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CONTENTS

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JOURNAL OF ANKARA MEDICAL SCHOOL Vol 18, No 2, 1996 61–63

USE OF IMMUNOHISTOCHEMISTRY IN HIRSCHPRUNG'S DISEASE

Bülent Mızrak* • **Görgün Bayraktaroğlu****

SUMMARY

Hirschprung's disease (HD) or congenital aganglionosis character istically presents with involvement of the sigmoid colon and rectum. There is an associated increases in mucosal nerve fibers in the affected bowel wall. Diagnosis of HD in the neonatal period is achieved via submucosal rectal biopsy, but it may be difficult because of ganglion cell immaturity. We retrospectively reviewed biopsy specimes from patients with suspected and proven HD, performed immunoperoxidase stains for chromogranin A, neuron specific enolase (NSE) and S100 protein. The results were compared to routine histologic findings. NSE and chromogranin A immunostaining produced staining of ganglion cell cytoplasm, greatly facilitating recognition of immature forms. With S100 staining increased numbers of nerve fibers in the muscularis mucosae and deep lamina propria were detected. All stains were helpful in demonstrating the overall pattern of microinnervation. We conclude that these immunostains are of value in suspected HD, and they may facilititate interpretation of rectal mucosal biopsies.

Abbreviated form of the title: Hirschprung's disease.

Key Words: *Hirschprung's disease, immunostaining, NSE, S100*

Detection of Hirschprung's disease (HD) in frozen or permanent sections remains one of the serious challenges facing the pathologist. The histopathologic diagnosis of HD is based onthe absence of ganglion cells in the submucosa and myenteric plexuses in the affected segment of the large intestine(6). Abnormal proliferation of nerve processes in the muscularis mucosae and lamina propria within the involved portion of bowel is another histopathologic finding.

A major advance in the diagnosis of HD was made when it was recognized that rectal suction mucosal biopsies could be used frequently to exclude that diagnosis(1). But the immature ganglion cells of Meissner's plexus in the infant are less distinctive in appearence than those in older patients or those of Auerbach's myenteric plexus. These immature cells may be confused with macrophages, fibroblasts, or Schwann cells (4).

Some studies have appeared that used the immunoperoxidase technique with antibodies against various nervous system proteins to stain ganglion cells in suspected cases of HD (3, 7). To determine their utility in this setting were trospectively reviewed 29 specimens from patients with suspected HD and performed immunoperoxidase stains using antibodies against neuron specific enolase (NSE), S100 protein and chromogranin A. The staining of ganglion cells and nerve fibers is documented, and results are compared to those obtained with hematoxylin-eosin stained sections.

MATERIALS AND METHODS

Twentyfive cases of HD dating from 1989 until 1995 were retrieved from the Pathology department of the Ankara University. These represented all cases during this time period for which sufficient tissue was available for additional study using immunocytochmeical technics. Data concerning the patient group are given in Table 1. Two autopsy and three biopsy specimens from children were used as control group.The control group consisted of patients unrelated to HD.

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Table 1. Description of cases studied

Number of patients	25
Males 14	
Females	11
Age range	6 days-6 years
Median age	12 weeks
Number of specimens	29
Mucosal biopsies	8
Full thickness or resections	21

For immunoperoxidase, unstained sections were cut at 6 micrometer. Staining was carried out using NSE, S100 and chromogranin A antibodies (all from Immunon). Diaminobenzidine (DAB) was used as the chromogen,and sections were counterstained with hemotoxylin.

RESULTS

Staining for NSE, chromogranin A, and S10 was, in general, good in both normal and HD patients. In the control group there was no false negative staining with these markers. Hemorrhage into the lamina propria did not interfere. In all instances, both ganglion cell cytoplasm and nerve fibers stained strongly with NSE and chromogranin A (Figure 1 and 2).Schwann cells remained negative. Immature ganglion cells stained as well as more mature cels. With S100 immunostaining ganglion cells were negative, while Schwann cells were positive (Figure 3).

In material from involved segments of the patients with HD, ganglion cells staining with NSE and chromogranin A was not seen, Neural elements

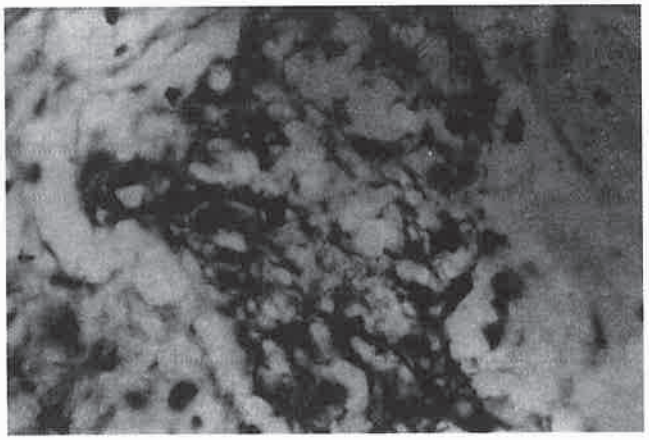

Figure 1. NSE staining of a submucosal ganglion. Both ganglion cell cytoplasm and nerve fibers are strongly positive (x400, DAB with hemotoxylin counterstain)

