, Infertility*

Testicular biopsy is a common procedure for the investigation of male infertility. The demonstration of the relationship between serum FSH levels and the histological appearance of biopsy specimens forced a reappraisal of the value of testicular biopsy (1). Some of the authors recommend testicular biopsy only for the cases where serum FSH levels and clinical evaluation are inconclusive (2) and the others recommended biopsy either in patients with FSH value less than three times the normal value (3), or some used a cutoff value of two times normal FSH levels (4). However recent improvements in newer assisted reproductive techniques particularly intracytoplasmic sperm injection (ICSI) have provided new impetus for testicular biopsy.

In order to further characterize the diagnostic significance of FSH in male infertility we re-examined the correlations between serum FSH levels and testicular morphology.

PATIENTS AND METHODS

Testicular tissue was obtained from men (age 20-42 years) attended to our infertility clinic. The patients were subjected to a thorough clinical investigation, including at least two semen analyses according to WHO guidelines (5). Serum levels of FSH were measured by immunoassay. Serum levels of more than 7 mIU/ml were regarded as elevated. Biopsies were performed either in patients with azoospermia in order to distinguish between obstructive and non-obstructive azoospermia or in patients with severely subnormal semen variables when history, clinical examination and hormone levels failed to explain infertility. Bilateral testicular biopsies were performed under local anesthesia and fixed for pathological examination as previously described (6) . Spermatogenesis was assessed as previously described (6). With regard to histopathological determinations four groups were identifi-

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Received: March 18, 1998 Accepted: June 24, 1998

ed: Normal spermatogenesis; hypospermatogenesis; maturation arrest and Sertoli Cell Only syndrome.

Statistical Analysis: The variable FSH was logarithmically transformed before analysis to achieve normal distribution. One-way analysis of variance was applied for testing differences between means. When overall F-test was significant, pairwise differences between group means were tested by a posteriori Duncan multiple comparison test for unequal sample size at a controlled significance level of a=0.05 and a=0.01.

RESULTS

The mean plasma FSH levels of four groups of patients were shown both in table and figure 1. Serum FSH levels were statistically significantly higher with sertoli cell only group and other three groups (normal, hypospermatogenesis, maturation arrest; p values: <0.01, <0.01 and <0.05 respectively). Although mean serum FSH levels were slightly elevated at two testicular pathology (hypospermatogenesis and maturation arrest) compared to normals, we did not observe any statistical significance.

DISCUSSION

Since the development of gonadotrophin RIAs in the 1970's it is generally accepted that measurement of serum FSH is of great value in assessing the state of the seminiferous epithelium in the infertile male (7). In azoospermic or severely oligospermic men with normal-sized testes, a normal level of FSH may indicate the presence of posttesticular obstruction of the excretory duct system. In men with azoospermia due to severely damaged germ cells, serum FSH levels are usually but not invariably elevated (8). It has been widely accepted that patients with persistent elevation of FSH concentrations (especially higher than three times normal) are considered to suffer from severe and irreversible testicular damage. Therefore diagnostic testicular biopsy has been regarded classically as unnecessary in such patients because they were not suitable for any form of conventional treatment (3). However with the advent of newer assisted reproductive techniques, particularly ICSI (9,10) and potentially round spermatid nuclear injection (ROSNI) (11) represent a notable beacon of hope for many patients previously considered beyond help. With the considerably higher fertilization and implantation rates being reported with ICSI and microepididymal sperm aspiration (MESA) or percutaneous epididymal sperm aspiration (PESA) the prospects for successful treatment in obstructive azoospermia have been considerably enhanced (12). Although persistent elevation of FSH concentration in the presence of azoospermia is synonymous with extensive and severe primary spermatogenetic failure, a minority of seminiferous tubules may still retain some degree of germ cell development so that can be called focal spermatogenesis (9,13,14). On the other hand, recently Gilbaugh, Martin-du-Pan and Wu emphasized the indirect nature of serum FSH as a marker of seminiferous tubular failure with distinct limitations (15,16,17). It has been reported that nearly half (48%) of a group of azoospermic patients with FSH elevated to three times that of the upper limit of normal has mature spermatozoa at testicular biopsy (15). Furthermore, the establishment of a pregnancy to 27 weeks gestation using testicular sperm from a patient with a FSH of 38.7 mIU/ml (normal range,1-12 mIU/ml) and bilaterally small testes has also been demonstrated (18). This particular patients biopsy showed a predominantly sertoli cell only pattern with less than 10% having hypospermatogenesis. Lastly, mature sperm in the testicular biopsy of 30% of men with azoospermia and significantly elevated serum FSH level (3 or more times normal) were reported by Kim et al (19).

Our results indicate that FSH plasma levels are of no diagnostic value in predicting any specific spermatogenic pattern except sertoli cell only syndrome which was the only pathology that we observed statistical significance with regard to normal spermatogenesis. Although with regard to our data and Bergman's (20) it could be speculated that plasma FSH levels can be used for diagnosing sertoli cell only syndrome (three times normal FSH values) we must not ignore that the minimal ingredients for successful fertilization with ICSI require only one haploid sperm DNA and the sperm centrosome (21). We think that, there are currently two indications for performing a testicular biopsy in an infertile man. The first is to differentiate testicular failure from obstruction in an azoospermic individual. The result of this and many previous studies, have already established that elevated serum FSH excludes the presence of repairable obstruction in these patients and therefore could be used as a selection criterion. The second reason to perform a testicular biopsy is to establish the presence of testicular sperm for use during assisted reproductive techniques in a patient with testicular failure. However FSH is not predic-

Table 1: FSH serum values in the four groups of patients.

	X	SD	n	p
Normal	6.84	2.46	26	<0.01
Hypospermatogenesis	9.06	6.60	39	<0.01
Maturation Arrest	9.69	4.74	19	<0.05
Sertoli Cell Only	17.09	12.57	21	

p values indicate differences between Sertoli Cell Only and other three groups.

tive of the presence of small numbers of sperm in the testis, since even man with sertoli cell only often have enough sperm present for ICSI (15,19). Therefore, testicular biopsy is not needed in these patients except as an adjunct to testicular sperm retrieval (TESE).

Our new approach to azoospermic or severely oligoasthenoteratozoospermic patients with highly elevated plasma FSH levels (three times normal) is, to ask to the patient if he and his wife is willing to undergo an in vitro fertilization (IVF) program. If the answer is no, than we do not see any reason to perform a testicular biopsy. On the other hand even if they are willing to undergo an IVF, a separate diagnostic biopsy would be again unnecessary since sperm are often present no matter what the testicular histology hence biopsy itself might cause adverse effects which may limit future success.

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THE NERVE DISTRIBUTION FOR ANKLE AND FOOT BLOCK ANESTHESIA*

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Güliz Tutar*** • Hakan E. Çubuk* • Alaittin Elhan*

SUMMARY

Foot surgery under ankle and forefoot block is gaining popularity as the benefits of regional anesthesia becomes more obvious. For a sufficient anesthesia of the foot, superficial and deep peroneal, sural, saphenous and tibial- nerves should be blocked. In this study these nerves mentioned above are dissected in the lower extremities of 20 formalin embelmed cadavers and 5 freshly amputated specimens and their anatomical distributions are studied. Landmarks which may help for locating these nerves are described. Although superficial peroneal, sural and saphenous nerves are subcutaneous and can be blocked with a skin wheal, others, tibial- and deep peroneal, are beneath fascial layers and precise knowledge of their anatomy is required for a successful block.

Key Words: *Block anesthesia, Foot and ankle, Nerve distribution*

Ankle block anesthesia is gaining popularity among the foot surgeons. The advantages of this technique are as follows (1,2,3):

1. Adverse effects of general anesthesia may be prevented,
2. It is more suitable for outpatient surgery,
3. Applied doses of local anesthetics cause little or no systemic toxicity,
4. Maybe time time saving for busy operating theaters.

Many foot surgery procedures can be performed with ankle block anesthesia especially using a mixture of short and long-acting local anesthetic agents(4):

1. Open reduction and internal fixation of tarsometatarsal, midtarsal and talocalcaneal injuries,
2. Decompression of the tarsal tunnel,
3. Osteotomies and arthrodesis distal to the malleoli,
4. All the soft tissue procedures about the foot,
5. Debridement of the infections of the foot.

Precise knowledge of topographic anatomical distribution of nerves as well as modifications around the ankle and foot is mandatory for a successful block. The aim of this study is to present the superficial and deep nerve distribution to ankle and foot.

MATERIALS AND METHOD

The nerves which should be infiltrated for an ankle block are presented depending on dissections of 20 adult formalin embelmed cadavers and 5 freshly amputated specimens performed at Ankara University Faculty of Medicine, Department of Anatomy. Twenty-four hours before dissections about 50 ml of latex solution (BE-KAT-SAN Ltd., Istanbul, Turkey) mixed with red Indian ink, was injected under manual pressure into the arteria femoralis of the formalin embelmed cadavers and to the main arteries of the freshly amputated specimens (5). This provided an excellent detail of the small arteries of the extremities. All the nerves were dissected around the ankle. Their locations, accompanying structures and variations were noted in detail.