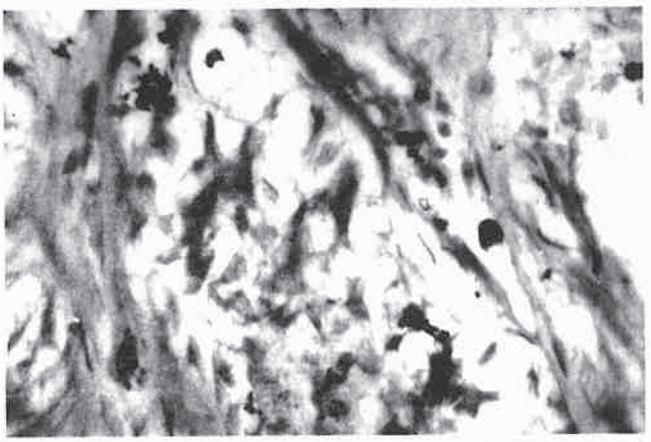

Figure 2. Chromogranin A staining of myenteric plexus of a normal infant. (x400, DAB with hematoxylin counterstain).

lacking ganglion cells were increased in prominence, ranging from large nerve trunks in the submucosa to indevidual fibers closer to the bowel lumen (Figure 4).

In general, the immunostaining results were in agreement with the interpretation originally rendered with the use of standard methods. However, the immunoperoxidase method greatly facilitated the positive identification of immature ganglion cells.

DISCUSSION

Several major advances greatly have facilitiated the management of patients who are suspected of having HD. After the demonstration that the level of aganglionosis of the submucosal plexus corre-

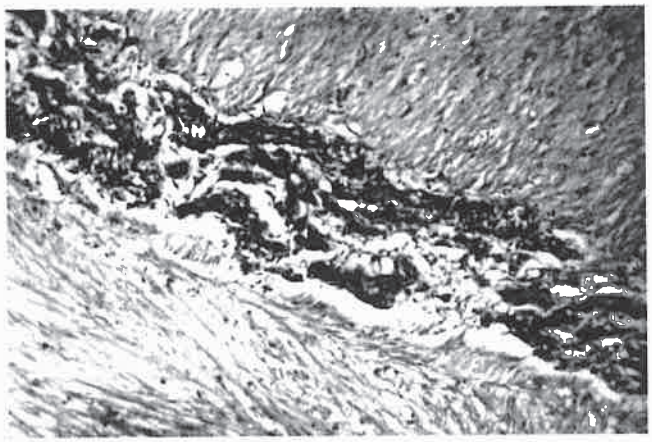

Figure 3. Normal rectal myenteric plexus of an infant with S100 immunoperoxidase. Ganglion cels are not stained, but are surrounded by positivestaining Schwann cells (x200, DAB with hematoxylin counterstain).

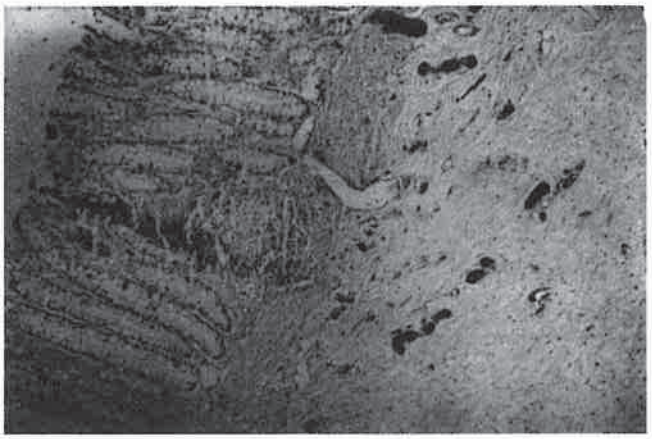

Figure 4. S100 staining of nerve fibers in Hirschprung's disease. Hyperplastic nerve fibers around muscularis mucosa. (x100, DAB with hematoxylin counterstain).

sponds to that of the myenteric plexus, the safer suction mucosal biopsies replaced full-thickness biopsies (1). However, the pathologist's duty is more difficult with this alteration. Immaturity of the ganglion cells of submucosa necessitates examining of serial sections of hematoxylineosin preparations.

The acetylcholinesterase stain is probably the method of choice in the hands of those who see large numbers of HD (4). However, it requires frozen tissue and its results may be difficult to interpret. Problems reported include interference with the image due to lamina propria hemorrhage, false negative reactions, and false positive reactions (3, 4, 7).

Immunostaining using antibodies to NSE and S100 protein has been shown to be an excelent technique for demonstrating the normal intervation of the gastrointestinal tract (5). Our findings document the efficacy of these stains in cases of suspected HD. In addition to these antibodies we also used chromogranin A, which reacts with neuroendocrine cells too. Our results are in agreement with those of previous reports. Cytoplasmic positivity with NSE and chromogranin A is higly specific for the ganglion cell.

The results of S100 immunostaining are less conclusive. The number and thickness of nerve fibres vary case from case. In addition of this fact, nerve fiber proliferation is reported in settings other than the congenital disorders of bowel innervation.

Recently there is an abundance of articles regarding the use of various antibodies to diagnose HD (2, 8, 9, 10). But they need to be approved, and much experince is necessary to be accepted as specific markers. Today the absence of ganglion cells in submucosa and myenteric plexuses is still the main diagnostic feature of HD; and in experienced hands only by examining serial hematoxylin-eosin stained sections the HD can be accurately diagnosed.

In conclusion, the use of immunohistochemistry has a complementary role in the diagnosis of HD. It is especially helpful in training the pathologist to recognise the immature ganglion cells. It may obviate to examine the necessity of several dozens of sections.

REFERENCES

1. Ariel I, Vinograd I, Lernau OZ, Nissan S, Rosenmann E: Rectal mucosal biopsy in aganglionosis and allied conditions. Hum Pathol 14: 991-995, 1983.
2. Deguchi F, Twai N, Goto Y, Yanagihara J, Fusbiki S: An immunohistochemical study of neurofilament and microtubule-associated Tau protein in the enteric innervation in Hirschprung's disease. J Pediatr Surg, 28:886-890, 1993.
3. Hall CL, Lampert PW: Immunohistochemistry as an aid in the diagnosis of Hirschprung's disease. Am J Clin Pathol. 83: 177-181, 1985.
4. Krishnamurthy S, Schuffler MD: Pathology of neuromuscular disorders of the smal intestine and colon. Gastroenterology. 93: 610-639, 1987.
5. Nakajima J. Watanabe S, Sato Y: An immunoperoxidase study of S-100 protein distribution in normal and neoplastic tissues. Am J Surg Pathol. 6: 715-717, 1982.
6. Qualman SJ, Murray R: Aganglionosis and related disorders. Hum Pathol. 25: 1141-1149, 1994.
7. Robey SS, Kuhajda FP, Yardley JH: Immunoperoxidase stains of ganglion cells and abnormal mucosal nerve proliferations in Hirschprung's disease. Hum Patrol. 19: 432-437, 1988.
8. Romanska HM, Bishop AE, Brereton RJ, Spitz L, Polak JM: İmmunocytochemistry for neuronal markers show deficiencies in conventional histology in the treatment of Hirschprung's disease. J. Pediatr Surg. 28: 1059-1062, 1993.
9. Tam PK, Owen G: An immunohistochemical study of neuronal microtubule associated proteins in Hirschprung's disease. Hum Patrol. 24: 424-431, 1993.
10. Yamataka A, Miyano T, Urao M, Nishiye H: Hirschprung's disease: Diagnosis using monoclonal antibody 171B5. J. Pediatr Surg. 2:820-822, 1992.

JOURNAL OF ANKARA MEDICAL SCHOOL Vol 18, No 2, 1996 65-68

ALUMINUM INTOXICATION and DESFERRIOXAMINE THERAPY IN CHRONIC HEMODIALYSIS PATIENTS

Neval Duman* • S. Deniz Kumbasar** • Kenan Ateş*** • Bülent Erbay* • Oktay Karatan*

SUMMARY

Aluminum is ubiquitious metal that is recently found to be toxic for man in high concentration. The two major excretory routes of aluminum are, the gastrointestinal and urinary systems. Because of the defective urinary aluminum excretion and increased exposure to aluminum containing chemicals, the patients with end-stage renal disease are prone to aluminum intoxication. We present two patient with end-stage renal disase and aluminum intoxication who were treated by desferrioxamine infusion followed by hemodialysis combined with Alukart hemoperfusion device.

Key Words: *Alukart, aluminum intoxication, chronic renal failure, desferrioxamine, hemodialysis.*

Aluminum (Al) is a ubiquitious metal that is found in many foods, cosmectic goods, parmeuticals and industrial materials. To date ny physiologic role of Al is not found in man, so it is not considered to be essential for man (4). Recently, it is found to be toxic for man in high concentrations that is presented clinically as progressive encephalopathy, microcytic anemia and osteomalacia (1, 3, 5, 6, 8, 10). In normal individuals Al enters to bodvia the respiratory and gastrointestinal systems by inhalation and foods. In patients, with chronic renal failure on hemodialysis treatment Al containing phosphate binders, dialysate and parenteral solutions contamined with Al are additiona sources of Al (4). The two major excretory routes of Al are the urinary and gastrointestinal systems. 20-25 mg of Al is excreted by kidney daily. Recently it hasbeen shown that it is also it has excreted by the biliary system in an amount more than that is excreted by the kidney (3, 4). Despite these excretory systems approximately 2 mg of Al is retained in the body in normal individuals which probably never causes any clinical manifestation (4). For those patients who are at risk of having Al intoxiciation, especially the ones with renal failure who are on chronic hemodialysis treatment and/or treated with Al containing phosphate binders, regular serum Al measurements are stressed (4). The first step of treatment is prevention which can be achieved by avoiding Al containing phosphate binders, dialysate and parenteral solutions that are contamined with Al, and by identifying the patients who are at risk and/or into0xicated (5), Curent recommendation for the medical treatment of Al intoxication in patients with renal failure who get hemodialysis treatment is the infusion of deserrioxamine (DFO) to mobilize Al form its stores, mainly the bone, followed by a high performance hemodialysis technique that is combined with a hemoperfusion device which has active charcoal (5, 9). The main side effects of DFO infusion are hypotension, Al encephalopathy, ototoxicity, eruptions, fatal bacterial (Yersinia enterocolitica) and fungal (Mucormycosis) infections (3, 5, 8).

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MATERIALS and METHODS

Being participated in a multicenter research program carried out by Antwerpen University, 68, patients, 46 males and 22 females aged between 12 and 63 years (mean age 32.2) were enrolled to the study. The patients were on chronic hemodialysis treatment in Ankara University Medical School, Hemodilaysis Unit. The mean time since the inita-tion of hemodialysis treatment in study population was 41.2 month. During the study, none of the patients received Al containing phosphate binders. The patients were clinically stable throughout the study and they did not have any signs attributable to renal osteodystrophy. Blood samples were drawn by special techniqueand equipments from a peripheral vein. Serum Al concentrations were determined by electrothermal atomic absorpion spectropotometry in the laboratory of Antwerpen University, Belgium, According to the research protocol, in patients with a serum al concentration above 50 µg/L, Al over-load/intoxication was considered and aDFO test was carried out but bone biopsy was not performed.