* This study was presented as a poster presentation in the '4. European Clinical Anatomy Congress' in Lille (September 1997)

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Received: Dec 29, 1998 Accepted: June 24, 1998

Findings

Superficial peroneal nerve A branch of the common peroneal nerve, descending the leg between extensor digitorum longus and peroneal muscles, pierces the fascia and becomes superficial at about the lower third of the leg. It divides into terminal branches above the ankle. Two main terminals are named as medial and intermediate dorsal cutaneous nerves ; which the former supplies sensation to the medial side of the hallux and the second and third dorsal web spaces and the latter to third and fourth dorsal web spaces (occasionally to fifth web space) (6,7). It is best to palpate the tip of the lateral malleolus and proceed proximally 8 to 10 cm. anterior to the subcutaneous border of the shaft of the fibula to block the superficial peroneal nerve (Fig. 1). In about one fourth of the cases the median and dorsal cutaneous brances arose independently from the superficial peroneal nerve a few centimeters proximal then the described above, that is name type A. The medial dorsal cutaneous dorsal nerve travels nearly the same in each type.

Intermediate dorsal cutaneous branch travels somewhat different in other types B and C (8).

Deep peroneal nerve Other branch of the common peroneal nerve, travels lateral to anterior tibial artery, and lies between the tendons of the tibialis anterior and the extensor digitorum longus. The anterior tibial artery can usually be palpated beneath the superior extensor retinaculum 4 to 5 cm. proximal to the joint line. If the artery is not palpable, then the lateral border of the tibialis anterior may serve as a landmark (Fig 1).

The nerve is just beneath the tendon and lies about 1 to 1.5 cm. deep to the skin. After the nerve passes beneath the extensor retinaculum, it accompanies the dorsalis pedis artery as it reaches the first intermetatarsal space. It may also be possible to block the nerve at this level, by palpating and avoiding the artery.(Fig. 2)

Sural nerve one of the branches of the tibial nerve may be reached at about 5 cm. proximal to the tip of the lateral malleolus, in between the peroneus longus tendon and the lateral border of the tendon calcaneus (Fig 1).

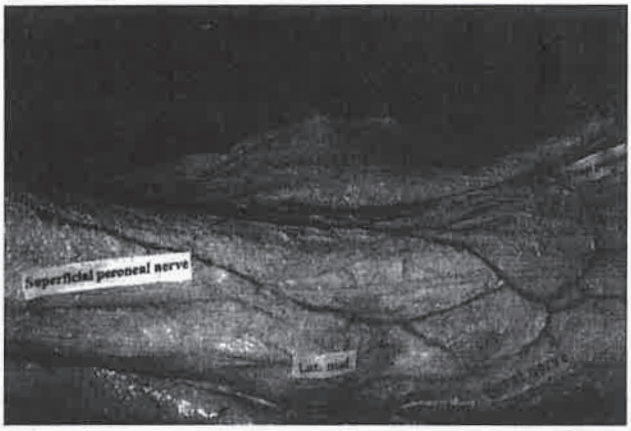

Fig. 1: The superficial peroneal, deep peroneal and sural nerves can be seen after removing the skin. At the same time the dorsal venous arcus of the foot is observed.

Saphenous nerve is the largest sensory branch of the femoral nerve, deriving its fibers from L3 and L4. This nerve supplies the skin over the medial side of the leg and ankle and skin over dorsomedial aspect of hindfoot and midfoot. It courses anterior to the medial malleolus. It may be blocked by palpating the tip of the medial malleolus and 3 to 5 cm. proximal to this landmark (Fig 2).

Tibial nerve is the largest division of the sciatic nerve. It supplies sensation to the skin of the heel and the medial side of the sole of the foot, as well as many

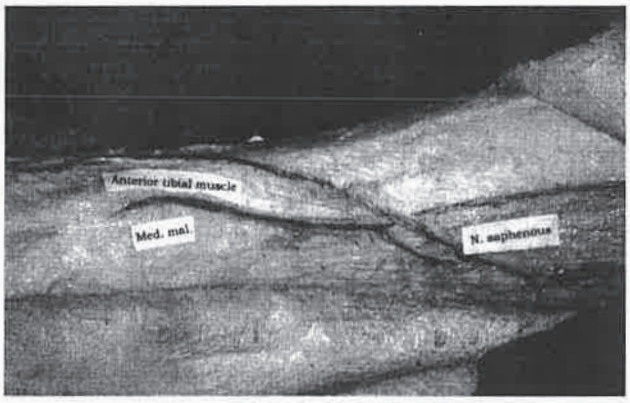

Fig. 2: The saphenous nerve coursing anterior to the media malleolus.

Fig. 3: Tibial nerve accompanying with the posterior tibial artery coursing posterior to the medial malleollus and under the aschill tendon.

muscular branches. It travels just posterior to the arteria tibialis posterior which can be palpated beneath the medial malleolus. To block the nerve one should palpate the artery in the most distal part around the medial malleolus (Fig 3).

DISCUSSION

Principles of nerve block anesthesia has been studied during the last century. Advances in drugs, new equipment for applications and anatomical studies of the peripheric nerves has increased effectiveness of the techniques.

Preservation of consciousness of the patient during the procedure may be an advantage of the regional block but an uncooperative patient or a patient who is not well prepared during the preoperative period may not want to live the anxiety of the operation. This may necessitate the support of the regional block with a mild general anesthesia or sedation.

Post operative analgesia provided by block anesthesia is another advantage. Successful application of the regional blocks requires precise knowledge of the anatomy of the peripheral nerves. Careful technique with slow injection and frequent aspirations prevent the possible complications of drug toxicity which may be caused by overdose or intravascular injections. Although test dose had been advocated as a precaution, slow injection is the easiest way to prevent it. Hypotension, sympathetic block and vasovagal reflex are among the other important complications reported. Trauma to the nerves by intraneural injection or neuritis caused by chemical or bacterial contamination of the drugs may end up with permanent disability and can only be prevented by strict attention to the details.

Mussurakis studied combined superficial peroneal and saphenous nerve block for ascending venography and recommended for all patients who are apprehensive or have already experienced pain on a first unsuccessful venipuncture attempt (9).

Elucidation of the anatomic course and variations of the nerves assist nerve protection during operative procedures as well as to help nerve localization for exploration (6-10). The location of the superficial peroneal nerve is especially important ; during fasciotomies and the fasciocutaneous flaps (11,12). Adkison et al (13). studied 85 cadavera legs to determine the course of the superficial peroneal nerve and reported that about 73 % of the cases the nerve coursed within the lateral compartment, in 14 % the nerve passed through the crural fascia from the anterior muscle compartment, in 12 % the nerve divided into two, with each one coursed in lateral and anterior compartments respectively.

Blair and Botte studied the superficial peroneal nerve under loupe magnification in 25 cadaver lower limbs. Their observation was three distinct patterns. Although there are some more variations reported in the literature, it is possible to block this superficial (subcutaneous) nerve as with olthers, the suralis and saphenous by a skin wheal, beginning about 9-11 cm. proximal to the tip of the lateral malleolus.

The deep peroneal nerve may be reached by palpating the anterior tibial artery beneath the superior extensor retinaculum 4 to 6 cm. from the ankle joint line. This neurovascular bundle lies between the etndons of tibialis anterior and extensor digitorum longus. When the artery is not palpable the tibialis anterior tendon can serve as a landmark. One may enter the skin lateral to the tendon to a 1-1.5 cm. deep to the skin.

The tibial nerve is the most important nerve to block for an adequate surgical anesthesia. About 5-6 cm. from the distal tip of the medial malleolus; the distance between the medial border of the calcaneal tendon and the posteromedial border of the tibia it is possible to palpate the posterior tibial artery. The nerve lies just posterior to the artery.

Although block anesthesia techniques have advantages, it is mandatory to have a thorough knowledge of not only the "normal anatomy" but the possible variations as well for a successfull and safe block and surgery.

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DILATED CARDIOMYOPATHY WITH FAMILIAL HYPERCHOLESTEROLEMIA IN A SIX-YEAR-OLD BOY*

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SUMMARY

Familial hypercholesterolemia, especially homozygous type is one of the risk factors of coronary atherosclerosis. Atherosclerosis-related diseases are the leading causes of death in the world. In this report, we presented a six-year-old boy with familial hypercholesterolemia and dilated cardiomyopathy secondary to coronary atherosclerosis. The family history revealed consanguinity between the parents. His parents and brother were also hypercholesterolemic. Two of his uncles had died from early myocardial diseases. Unfortunately, the patient died because of late diagnosis.The therapy of homozygous familial hypercholesterolemia should start as early as possible, before symptoms appear. Therefore, pediatrician should identify primary hyperlipidemia in childhood.

Key words: *atherosclerosis, dilated cardiomyopathy, familial hypercholesterolemia*

Familial hypercholesterolemia (FH), an autosomal dominant inherited disease due to deficiency or absence of cell receptors for low density lipoprotein (LDL) is well known (1). The frequencies in white population vary from 1:106 to 1:500 (2). Patients with FH are known to have increased risk of coronary heart disease as compared to normolipemic subjects (1-3). In this paper, we report the case of a six-year-old patient with homozygous FH who has developed dilated cardiomyopathy presumably due to coronary atherosclerosis.

CASE REPORT

A six-year-old boy was admitted to our hospital because of abdominal pain, fatique, palpitation and dyspnea. He had xanthoma on bilateral Achilles tendons when he was two years old, and other xanthomas developed on the hands, elbows, knees, gluteal and popliteal regions with age. His parents were first degree cousins. They and his brother were hypercholesterolemic too. Two of his uncles had died from early myocardial infarction.

On admission the patient was dyspneic and tachypneic. The blood pressure was 85/55 mmHg and heart rate was 156/min. His height and weight were below the third percentile for this age. He had cutaneous xanthomas on bilateral hands, knees, elbows, buttocks and popliteal regions and tendon xanthomas on Achilles tendons (Fig. 1A,B). The precordium was hyperactive. There was a gallop rhythm and 2/6 pansystolic murmur at the lower left sternal border and apex. The liver edge was 3 cm below the right costal margin.

Laboratory studies revealed the following values: Hemoglobin was 9 g/dl, hematocrit was 30% and white blood cell count was 7500/mm^3. The liver and renal function tests were normal. The patient's serum total cholesterol level was 673 mg/dl. The results of the lipid electrophoresis of the patient and the other mem-

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Received: Oct 30, 1997 Accepted: April 22, 1998

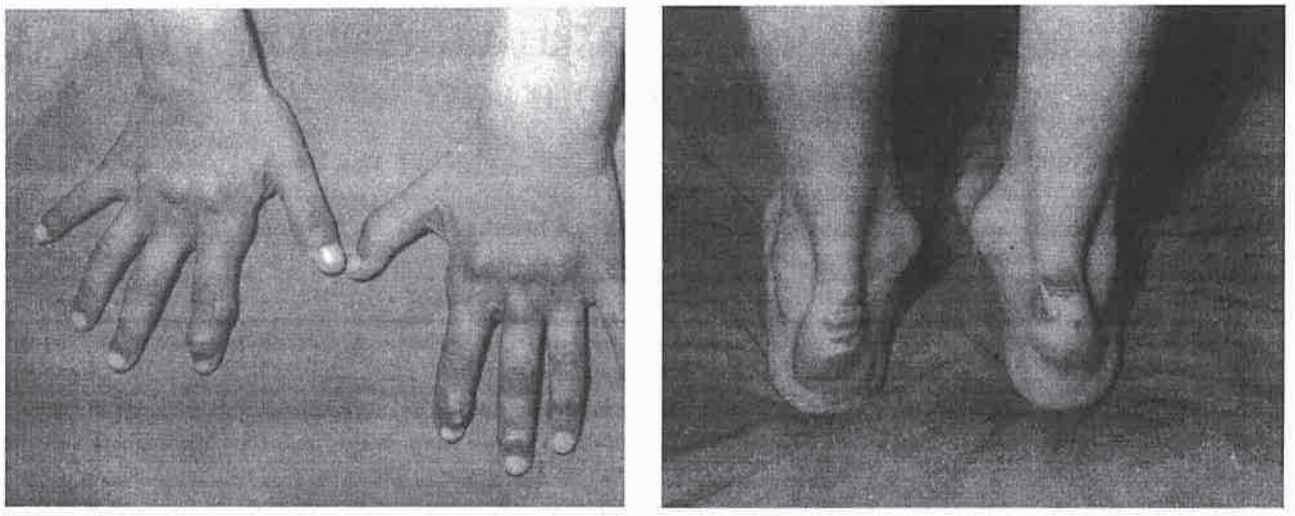

Fig. 1: Cutaneous xanthomas on the hands (A) and tendon xanthomas on Achilles tendons (B) are seen.

bers of his family are listed in Table 1. The electrocardiography showed sinus rhythm and left ventricular hypertrophy with ST-T wave abnormalities in V5 and V6. Chest radiography revealed cardiomegaly. On two dimensional echocardiography; left ventricular end-diastolic dimension was 42.6 mm (normal range for this age: 24 - 38 mm), and left ventricular end-systolic dimension was 38.7 mm. The ejection fraction and shortening fraction were decreased to 28% and 13% respectively.

The distance between the E point of anterior mitral leaflet and interventricular septum was reduced (Fig. 2).

Doppler echocardiography revealed moderate mitral regurgitation. These findings were confirmed by cardiac catheterization and angiocardiography. The left ventricular wall motions were decreased. Left ventricular angiogram demonstrated a third degree mitral regurgitation. Left coronary angiography revealed 85 percent occlusion of proximal one-third of the

Table 1. Values of Triglyceride and Cholesterol (mg/dl)

	Age	Triglyceride	Total Cholesterol	LDL Cholesterol	HDL Cholesterol
Patient	6	91	673	883	400
Mother	26	94	355	696	320
Father	30	136	573	756	210
Brother	5	195	228	ND*	ND*
Sister	8	78	167	ND*	ND*

Reference values(1,10):

Triglyceride :	5-9 yr male :	28-85 mg/dl
	Adult male :	40-160 mg/dl
	Adult female :	35-135 mg/dl
Total cholesterol :	5-9 yr male :	125-189 mg/dl
	25-34 yr male :	133-524 mg/dl
	25-34 yr female :	128-230 mg/dl
LDL cholesterol :	5-9 yr male :	63/129 mg/dl
	25-34 yr male :	70-185 mg/dl
	25-34 yr female :	71-136 mg/dl
HDL cholesterol :	5-9 yr male :	38-74 mg/dl
	25-34 yr male :	31-63 mg/dl
	25-34yr female :	36-77 mg/dl

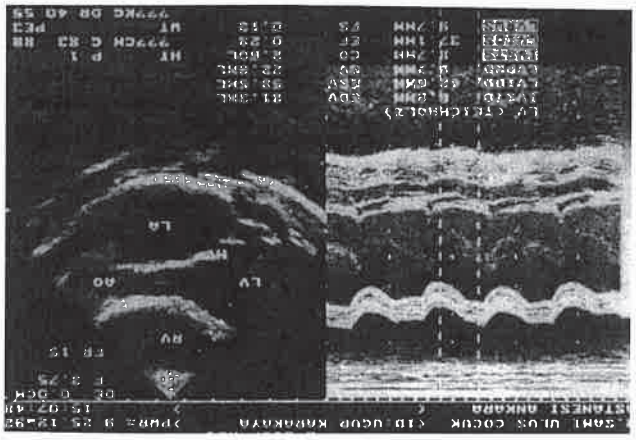

Fig. 2: M-mode and two dimensional echocardiographic view of the patient in parasternal long axis position showing markedly dilated left ventricle. AO:Aorta, LA:Left atrium, LV:Left ventricle, MV:Mitral valve, RV:Right ventricle.

circumflex artery. There were 80 percent and 70 percent narrowing of left anterior descending artery before first septal branch and proximal region of first diagonal branch, respectively. The catheter could not be entered to the ostium of right coronary artery. On the aortic root injection the right coronary artery was not opacified.

Homozygous FH with dilated cardiomyopathy due to coronary atherosclerosis was diagnosed. Initial therapy included digoxin, captopril and furosemid. In order to decrease plasma cholesterol, he was treated with cholesterolamine and prudent diet. The patient died from heart failure following the cardiac catheterization. Autopsy could not be performed.

DISCUSSION

FH is an inherited disease characterized by raised blood cholesterol, accumulation of cholesterol in the skin, tendons and arterial wall, and accelerated atherosclerosis(1). FH arises from mutations in a particular gene which codes in all nucleated body cells for a single polypeptides chain : The LDL receptor. The hepatic LDL receptors have a reciprocal hand in both formation and the removal of plasma LDL(4).

The clinical diagnosis of homozygous FH is not difficult. Patients are likely to be identified early in childhood because of xanthomas associated with high plasma cholesterol levels. The diagnosis of homozygous FH in our patient was diagnosed by family history, juvenile xanthomatosis and high serum total cholesterol level (above 600 mg/dl). Coronary atherosclerosis frequently has his onset before 10 year of age; most patients die of complication from heart diseases before 30 year of age.(1).

Although patients with xanthomatosis and hypercholesterolemia associated with valvular heart diseases have been reported as a uniqe feature of the homozygote FH, it is not found in heterozygote form (5,6). To the best of our knowledge, dilated cardiomyopathy with homozygous hypercholesterolemia in children has not been reported previously. It is to be antipicated, that ischemia due to coronary atherosclerosis would exert profound detrimental effect on the heart's contractile machinery. Interruption of coronary flow (experimentally or clinically) is rapidly followed by hemodinamic evidence that contractility of the ischemic myocardium is dramatically impaired (7). Ischemia or hypoxia can cause irreversible changes in the heart's contractile proteins. A change in the Ca-receptor protein of the contractile apparatus in the ischemic heart may be a major factor in decreasing myocardial contractility. It has been suggested that hypoxia or ischemia, by inhibiting the Na-pump, could lead to Na accumulation at a membrane binding site located at a portion of the myocardial fiber in contact with the extracellular fluid. This accumulation of Na could thereby impair the release of Ca to the conractile proteins (8).