In the DFO test, a baseline Al value was obtained prior to a hemodialysis session (sample 1), then 10 mg/kg of DFO in 150 ml of 5 % dextrose solution was infused into a enousline during the last 30 min-utes of the same hemodialysis session, a second sample was taken within 5 minutes after the end of the DFO infusion (sample 2), at the start of the next hemodalysis session (44 hours after DFO adminis-tration), a third serum sample was taken. The test was considered to be positive if the rise in serum Al concentration 44 hours after DFO administration (sample 3) was more than 50 µg/L from the baseline (sample 1) serum Al concentration. The patents who were diagnosed to have Al intoxication, were treat-ed with 30 mg/kg DFO infusion, 48 hours later folowed by a hemodialysis combined with Alukart hemoperfusion, and then a second hemodialyss without prior inusion of DFO but combined with Alukart hemoperfusion for two months, and blood saples were collected before and after the hemodial-ysis session. All the samples collected throughout the study were sent to the Antwerpen University to be studied for Al concentrations.

TABLE 1: Serum aluminum concentrations in two patient with aluminum intoxication, before and afer treatment by hemodialy-sis combined with hemoperfusion.

PATIENT NO 1		Serum Aluminum Levels (mg/L)
1st treatment with Alukart	Predialysis Postdialysis	315 117
2nd treatment with Alukart	Predialysis Postdialysis	117 81
3rd treatment with Alukart	Predialysis Postdialysis	251 100
4th treatment with Alukart	Predialysis Postdialysis	121 92
5th treatment with Alukart	Predialysis Postdialysis	396 216
7th treatment with Alukart	Predialysis Postdialysis	267 110
8th treatment with Alukart	Predialysis Postdialysis	11 76
PATIENTS NO 2		
1st treatment with Alukart	Predialysis Postdialysis	308 172
4th treatment with Alukart	Predialysis Postdialysis	183 111

RESULTS

In our Hemodialysis Unit 68 patients were screened for possible Al intoxication. The mean serum Al concentration in these group of patients was 2.63 µg/L which is much below the mean values of outstanding European and Turkish hemodialysis centers (Figure 1). Eight of these patients (11.7 %) were found tohave values more than 50 µg/L and they needed further evaluation with DFO test. After the DFO test two patients (2.9 %) were found to be Al intoxicated, and were treated according to the above metioned protocol. Before the DFO test, patient 1 and 2 had serum Al concentrations of 51 and 79 µg/L, respectively. The serum Al concentrations after DFO test were 147 µg/L for patient 1 and 253 µg/L for patient 2, reflecting a positive test for Al intoxication in both of these patients. These patient were treated by DFO infusion followed by hemodialysis combined with Alukart hemoperfusion device for two months, according to the above mentioned protocol. Some of the serum Al values of these patients obtained during the treatment are listed in Table I. Patient 2 had frequent coagulation problem within the Alukart hemoperfusion device despite increased anticoagulant dose, so he could only have two succesful treatment sessions. It can clearly be seen that much of the serum Al is extraced effectively by the procedure.

DISCUSSION

Increased awareness on toxic effects of Al burden has led to restricted use of Al containing phosphate binders and took further attention on control possible contamination of dialysate with Al, and these resulted in decreased incidence of Al intoxication in patients with renal failure for the past few years (4). Although this study in our Hemodialysis Unit revealed that the incidence of Al intoxication was below the average of many centers in Europe