Atherosclerosis-related disease, particularly coronary heart disease, is the leading cause of death in the world. It is known that atherosclerosis begins in early life. It was described as a pediatric disorder almost 30 years ago, and evidence of advanced coronary atheosclerosis was found at autopsy in 20 to 22-year-old soldiers who were killed in the Korean and Vietnam wars (9). Hypercholesterolemia should be treated in childhood otherwise hypercholesterolemic children are likely to become hypercholesterolemic adults. In conclusion, we emphasize that pediatrician should identify primary hyperlipidemia in childhood and attend to prevent the associated risk of premature coronary disease by describing appropriate diet and cholesterol-lowering drugs. Therapy is more effective if started early and decreases the risk for myocardial disease.

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JOURNAL OF ANKARA MEDICAL SCHOOL Vol 20, No 3, 1998 161-164

RUPTURED MYCOTIC ANEURYSM PRESENTING AS ACUTE SUBDURAL HEMATOMA: A CASE REPORT AND REVIEW OF THE LITERATURE

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SUMMARY

The case of mycotic aneurysm presenting as acute subdural hematoma is described. A 21-year old man with a history of headaches and vomiting was admitted to hospital. Brain computed tomography scan was revealed a left temporal parietal acute subdural hematoma. Angiography showed an aneurysm on the distal branch of the left middle cerebral artery.

Key Words: *Mycotic aneurysm, rheumatic heart disease, endocarditis, subdural hematoma*

A ruptured intracranial aneurysm presenting as an acute subdural hematoma is not a very common case. There have been rare reported cases in the literature (1, 2). Since the criteria of examination, diagnosis and treatment of mycotic aneurysm presenting as acute subdural hematomas are not clearly defined in the literature yet, this case is discussed in the light of available literature.

CASE REPORT

A 21-year old man was brought to the emergency room with the complaints of headache and vomiting. There was no history of trauma. The patient was being followed up for rheumatic heart disease and receiving prophylactic antibiotic treatment. Three months prior to his admission to our hospital he had been diagnosed having an aortic insufficiency and hypertension. Cardiac auscultation revealed a grade 3 systolic murmur. Patient had a subfebril fever (37.2 C) and white blood cells count was 12.800/ml. There was no deficiency in the patient's neurological examination. Brain computed tomography revealed a left temporal parietal acute subdural hematoma (Figure 1). Considering the patient's rheumatic heart disease and having no history of trauma, it was suspected that he could have a mycotic aneursym. A cerebral angiography was performed. Angiography showed an aneurysm in the left middle cerebral artery distal branch (Figure 2). All the cultures failed to elucidate any source of infection. An echocardiogram demonstrated a mitral valve prolapsus and an aort insufficiency grade 2-3. The patient was started on an intravenous antibiotic treatment. Following the treatment he was taken to operation. During the operation a left temporal parietal craniotomy and aneurysm clipping were performed (Figure 3). At the pathologic examination; the slides were stained with hematoxylin eosin and in the study of the material, a thin layer of intima, hemorrhages, fibrin depositions and exuda were observed (Figure 4). The patient suffered no surgical or internal problem postoperatively. Three months following the first operation an aort valve replacement was performed on the patient.

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Received: May 5, 1997 Accepted: April 22, 1998

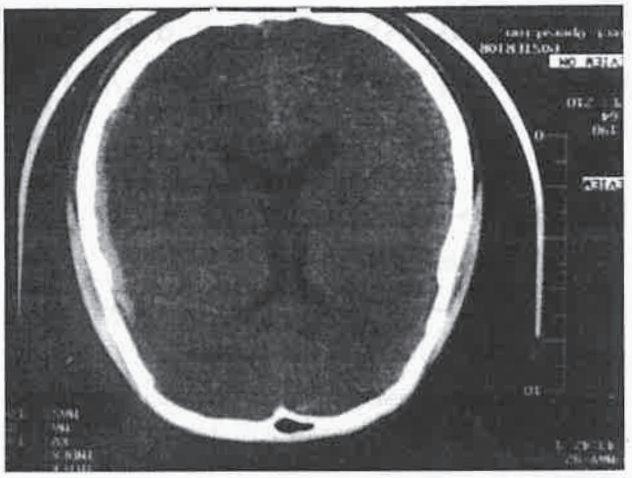

Fig. 1: Left temporal and parietal subdural hematoma at the brain computed tomography.

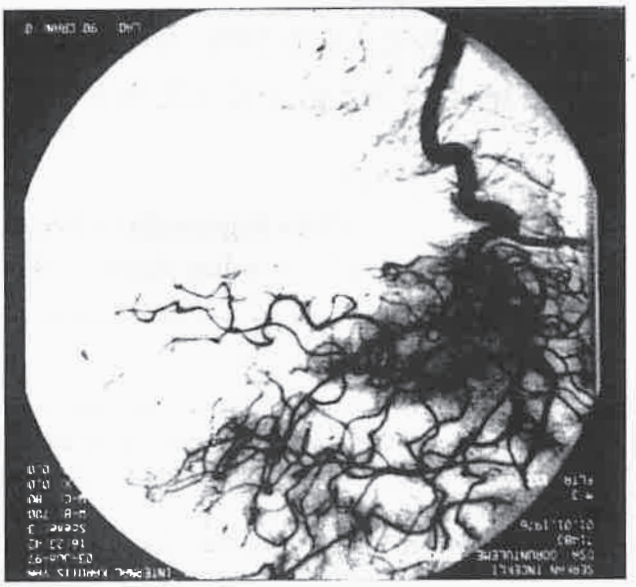

Fig. 3: After the operation clipping the aneurysm.

DISCUSSION

In 1869 Church was the first person to trace a casual relationship between the formation of an intracranial aneurysm and vegetative endocarditis (1). Osler, on the other hand, was the first person to use the term "mycotic" (2). Bohmfalk and collagues used the term "Bacterial aneurysm" for the first time (3). Mycotic aneurysms constitute 2.5 % - 4.5 % of all intracranial aneurysms. Four-10 % of the patients with bacterial endocarditis also suffer from intracerebral aneurysm (4, 5, 6). Most of the patients have congenital heart disease and rheumatic heart disease. A small number of patients are found to have conditions such as meningitis, immunosupression, cavernous sinusitis, pharengitis or drug abuse (3, 5, 7). In most of these patients while there are traces of acute subdural hematomas (8), in the literature intraparenchymal hemorrages due to the mycotic aneurysm were also reported (9). In the literature the true incidence of ruptured mycotic aneurysms is not defined whereas a 0.3 % to 7.9 % incidence of acute subdural hematoma related to rupture of any intracranial aneurysm is defined. The incidence of 2.5 % to 4.5 % for all intracranial aneurysms associated with acute subdural hematoma is quite low (10, 11, 12). The results of the mycotic aneurysm treatment in the literature were extremely poor (13, 14). Later on the results of larger series in the literature were better (7, 15). That the main pathogenesis started at the vaso vasorum and a vascular wall destruction existed in the mycotic aneurysm was pointed out in some studies (16, 17, 18). Mycotic aneurysms were observed mostly in the middle cerebral artery distal branches (8, 19, 20, 21). Subdural hemorrhage in intracranial aneurysm was explained by two theories (11, 22). The first one, through adhesions with the arachnoid membrane, the aneurysm bleeds directly into the subdural space. Second, blood streaming from ruptured aneurysm disrupts the arachnoid layer and forces its way in to the subdural space. In this case we believe that the first theory would apply better. In the mycotic aneurysm another discussion topic is the method of the treatment. There are various views on this issue.

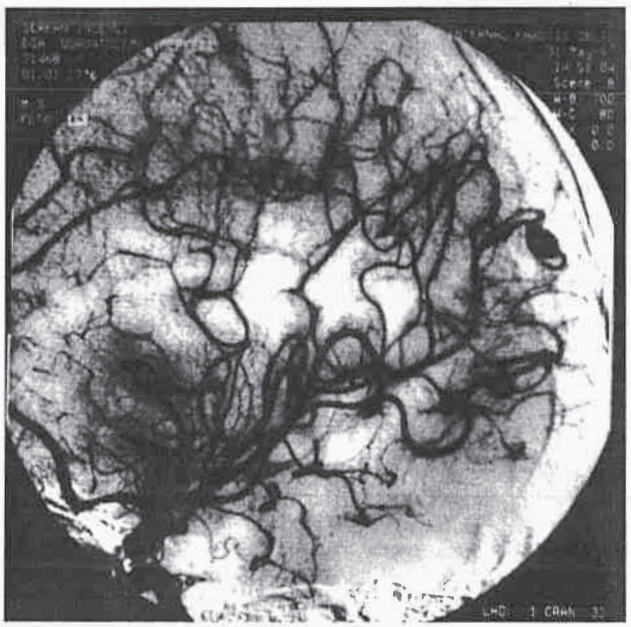

Fig. 2: Aneursym in the left middle cerebral artery distal branch.