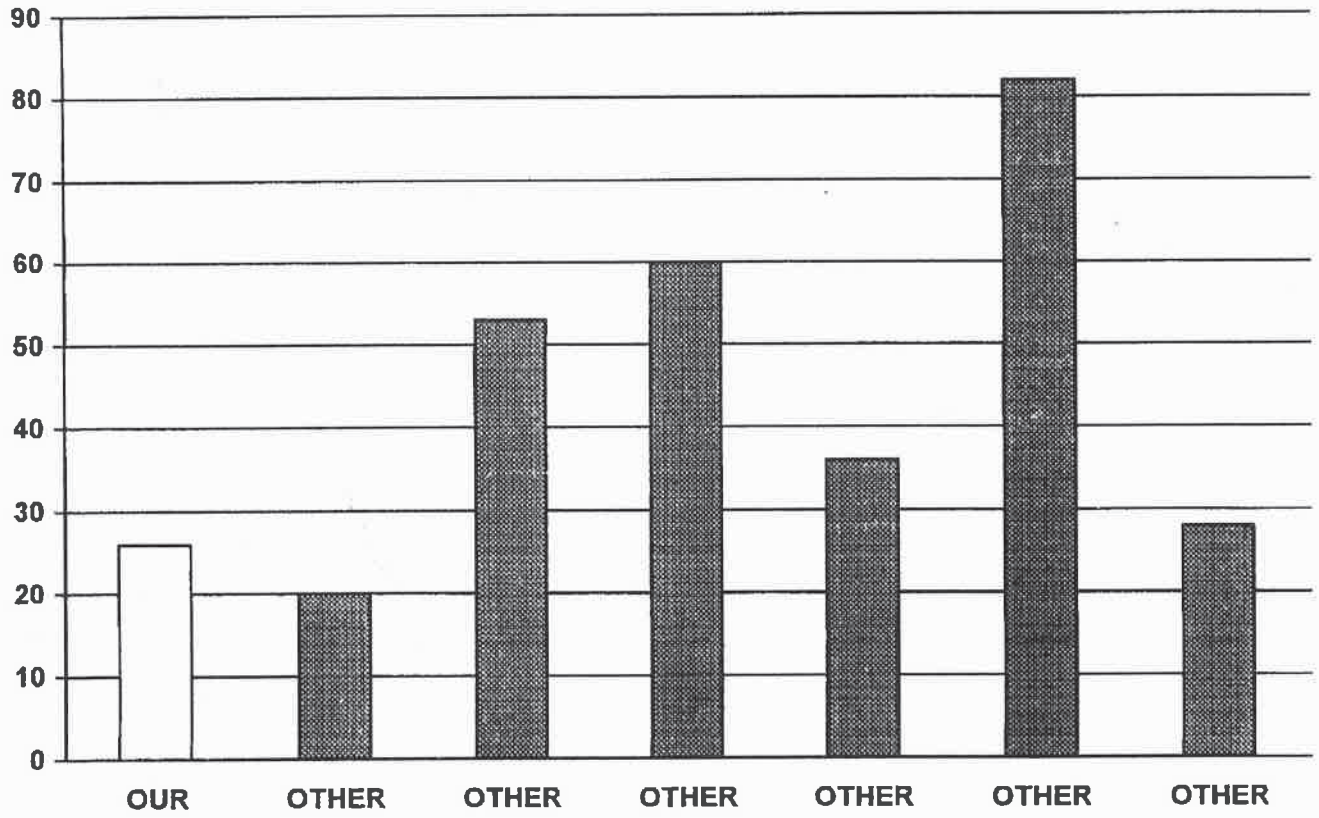

FIGURE 1: Meán serum aluminum concentrations in patients with end-stage renal disease, obtained in several hemodialysis centers.

and Turkey (Figure 1), it does not reflect the incidence nationwide but can only give an idea for a group of patients in one center in Turke. The first most important step to be taken to control Al intoxication is prevention by means of giving enough importance to physician education in prescribing Al containing phosphate binders and the use of appropriate dialysate in the hemodialysis centers. Athough it is expensieve and not readily available it is recommended to screen the patients wth renal failure for Al intoxication regularly (1, 2), imaging the economic burden of such a protocol on the health insurance in our country, wemay advocate the determination of serum Al only in those patients with clinical signs and symptoms. Al intoxicated patients must be treated with DFO infison followed by hemodialy sis combined with a hemoperfusion device that has active carcoal. When this hemoperfusion device is combined with a hemoperfusion device that has active charcoal. When this hemoperfusion device that has active charcoal. When this hemoperfusion device is combined with a high-flux polysulphone hemodialysis membrane, best results are achieved (4, 5, 9).

Whether giving enough emphasis and treating Al intoxication increase the quantity of lifein patients with renal failure remains to be proved but they surely increase the quality.

REFERENCES

1. Brem AS, DiMario C, Levy DL: Perceived aluminum related disease in a dialysis population. Arch Intern Med 151: 2541-2544, 1989.
2. Chazan JA Lew NL, Lowrie EG: Increased serum aluminum. Arch Intern Med 151: 319-322, 1991.
3. delmez J, Weerts C, Lewes-Finch J, et al: Accelerated removal of deferoxamine mesylate chelated aluminum by charcoal hemoperfusion in hemodialysis patients. Am J Kidney Dis 13: 308-311, 1989.
4. D'Hase PC, Couttenye M, Lamberts LV, et al: Diagnosis and treatment of aluminum related bone disease in dialysis patients, IIPJ 5: 47-57, 1993
5. Dimitros MV, DHase PC, Labrets LV, et al: Removal of aluminoxamine and ferrioxamine by charcoal hemoperfusion and hemodialysis. Kidney Int 41:1400-1407, 1992.
6. Grutzmacher P, Ehmer B, Messinger D, et al: Effect of aluminum overload on the bone marrow response to human recombinant erythropoietin. Contrib Nephrol 76: 315-323, 1989.
7. Joffe P, Olsen F, Heaf JG, et al: Aluminum concentrations in serum, dialysate, urine and bone among patients undergoing continuous ambulatory peritoneal dialysis. Clin Nephrol 32: 133-138, 1989.
8. Margaret JB, Cooper K, Schnall S, et al: Aluminum induced anemia: Pathogenesis and treatment in patients on chronic hemodialysis. Kidney Int 36: 852-858, 1989.
9. McCarthy JT, Milliner DS, Schmidt DF, et al: Deferoxamine and coated charcoal hemoperfusion to remove aluminum in dialysis patients.kidney Int 34: 804-08, 1988.
10. Novak M, Freundlich M, Zilleruelo G: Aluminium exposure and toxicity. J. ed Gastroenterol Nutr 9: 267-268, 1989.

JOURNAL OF ANKARA MEDICAL SCHOOL Vol 18, No 2, 1996 69–71

TUMOR MARKERS IN HEMODIALYSIS PATIENTS

Murat Duranay • Mehmet Şahin • Fahri Bayram • Musa Bali • Murat Kahraman*

SUMMARY

Serum levels and the incidence of elevated levels of several tumor markers were measured in 22 hemodialysed patients without clinical evidence of neoplasm. The tumor markers evaluated were carcinoembryonic antigen (CEA), CA 125, CA 15.3, CA 19.9, α-fetoprotein and beta human chorionic gonadothropin (ß-HCG). Several tumor markers (CEA, CA 125, Ca 15.3, CA 19.9) show a high false positive rate and may be unraliable for monitoring malignancies in hemodialysis patients, while the other markers (ß-HCG and α-FP) evaluated appear to maintain their specificity in this situation.