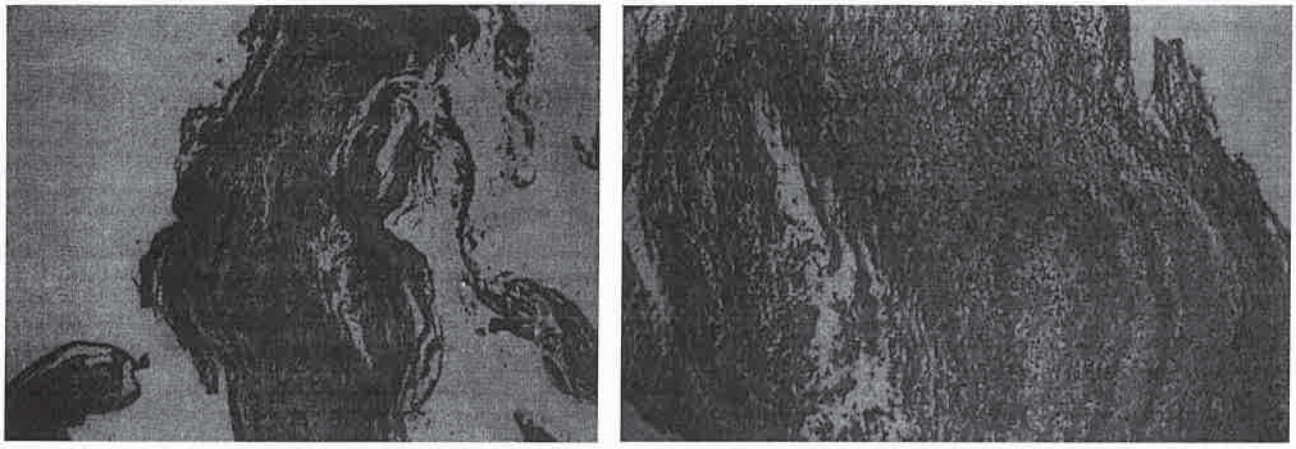

Fig. 4: Pathologic examination shows a thin layer of intima, hemorrhage, fibrin and exuda.
a) H.E X 10 b) H.E X25

When Frazee and collagues (15) compared the results of elective surgical therapy with the non surgical therapy results, the outcome was optimistic. As for the results of the series they had used, it was clearly pointed out that a series of angiography should be performed on the patients suffering from headaches and experiencing focal neurological deficiencies. It should also be considered while planning an operation that the angiography could be combined with antibiotic treatment and there may be multiple aneurysms. Molizari and collagues had studied the time period of aneurysm constitution following the placement of an infective agent into the cerebral vessel and found out that in patients who did not receive antibiotic treatment, an aneurysm developed in 1-3 days whereas this period was extended to a full week in the patients who received antibiotic treatment. But in those with bacterial endocarditis, although they had received the proper antibiotic treatment, it was shorter than a week that an aneurysm developed (16, 20). Serial angiography was suggested accompanying the antibiotic treatment (15). Bingham and collagues report on the patient with total aneurysm resolution with serial angiograpies (23). Many authors suggest a surgical treatment in the patients with a rupture and having no response to antibiotic treatment (3, 7, 15). While taking this decision the lesion's being in a single and easy-to-reach location will be adventageous. There are different views on the treatment of proximal and multiple aneurysms. We believe that results of a larger series are needed to have a general concensus on this issue.

CONCLUSION

There is a high mortality and morbitity of the non-surgical therapy in the ruptured mycotic aneurysms.

The results of surgical treatment carried under elective conditions are better.

Since new mycotic aneurysm may develop during the antibiotic treatment, serial angiographies must be performed.

In the preoperative preparation the possibility of multiple aneurysm, must be taken into consideration.

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JOURNAL OF ANKARA MEDICAL SCHOOL Vol 20, No 3, 1998 165-168

A PATIENT WITH SYSTEMIC SCLEROSIS WITH ADVANCED CARDIAC AND SKELETAL MUSCLE INVOLVEMENT (A Case Report)

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SUMMARY

This report describes a patient with progressive systemic sclerosis with polymyositis who had myocardial infarction. Myocardial involvement in systemic sclerosis is due to two reasons: Noninflammatory and inflammatory involvement. The former group is due to noninflammatory intramyocardial vasospasm similar to peripheral vasospasm, and the later is from inflammatory myocarditis, that associated with peripheral "inflammatory myositis". It is important to differentiate these two subgroups, because the inflammatory myositis, like their polimyositis-dermatomyositis counterparts, has an excellent response to anti-inflammatory therapy. Myocarditis rarely been reported in some patients with systemic sclerosis in association with myositis. So we reported this case as an cardiac and skeletal muscle disease in systemic sclerosis.

Key words: *Systemic sclerosis, Myocarditis, Myositis.*

Systemic sclerosis is a multisystem disorder of unknown cause characterized by fibrosis of the skin, blood vessels, and visceral organs, including the gastrointestinal tract, lungs, heart, and kidneys. The degree and rate of skin and internal organ involvement vary among patients [1]. Patients with systemic sclerosis are known to be at risk for development of myocardial dysfunction and skeletal myopathy [2-4]. Although rare, clinically severe myocarditis has been reported in the setting of systemic sclerosis [5-9]. We describe a patient with advanced, and progressive clinic of cardiac and skeletal muscle, skin, lung, and gastrointestinal tract involvement of systemic sclerosis.

CASE REPORT

A 47-year-old woman has admitted to İbn-i Sina Hospital Department of Immunology, in May 1994 because of swelling, and stiffness of her hands and fingers, and Raynaud's phenomenon. The diagnosis of systemic sclerosis was based on ARA criteria, and started to interferon α-2a, calcium channel blocker, and low dose aspirin therapy. Noticeable alterations in gut habits (diarrhea and constipation periods) was started 1 year later from the diagnosis. As the patient didn't benefit from interferon therapy, d-penicillamine was started in June 1995. But even with this therapy her clinical status got worsened. She charged to our hospital in October 1995 again for evaluation of worsening clinical status. She was suffering from generalized fatigue, severe myalgias, loss of weight due to dysphagia and dyspepsia, and stiffness of her hands and arms, and arthralgias.

On examination her blood pressure was 100/70 mm Hg with a regular heart rate of 88 beats/min. She had skin thickening, and swelling from her fingers to shoulders and active Raynaud's phenomenon. There was mild limitation of mouth opening. Her lungs were clear to auscultation. The cardiovascular examination was normal, and epigastric pain was noted on abdomen. Motor examination revealed marked proximal weakness of the upper and lower extremities.

The laboratory test results confirmed moderate anemia and the following values: Hemoglobin, 8,9 g/dl; hematocrit, 27%; leukocyte count, 12000/mm3; platelet count, 617000/mm3; sedimentation rate, 100

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Received: Dec 19, 1997 Accepted: Feb 11, 1998

mm/h. Serum urea nitrogen, creatinine, sodium, potassium, calcium, uric acid, alkaline phosphotase, bilirubin, and transaminases were normal. Albumin was 2,8 g/dl (normal: 3-5,5); lactate dehydrogenase level was 277 IU/L (normal: 101-233); serum creatinine phosphokinase (CPK) level was 287 IU/L (normal:24-180); with MB fraction 37 IU/L (normal: 0-25); aldolase level was 8,5 IU/L (normal: 2,7-5,3). Antinuclear antibody (ANA) was positive, with a homogeneous pattern; anti ds-DNA was normal. Anti-streptolysin O antibody level was 567 IU/L (normal: 0-200); C-reactive protein was 110 mg/L (normal: 0-5); rheumatoid factor level was normal. Immunoglobulin (Ig) G was 22,52 g/L (normal: 6,5-16); Ig M was 3,73 g/L (normal: 0,6-3,7); and Ig A was normal. Anti-SCl-70 antibody was positive. Thyroid function tests were normal with antimicrosomal thyroid antibody 818,9 IU/ml (normal: 0-50) Urinalysis was normal. 24-hour-urinalysis revealed 65 mg/day creatinuria (normal: 0-80). Proteinuria was absent, and creatinine clearance was normal.

Thoracic CT revealed esophageal dilatation, and diffuse, mild interstitial changes and emphysematous areas in some places in the lung parenchyma. Lung function tests, gas exchange (blood gases and diffusion capacity for carbon monoxide) tests were normal. Skin biopsy was consistent with systemic sclerosis.

Because of the progressive myalgias, muscle weakness, and increased serum creatin phosphokinase and aldolase level, and decreased nerve conduction velocity on sural nerve, by electroneuromyography, muscle biopsy was made, and showed interstitial and perivascular lymphocytic infiltrations, marked degeneration of muscle fibers, that's consistent with inflammatory myositis.