Key Words: *Chronic renal failure, Tumor markers, Hemodialysis.*

Tumor markers are important parameteres for the diagnosis and prognosis of many malignancies. These high molecular weight proteineous substances used in estimating the response of malignancy to therapy are produced by the metabolism of neoplastic or embryogenic cells (9).

Different numbers of clinically used tumor markers are present in the sera of healthy individuals though at low levels. Sensitivity and specificity of these markers are low and know ledge about their metabolism is scarce (3).

There is still controversy as to whether or not the incidence of malignancies is increased in uremic patients. Serum level of tumor markers in these patients have some features, about which some trials were published (1, 4, 6, 7, 8).

In this study serum leves of several tumor markers were measured in patients who had chronic renal failure and regularly hemodialysed.

MATERIALS AND METHODS

Twenty-two patients, 9 female and 13 male, with end-stage chronic renal failure and having regular hemodialysis are included in this study. They did not have any neoplasm clinically.

24 hours after the hemodialysis blood samples were drawn and by solid phase immunoradiometric method, serum levels of CEA, αFP, ßHCG, CA 15.3, CA 19.9 and CA 125 were measured.

Mean age of the patients was 31.18 ± 6.91 (ranging between 25-65 years) and the length of hemodialysis program was 22.36 ± 10.09 months on the average (2-92 month). Knowledge about patients are summarized in Table I.

Table I. Patients Characteristic's.

	n(%)
Age (year)	31.18 ± 6.91
Sex (F/M)	9/13 (41/59)
Time on dialysis (months)	22.36 ± 10.09
Primary Diagnosis	
Chronic Glomerulonephritis	9 (41 %)
Chronic Pyelonephritis	5 (22.7 %)
Polycystic Kidney	2 (9.1 %)
Hereditary Nephritis	1 (4.5 %)
Unknown Etiology	5(22.7 %)

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Table II. Mean Values and percentage of patients with increased serum levels of the different tumor markers studied.

marker	patient group	control group	increase n (%)	normal values	P
B-HCG (MU/ml)	6.46 ± 0.96	3.73 ± 0.51	21/22 (95)	0.0-10.0	NS*
CEA (ng/ml)	4.52 ± 1.3	1.44 ± 0.66	7/22 (32)	0.0-3.0	<0.05
αFP (ng/ml)	2.40 ± 0.43	2.08 ± 0.41	0/22 (0.0)	0.5-8.5	NS
CA 19.9 (U/ml)	31.3 ± 9.2	9.55 ± 1.60	9/22 (41)	0.0-24.0	<0.05
CA 15.3 (U/l)	21.62 ± 2.7	10.70 ± 1.3	7/22 (32)	0.0-20.0	<0.01
CA 125 (U/ml)	47.20 ± 21.0	5.90 ± 1.2	10/22 (45.4)	3.0-28.0	<0.05

* Not Significant

A group consisting of 17 healthy people, 7 female and 10 male, with mean age of 27.61 ± 3.45 (22-38 years) was used as a control.

Student square test and regression analysis were used for the statistical evaluation of the results. $p < 0.05$ was assumed statisticaly significant.

RESULTS

Table II summarize the levels of the different tumor markers in patients and control groups.

Serum levels of CEA, CA 15.3, CA 125 and CA 19.9 were significantly higher in the study group with respect to control group. On the other hand no significant difference was observed for ßHCG and αFP between two groups.

Multiple variance analysis showed no statisticaly significant increase in more than one tumor markers. No correlation was found between the increased serum level of tumor markers and patient's age, duration of hemodialysis and duration of the disease. Similarly, no correlation was found between serum levels of these markers and serum creatinine or BUN.

DISCUSSION

Tumor markers are produced by neoplastic cells. But normal tissues can produce them in low amounts, so they may be observed in healthy individuals at low concentrations. Their levels may increase in some non-malignant diseases (chronic bronchitis, pancreatitis, ulserative colitis, cirrhosis) (1, 3).

In our study CEA level was high in 32 % of patients, and it's compatible with literature. Serum CA 125 level was found high in 45 % of the patients. It was interesting to find the serum level of CA 125 fifteen times higher than normal in a patient with dialysis ascites. It has been reported that serum levels of this marker are increased in patients with ascites due to different etiologies (2, 3, 5). In fact, CA 125 having high specificity and sensitivity for over adeno ca, is known to be increased in all ascitic cases (2). As well-known, CA 19.9 is increased in cancer of pancreas. In this sutdy it was normal in 41 % of patients. CA 15.3 which is an important marker of breast cancer was found high in 7 patients (32 %). Result for CA 19.9 and CA 15.3 were similiar to those in previous studies (3, 7). There are also some studies reporting no significant difference in the level of these markers (4).

In all of our patients, serum α-FP level was normal. This result is similar to those of Cases et al (4) but not consistent with that of Zeferau et al (9).

One possible explanation for the elevated serum leves of some tumor markers in uremia is the fact that renal tubules play an important role in the metabolism of peptides and proteins (3). Their clearance decreases in renal failure. Besides, their clearence through dialysis membrane is also insufficient. It's difficult to explain normal α-FP level in uremic patients by this mechanism. It may be due to increase in production and to decrease in renal metabolism (3, 9).

As a result, in the presence of chronic renal failure several tumor markers (CEA, CA 125, CA 15.3, CA 19.9) are elevated above reference values. In a substantial number of patients, making them unreliable for monitoring malignancies in uremic patients, while the other markers evaluated appear to maintain their specificity. Since they are expensive tests, especially in patients with renal failure and hemodialysis, they should be requested according to their sensitivies.

REFERENCES

1. Ammon A, Eiffert H, Weber MH, Rummel J, Niemann J: Tumor markers in dialysis-dependent renal failure. A comparison of the mucin-like carcinoma antigen, CA 15.3, CA 125, CA 19.9 and CEA antigens. Onkologie, 11 (6): 260-262, 1988.
2. Bergmann JF, Beaugrand M, Labadie H: CA 125 (Ovarian tumor-associated antigen) in ascites liver diseases. Clin Chim Acta, 155: 163-166, 1986.
3. Cases A, Filella X, Molina R, Ballesta AM, Lopez-Pudret J, Revert L: Tumor markes in chronic renal failure and hemodialysis patients. Nephron 57: 183-186, 1991.
4. De Santo NG, Veneroso S, Capodicasa G, Crisel A, Giardano C. Tumor markers in uremia: Carcinoembrionic antigen, neuronspecific enolase, carbohydrate antigen CA 50 and alpha-fetoprotein. Am J Nephrol, 6: 458; 463, 1986.
5. Durand-Zaleski I, Rymer JC, Roudot-Thoraval F, Revuz J, Rosa J: Reducing unnecessary laboratory use with new test request form: Example of tumour markers. Lancet 342: 150-153, 1993.
6. Filella X, Cases A, Molina R, Jo J, Bedini JL, Revert L, Ballesta AM: Tumor markers in patients with chronic renal failure. Int J Biol Markers, 5(2). 85-8, 1990.
7. Odagiri E, Jibiki K, Takeda M, Sugimura H, Iwachika C, Abe Y, Khira K, Khiara Y, Iton M, Nomura T: Effect of hemodialysis on the concentration of the seven tumor markers carcinoembryonic antigen, alpha-fetoprotein, squamous cel carcinoma-related antigen, neuron-specific enolase, CA 125, CA 19.9, CA 15.3 in uremic patients. Am J Nephrol, 11(5), 363-8, 1991.
8. Waltz G, Kunzendorf U, Keller F, Fitzner R, Offermann G, Elevated tumor markers in hemodialysis patients. Am J, Nephrol, 8(3), 187-189, 1988.
9. Zeferos N, Digenis GE, Christophoraki M, Alexopoulos I, Kostakis A, Gyftaki H, Moulopoulos S: Tumor markers in patients undergoing hemodialysis or kidney transplantation. Nephron 59: 618-620, 1991.

JOURNAL OF ANKARA MEDICAL SCHOOL Vol 18, No 2, 1996 73–77

POSTPARTUM THYROID DYSFUNCTION; A REPORT FROM ANKARA

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SUMMARY

A high prevalence of postpartum thyroid dysfunction (PPTD) has been reported in several countries, but there have been no systematic studies of its prevalence in Turkey. In the present study, 24 euthyroid pregnant women with Grade I A or I B goiter (according to WHO criteria) who have been residing in Ankara and who never had any medications for thyroid disease, were evaluated clinicaly and with hormonal measurements during pregnancy and at postpartum 3rd, 6th, 9th, and 12th months. PPTD, which has detected in 4(16.6%) of the 24 women, developed at the 3rd postpartum month in one women and at the 6th postpartum month in the other three women. 2 of these 4 PPTD cases had high antimicrosomal (anti-M) antibody titers during the gestation periods; anti-M antibody titers of the other two PPTD cases were within normal ranges during pregnancy. During the postpartum period, 7 women had high anti-M antibody titers (29.1 %), and PPTD developed in 4 of them, as mentioned above. Of the 4 PPPTD cases, only one had a high antithyroglobulin (anti-Tg) titer during pregnancy. At the postpartum period 4 of the 24 women showed high anti-Tg antibody titers and PPTD was detected in two of them including the above mentioned case, who had a high titer of anti-Tg antibody during pregnancy.

PPTD is a common condition that occurs postpartum period. On the basis of the observation we suggest that only the women, who have high anti-M antibody titers and who show the clinic sings of thyroid dysfunction at postpartum period, should be evaluated with the thyroid function tests.

Key Words: Postpartum thyroid dysfunction, anti-M antibody.

The increased prevalence of postpartum thyroid dysfunction (PPTD) was called in to attention in some countries, especially in the regions, where the iodine intake was high (1, 2, 7, 9, 14, 15). The first well documented accound of PPT was by Robertson, a general practioner in New Zealand who described women from an iodine deficient area who developed hypothyroidism postpartum (13). The first report of PPT from Turkey was Koloğlu et al, who described 4 women developed painless thyroiditis in postpartum period (6). In general PPTD was declared to be occur in 5-7 % of all women (7). However, while a very high prevalence of PPTD, as 16.7 % was reported from Britain, some investigators emphasized an occurance rate of 1.1 % (2, 12). Genetic and environmental factors and using different criteria for the diagnosis of PPTD were suggested to be the source of these diversities between studies (3, 5, 12, 14). Besides this rather high prevalence of PPTD reported from Britain might be resulted from the selection of only the women who were positive for thyroid autoantibodies during their pregnancies (2). On the other hand predictive value of the high of anti-microsomal (anti-M) antibodytiters during pregnancy for the development of postpartum thyroid dysfunction, is a general opinion (2, 7, 11, 14, 15, 17). Contrary to this, a weak correlation between PPTD and antithyroglobulin (anti-Tg) antibodies was reported (1, 2, 4).

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The present study is planned to evaluate the prevalence of PPTD among women residing in Ankara, a region in Turkey, where the iodine intake is relatively lower than some other areas and to evaluate the relation between the antithyroid antibody levels during pregnancy and the occurence of PPTD.