The electrocardiogram showed the absence of R wave progression on the inferior derivations, left anterior fascicular hemiblock, and left axis deviation. Echocardiography showed poor contraction of ventricles, although it was normal previously. CKMB level increased to 56 IU/L, and AST level to 49 IU/L. Coronary arteries found normal with coronary angiography. Ventriculography revealed hypokinesia on the anterolateral wall of the left venticle. Myocardial thallium-201 scintigraphy with SPECT imaging revealed ischemia in the inferoapical site of the left ventricle, and fixed perfusion defect on the inferior wall. Recumbency MUGA scanning showed normal (%51) left ventricle global ejection fraction with hypokinesia on the apex.

We started to the patient prednisolon 1mg/kg/day for her cardiac and skeletal muscle disease. After a few days her muscle weakness and fatigue decreased apparently, and CPK, CKMB, and LDH levels got to normal.

DISCUSSION

Cardiac involvement in systemic sclerosis is relatively common, and if clinically evident, usually portends a poor prognosis. Cardiac manifestations of systemic sclerosis include arrhythmias, congestive heart failure (CHF), angina pectoris with normal coronary arteries, and sudden death [1, 4, 7, 8]. Although myocardial fibrosis is present in a majority of patients at autopsy, clinically evident myocardial disease is uncommon [6, 11]. When clinically evident, cardiac involvement has been shown to indicate a poor prognosis for survival [2, 3, 5-8].

Approximately 50% of patients with systemic sclerosis have abnormal ECG findings. Left anterior fascicular block is seen in 52% of these patients. Septal infarction pattern is approximately 10 to 20% of patients with systemic sclerosis. Symptomatic arrythmias are also common in systemic sclerosis. Seventy-two percent of patients have sustained symptomatic arrhythmias, including documented ventricular tachycardia in 24% and high-grade atrioventricular block or severe bradycardia in another 20% Fifty-six percent of patients have sustained tachyarrhythmias. Most importantly, 48% of patients die suddenly, which accounted for 67% of all deaths [2].

Patients with systemic sclerosis and skeletal muscle disease are at risk for development of coexisting myocardial disease. Patients with myopathy had a significantly greater prevalence of myocardial involvement (21-50-80% at different studies), clinical CHF (10%), and cardiac death (8%) than did patients without myopathy [2, 3, 12]. As a corollary, patients with systemic sclerosis who had at least one documented elevation of serum CK had a similarly risk of myocardial involvement (23%), CHF (10%), and cardiac death (9%).

It is clinically difficult to differentiate primary myopathy from myopathy that is due to atrophy from disuse, coexisting articular disease, or use of systemic corticosteroids. Elevations of serum CPK are present in a comparatively low percentage of patients, whereas increases in serum aldolase level may occur more often. Abnormalities as determined by electromyograp-

hic examination are common, but may be nonspesific. Muscle biopsy may increase detection of disease [2].

Our patient had a 1,5-year history of rapidly progressive face and hand swelling followed by diffuse skin tightening, Raynaud's phenomenon, and dysphagia despite treatment with d-penicillamine, and interferon. She had a 4-month history of proximal muscle weakness, and deteriorated clinical status. Her serum CPK, CKMB, and aldolase levels were elevated. Muscle biopsy revealed myopathy. She had an unstable angina pectoris (UAP), with normal coronary arteries. MUGA scanning and SPECT Thallium-201 myocardial perfussion imaging showed anterolateral fixed perfussion defect. SPECT imaging is more sensitive and specific for detecting coronary artery diseases [13].

Myocardial infarction or UAP are rarely seen in systemic sclerosis with normal coronary arteries. Bulkley et al. [14] reported a high prevalence of myocardial contraction-band necrosis that's a histologic lesion seen in the setting of ischemic injury followed by reperfusion and speculated that myocardial fibrosis results from intermittent spasm of the small coronary arteries, a form of "myocardial Raynaud's phenomenon".

The development of myocardial disease in systemic sclerosis attributed to two mechanism in the literature. The first reason is the noninflammatory contraction band necrosis and fibrosis from vasospasm of intramyocardial arterioles similar to peripheral Raynaud's phenomenon. The other reason is the inflammatory myocarditis, and has been well described by Clements et al [15]. This subgroup may be identifiable by the presence of peripheral myositis and an elevation not only of the total serum CPK, but also of the CPK-MB isoenzyme. The inflammatory infiltrates on muscle biopsy, classified as "inflammatory myositis" indistinguishable histologically from polymyositis-dermatomyositis (PM-DM). It is important to making the distinction between these two groups of systemic sclerosis patients with muscle disease, because those patients with inflammatory myositis, like their PM-DM counterparts, had an excellent response to anti-inflammatory therapy [15]. According to this subdivision, our patient must consider as an inflammatory myocarditis.

As the therapy that is recommended for these patients is steroid [2,3,5-8], we started prednisolon 1 mg/kg to her. After a few days her muscle weakness decreased, and her status performance improved. But in the previous reports that given steroid alone, even at high doses, the patients die approximately 6 months later because of the progressive left ventricle failure [6-8].

In summary myocarditis may accompany peripheral myositis in some systemic sclerosis patients. Our patient's clinical course of systemic sclerosis was so progressive that it didn't reply to interferon and d-penicillamine treatments. She had systemic sclerosis with skin, gastrointestinal tract, respiratory, cardiovascular, and neuromuscular system involvements. As the association of the cardiac and skeletal muscle disease in an advanced systemic sclerosis is very seldom we described her.

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A PATIENT WITH MIXED CRYOGLOBULINEMIA WHO HAS DEVELOPED LOW-GRADE MALIGNANT LYMPHOMA: (Case Report)

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SUMMARY

A close relationship has been established between mixed cryoglobulinemie and low-grade malignant lymphoma. Indeed, the risk of malignant lymphoma significantly increases during the course of type II mixed cryoglobulinemia. In this short case report, we aimed at presenting a patient with essential mixed cryoglobulinemia (54 years old, female) who has developed a low grade malignant lymphoma and to discuss this relationship.

Key Words: *Mixed cryoglobulinemia, Malignant lymphoma*

Mixed cryoglobulinemia (MC) is considered as a lymphoproliferative disorder charactererized by arthralgia, weakness, purpura, and organ involvement such as glomerulonephritis, peripheral neuropathy, vasculitis and chronic liver disease (1). Three types of cryoglobulinemia (Cryolg) are usually recognized according to the immunochemical findings (2). Type I Cryolg is characterized by a single monotypic component which is substained by a lymphoproliferative disorder. On the other hand, type II and III Cryolg consist of a mixture of two or more immunoglobulin components which are produced under the influence of conditions yet to be fully understood. One of these components is monotypic in type II Cryolg, while they are all polytypic in type III Cryolg (2).

The development of malignant B cell lymphoma has been reported in a variable fraction of these patients (3,4). In this case report, we presented a patient with essential mixed cryoglobulinemia who has developed a low grade malignant lymphoma.

CASE REPORT

A 54 year old female (Name : S.I. protocol number : 24271) presented to the our clinic at the Ankara University Medical School with a complain of arthralgia, weakness and myalgia in 1976. In 1984, she had been hospitalized because of a purpuric rash in the lower extremities and an oral aphthous lesion. At this time, physical examination revealed some brown pigmentation on the abdominal and thorasic area associated with hepatomegaly. Remaining examination was unremarkable.

A mild anemia (hemoglobin of 12 gr/dl) was observed, associated with a high sedimentation rate (115 mm/h) and circulating cryoglobulins. Electrolites, liver panel and immunologic tests were all in normal limits. Bence-Jones proteinuria and Hepatitis B surface antigen were negative. Antihepatitis B surface antigen was positive. Serum IgA level; 308 mg/dl (90-450 mg/dl); serum IgG level; 1680 mg/dl (80-1800 mg/dl);and serum IgM level was 5000 mg/dl (60-250 mg/dl). Serum immunoelectrophoresis have a monoclonal IgM component. Telecardiography was normal. Abdominal ultrasonography showed a mild hepatomegaly. Skin biopsy, including histopathology and immunoflouresans examinations, was normal.

The patient was diagnosed with an essential mixed cryoglobulinemia based on these clinical and laboratory findings, and treated with glucocorticoids.

In 1992, the patient developed with an autoimmune hypothyroidism. Abdominal ultrasonography

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Received: Dec 19, 1997 Accepted: Feb 11, 1998

showed hepatosplenomegaly associated with paraaortic and periportal lymphadenopathies (2x0,5 cm.). Incisional biopsy of the axillar lymphadenopathy was performed and low grade malignant lymphoma was diagnosed. The patient was treated with glucocorticoids far 10 months but died of in 1993.

DISCUSSION

The development of a low grade malignant lymphoma has been reported in patients with cryoglobulinemia. Monteverde et al 's series displayed quite homogeneous findings on clinical grounds (5) : those were more often middle-aged women, with a history of purpura, arthralgia and asthenia lasting some years. In that study, twelve patients with essential mixed cryoglobulinemia underwent multiple liver and bone marrow biopsies. In 9 of 12 cases , routine histology revealed an infiltration of the liver portal tracts, lobules and sinusoids by small lymphocytes suggesting the cytological characteristics of the LP immunocytoma of the Kiel classification. At the immunophenotyping, these elements expressed the CD22 antigen and bore the same type of immunoglobulin as the monotypic component in the serum (5). In 7 of 9 patients repeated bone marrow needle biopsies showed multiple foci of infiltration by plasmacytoid cells. On the basis of these findings, Monteverde et al discussed the hypothesis that most essential mixed cryoglobulinemia are substained by a low grade malignant lymphoma. In 1968, Dini et al , who suggessed that cryoglobulinemia seems to be related to a B cell malignant lymphoma, studied bone marrow biopsies of cryoglobulinemic patients (5). At the early phase of disease, monoclonal proliferation of B lymphocytes seems to be limited but as time goes by often evolves into non-Hodgkin's lymphoma (NHL). Viral infection could play a direct role in the development of these hematologic malignancies.

A number of recent studies have repeatedly implicated the hepatitis C virus (HCV) as the possible major etiologic factor of the type II mixed cryoglobulinemia (6,7,8,9,10). It has been speculated that HCV may sustain the clonal expansion of B cells secreting IgM monoclonal rheumatoid factor in this disease. In a multistep model of lymphomagenesis, such benign B cell clonal populations may be more prone to a series of genetic events causing the transition to a malignant B cell phenotype (11,12). Indeed, the risk of a frank B cell malignancy significantly increases in the course of the type II mixed cryoglobulinemia. (13). A putative pathogenetic role of HCV in the development of mixed cryoglobulinemia associated B cell malignancies has also been speculated. Salvatore et al (14), reported the localization of HCV within a parotid non-Hodgkin's lymphoma lesion diagnosed during the course of a HCV- related mixed cryoglobulinemia.

In result, mixed cryoglobulinemia is associated with a high prevalence of low-grade non-Hodgkin's lymphomas.

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HYPERTROPHIC CARDIOMYOPATHY WITH MIDVENTRICULAR OBSTRUCTION ASSOCIATED WITH CORONARY ARTERY DISEASE (A CASE REPORT)

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Çetin Erol* • Sait Kenan • Derviş Oral***

SUMMARY

Midventricular obstruction is an uncommon variant of hypertrophic cardiomyopathy (HCM) in which the hypertrophic process predominantly occurs at the left ventricular (LV) papillary muscle level, causing functional separation of the apical region from the outflow tract. In the clinical course, mid-ventricular obstruction (MVO) is known as a cause of chest pain, usually occurring as typical angina on effort or atypical chest pain, and also resulting in some cases, apical myocardial infarction in the absence of coronary artery stenosis. In this case we present a patient with MVO who had atypical chest pain. Coronary angiography revealed significant stenosis at circumflex artery and chest pain was eliminated after successful percutaneous transluminal coronary angioplasty. Though chest pain can be seen in patients with MVO due to oxygen supply/demand mismatch, coronary artery disease should be kept in mind even in the absence of typical angina.

Key Words: *Hypertrophic cardiomyopathy, Midventricular obstruction, Chest pain, Coronary artery disease, Percutaneous transluminal coronary angioplasty*

Midventricular obstruction is an uncommon variant of hypertrophic cardiomyopathy (HCM) in which the hypertrophic process predominantly occurs at the left ventricular (LV) papillary muscle level, causing functional separation of the apical region from the outflow tract.(1) In the clinical course, mid-ventricular obstruction is known as a cause of chest pain, usually occurring as typical angina on effort or atypical chest pain, and also resulting in some cases, apical myocardial infarction in the absence of coronary artery stenosis.(1-3) In this case we present a patient with midventricular obstruction who had atypical chest pain accompanied by significant coronary artery stenosis dilated by performing successful percutaneous transluminal coronary angioplasty (PTCA).

A 58-year-old man was referred to the cardiology department because of atypical chest pain. He was a heavy smoker. No history of hypertension was reported. On admission, heart rate was regular at 76 beats/min and blood pressure was 130/70 mm Hg. Physical examination revealed only mild systolic ejection murmur at the apex. The electrocardiogram (ECG) showed LV hypertrophy with negative T waves (maximum 4 mm in depth), in leads D1, aVL and V2 through V6. Two dimensional echocardiography (ECHO) revealed marked LV hypertrophy confined to apical half below the papillary level. There was significant obliteration of the LV cavity at the level of the papillary muscles. The thickness of the septum and the posterolateral wall were, respectively, 1.8 and 1.6 cm at the midcavity and normal at the base; the apical region showed a lesser degree of hypertrophy. The mitral valve motion was normal. From the apical window sampling by continuous-wave Doppler at the site of midventricular obstruction (Fig. 1) revealed an abnormal systolic pressure gradient between the apical region and the basal region (maximally 57, mean 31 mm Hg). At cardiac catheterisation, the LV pressure in

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Received: Fab 4, 1998 Accepted: April 22, 1998

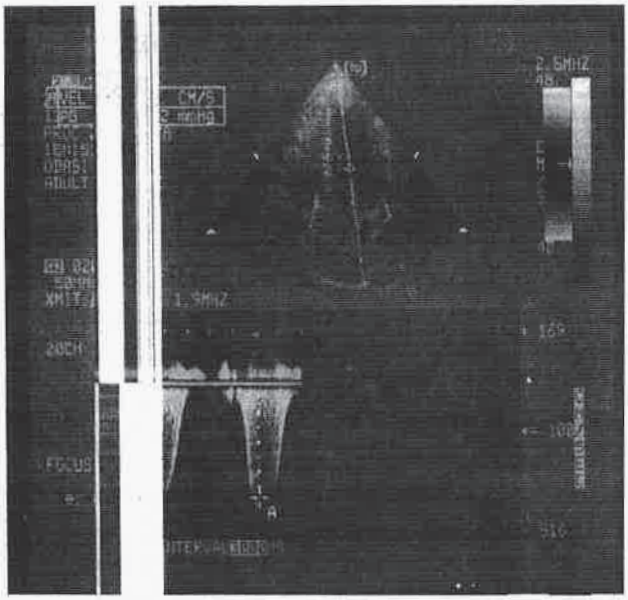

Fig. 1: Apical four-chamber view of the left ventricle at the systole showing continuous-wave Doppler tracing of abnormal systolic velocity pattern.

the base and apical chamber were, respectively, 140/18 and 180/32 mm Hg, showing 40 mm Hg pressure gradient in systole and 14 mm Hg in diastole without outflow gradient. Left ventricular cineangiography in the 30-degree right anterior oblique projection revealed marked muscular systolic and diastolic narrowing at the midventricular level (Fig 2). The LV wall motions were normal and ejection fraction was %78. Coronary angiography (CAG) revealed a discrete %70 stenosis in the proximal left circumflex (Cx) artery and a segmentary %30 stenosis in the mid right coronary artery. LAD was patent. After premedication with 15.000 U heparin and 250 mg aspirin successful PTCA was performed in the left Cx artery. During the 24-hours clinical follow-up no cardiac event was observed. The patient was later discharged and he was symptom free at the end of the first month.

DISCUSSION

Midvenricular obstructive HCM has been known since 1976(1) and occured much less common than the subaortic obstructive form. Characteristical feature of this variant of HCM at two dimensional echocardiography or cineangiography is midcavity obliteration due to systolic apposition of hypertrophied walls and papillary muscles at the midventricular level(2). Systolic midventricular obstruction (MVO) causes functional separation of the apical region from the outflow tract and result in a high pressure apical chamber in terms of basal chamber.(1-3) Diastolic intraventricular narrowing with a particular Doppler echocardiography pattern has been also reported, especially in patients with apical HCM.(4-6) In our case, we demonstrated both systolic and diastolic midventricular narrowing with the pressure gradient. Myocardial ischemia in patients with MVO have been well demonstrated.(2-4) Evidence of ischemia, subjective or objective, is frequent, usually occurring as typical angina on effort or atypical chest pain.(2) Apical transmural myocardial infarction (MI) with aneurismal formation has been also described with normal major coronary arteries in many, if not most, cases.(1-5) Although the mechanism for the myocardial ischemia and MI in the

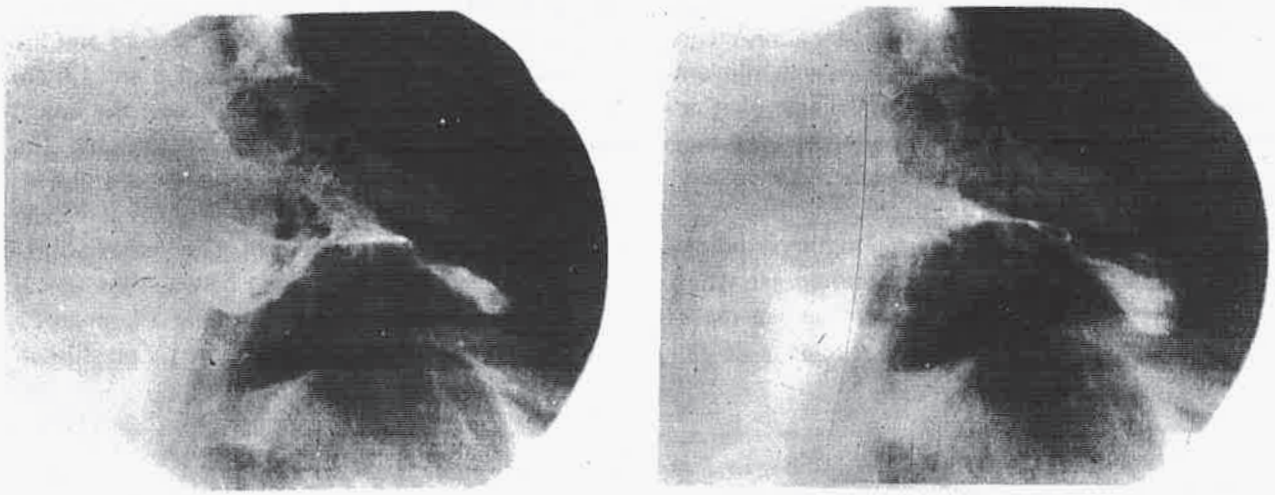

Fig. 2: Left ventricular cineangiographic frames 30-degree right anterior oblique projection at end diastole (left) and systole (right) showing severe midventricular narrowing in both frames.

absence of coronary artery disease (CAD) is not entirely clear, these clinical events are primarily attributed to oxygen supply/demand mismatch.(2) According to this, prolonged increase in pressure within the apical chamber resulting from the systolic and/or diastolic midcavity obstruction may result in regional ischemia and thus may explain angina or MI in some patients with MVO and normal coronary arteries.

Our patient had an atypical chest pain. Since previous reports declared that exercise testing and thallium-201 scintigraphy has limited value in the diagnosis of CAD in patients with HCM, we performed CAG. Significant left Cx artery lesion was observed and successful PTCA was performed. Chest pain was disappeared after PTCA and in 1 month period the patient is still symptom free. To our knowledge our case is the first with midvenricular obstructive HCM associated with CAD whose chest pain was disappeared by successful PTCA.

This case suggest that coronary artery disease should be kept in mind in patients with midventricular obstruction even in the absence of typical angina.

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SURGICAL TREATMENT OF DOUBLE AORTIC ARCH WITH RIGHT DOMINANT ARCUS: Report of three cases*

Mustafa Yılmaz • Murat Güvener** • Assem Miari*** • Alpay Çeliker**** Yurdakul Yurdakul*****

SUMMARY

We present three cases, surgically treated for double aortic arch (DAA). Age of the patients were three months old, twenty four months old and thirty months old.

The major symptoms were difficulty in breathing, stridor, recurrent respiratory infection, intermittant cyanosis and dysphagia. Symptoms were noted at birth but diagnosis delayed because of that underlying condition was not suspected by the primary physician. Angiocardiograpy were performed in all patients. Aortography showed DAA with hypoplasia of the left aortic arch and dominant right arch. Surgical division of hypoplastic left arch has been performed without mortality in these three patients. Symptomatic improvement was achieved in all patients.

Key Words: *Double Aortic Arch, Surgical treatment*

Double aortic arch is relatively rare congenital anomaly believed to be the result of persistence the hypothetical double aortic arch system proposed by Edwards(1)

During the fourth week of fetal life the aortic trunk divides into a symmetric ring consisting of right and left components that pass on either side of trachea and esophagus are encircled by this vascular ring. Normally, absorption of the right (posterior) arch will take place between the right subclavian artery and its junction with the descending aorta. The remnant of the right arch becomes the right innominate artery and leaves a left (anterior) arch as normal, freeing the trachea and esophagus(2-3). Failure of this process of absorption in the right arch produces a vascular ring and causes extrinsic tracheoesophageal compression. Successful surgical correction of DAA was first accomplished in 1945 by Gross(4).

CASE REPORTS

Three patients were transferred to our hospital because of respiratory distress, hypoxemia, cyanosis, stridor, noisy breathing and dysphagia. Their ages were 3,24,36 months old. The ages of mothers were 26,33,35 years old. There were no history of drug intake or illness during their pregnancy. Echocardiographic examinations were normal. In all patients, bronchoscopies were performed and tracheal compression were observed. Esophagograms demonstrated smooth extrinsic compression on the lateral and posterior aspect of the esophagus. Aortographies showed double aortic arch with hypoplasia of the left (anterior) arch and dominant right (posterior) arch (Figure 1) (Mayo type 1A)(5). Two of these cases, there were ductus arteriosus on the left and aortic(Kommerell's) diverticulums. There were no other anomalies. The patients were explored through left thoracotomy thro-

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Received: Fab 26, 1998 Accepted: April 22, 1998

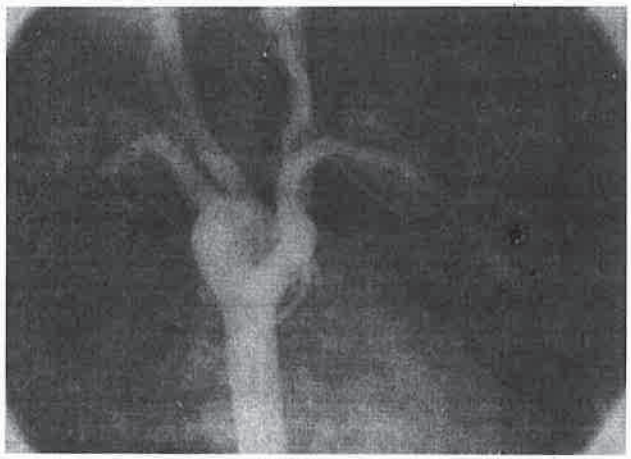

Fig. 1: Angiocardiography showing DAA. Notice the right dominant arcus.

ugh fourth intercostal space (Figure2). In all three patients, operation findings were same. There was a large aortic arch, the smaller left aortic arch, gave rise to the left innominate artery and then coursed posterior to the trachea and esophagus to connect to the right arch. The dominant right arch gave rise to the right carotid and right subclavian arteries. In two patients there were patent ductus arteriosus (PDA) and aortic(Kommerell's) diverticulum. At operation, first PDA was divided by division, then the left arch was divided just proximal to its entrance into the descending aorta, Aortic diverticulums were excised.

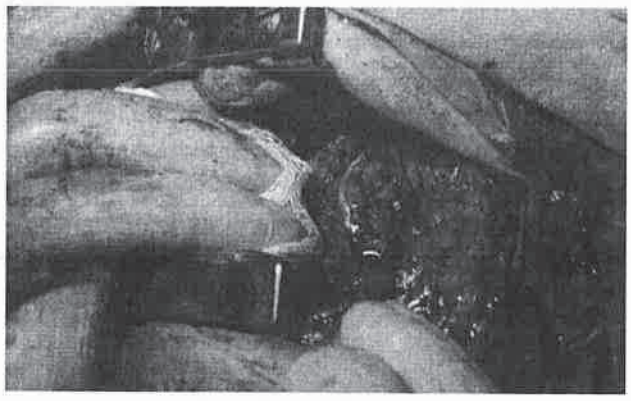

Fig. 2: Peroperatif wieving of DAA

DISCUSSION

Double aortic arch is a relatively rare congenital anomaly, and the most common types of vascular rings. It represent a persistance of both right and left dorsal aortic arches. It arise from the ascending aorta anterior to the trachea, cross dorsally on both sites of the trachea and esophagus and join posteriorly to form the descending aorta. Each arch gives rise to its common carotid and subclavian arteries or innominate artery(6). Ductus arteriosus may be present on the left or right side or it may be bilateral. Ductus arteriosus is most often left sided. Both two of our cases, PDA's were on the left side. The relative sizes of the arches are important, because, at operation, the surgeon divides the smaller one(7).

By for the majority of vascular rings consist of a dominant right arch. The surgical relevance of this fact is that almost all vascular rings are most conveniently approached through a left thoracotomy. For the diagnosis of the double aortic arch, barium swallow, aortography and magnetic resonans imaging(MRI) are usefull(8).

If either respiratory or dysphagic symptoms are present, surgical division of the ring is indicated. If the child is asymptomatic, surgery may be deferred. Clinical evidence suggests that the diverticulum may be major cause of residual tracheal or esophageal compression.(9).Because of that we excised aortic (Kommerell's) diverticulums. It suggested that aortopexy of the aortic diverticulum is an alternative technique to excision in some cases by some authors(10). Correction in early infancy relieves dyspnea and dysphagia, prevents aspiration-induced pneumonia and other respiratory infections, and most importantly allows for normal tracheal growth. Surgery shouldn't be delayed because of the respiratory infection, as division of the ring, which allows more adequate clearing of respiratory secretions, is most effective treatment of infection(6,7,8). In our patients, although their recurrent respiratory infections resistant to antibiotics therapy, surgical division has been performed without mortality. The mean postoperative hospital stay was 12 days. Symptomatic improvement was observed at first control, a month after the discharge.

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