SUBJECT AND METHODS

Twenty-four euthyroid pregnant women with grade I A or I B goiter according to WHO (Word Health Organization) classification who attended out-patient clinics of the Department of Obstetrics and Gynecology Disease of AnkaraUniversity Medical School between January 1991 to August 1994 were included in the study. Neither of the women had had any medication for thyroid disease and they had been residing in Ankara for at least 20 years. The mean age was 26.7 ± 3.8 (x ± SD) and clinical and hormonal evaluations were made during pregnancy and at postpartum 3rd, 6th, 9th and 12th months. Anti-M and anti-Tg antibodies were accepted as high when the titer was above the upper limit 50 IU/ml. Hormonal and clinical details of the cases, during pregnancy and after parturition are given in Table I.

Free thyroxine (Ft4) and free triiodothyronine (FT3) levels were measured by radioimmunoassay (RIA) (Amerlex-M kit for FT3, Gammacoat two step kit for FT4). Sensitive thyroid stimulating hormone (S-TSH), antimicrosomal antibody (anti-M) and antithyroglobulin antibody (anti-Tg) titers were determined by immunoradiometric (IRMA) method (IDS-Gamma BCT kit for s-TSH, TMab coated tubes ref. BC 1005 kit for anti-M, and TGab coated tubes ref. BC 1006 kit for anti-Tg) Al hormonal evaluations were made at the Endocrinoogy and Metabolic Disease Laboratory of Ankara University Medical School.

RESULTS

We found PPTD in 4 (16.6 %) of the 24 women, who were followed during pregnancy and postpartum one year (Tables I and II).

Anti-M antibody titers were high, during pregnancy, in 4 of 24 women, and PPTD was detected later,in two of these four cases (8.3 % of totals) at 3rd and 6th months of postpartum period (Table II, case no 5 and 10). However, in cases 3 and 20, who also developed PPTD, anti-M antibody titers were found to be within normal ranges during pregnancy. As seen in Table I, all patients with PPTD, showed high anti-M antibody titers, at the time of the diagnosis of PPTD. However, in one patient (case 10), although the anti-M antibody titer was high when PPTD developed, it was lower than the titer observed when this patient was pregant.

During the postpartum period, a total of seven patients had high anti-M antibody titers (29.1 %) and four of these seven developed PPTD as mentioned above. In one case, who had high anti-Tg antibody titer during the course of pregnancy and who developed PPTD at the 3rd onth postpartum, a higher level was observed at the time of PPTD diagnosis However, during the postpartum period, 4 of the 24 women exhibiedhigh anti-Tg antibody levels and PPTD was diagnosed in only two of them, including the above-mentioned case (case 3 and 5).

Serum FT3 and FT4 levels of the patients with PPTD were within normal range, except one patient who had elevated FT4 level (Table II, Case 20). In all cases with PPTD, who were clinically euthyroid, supression of s-TSH leve indicating a subclinical state of thyrotoxicosis, was observed. A diagnosis of PPTD was detected at the 6th month in three cases and at the 3rd month in one case. The elevated F4 level in one patient and the suppressed s-TSH levels in all PPTD cases, returned to normal during the follow-up period.

No clinical or subclinical hypothyroidism was observed in any case.

DISCUSSION

The clinical course of the postpartum thyroiditis (PPT) the most frequently seen form ofthe postpartum thyroid dsyfunction, generally, consist of these four phases (8).

1. Thyrotoxicosis as a result of the destructive phenomenon caused y an inflammatory process.
2. Euthyroid phase.
3. Hypothyroid phase.
4. Recovery phase.

Thyrotoxic phase occurs at 1-3 months postpartum and lasts for 1-2 months (14). In most ofthe patients, either the thyrotoxic or the hypothyroid

Table I. Hormonal and Clinical Charactheristics of our Patients During Pregnancy and Postpartum Period

		PREGNANCY (MEAN VALUES)				POSTPARTUM PERIOD (MEAN VALUES)				
PATIENT NR	AGE	ST_3	ST_4	TSH	ANTI-M	ST_3	ST_4	TSH	ANTI-M	CLINICAL STATUS
1	23	4.6	12.80	2.10	30.00	5.95	19.90	1.25	190.00	EUTHYROID
2	23	3.00	12.10	1.80	6.00	6.75	17.88	1.43	3.45	EUTHYROID
3	31	4.90	9.50	2.20	13.90	5.80	15.48	1.99	58.28	EUTHYROID
4	34	5.80	14.30	1.80	510.00	5.93	12.83	1.52	224.15	EUTHYROID
5	24	4.70	14.10	4.30	440.10	5.45	18.83	1.55	830.60	EUTHYROID
6	26	3.70	12.30	0.51	1.10	6.13	14.80	0.97	10.43	EUTHYROID
7	27	6.80	14.90	1.10	0.30	5.83	14.79	2.35	11.15	EUTHYROID
8	31	6.00	22.00	1.40	12.00	6.60	13.95	1.23	15.83	EUTHYROID
9	27	2.90	12.90	0.45	23.00	5.00	18.98	1.16	15.25	EUTHYROID
10	25	5.20	10.20	1.40	178.00	6.25	16.20	1.23	155.0	EUTHYROID
11	27	6.00	20.00	1.00	10.00	6.23	18.35	1.08	6.13	EUTHYROID
12	34	6.40	14.20	2.00	4.00	5.53	19.60	0.72	2.93	EUTHYROID
13	20	5.60	17.30	1.20	20.00	6.80	14.15	1.78	32.20	EUTHYROID
14	24	4.00	14.00	0.59	0.50	6.65	15.75	0.87	3.80	EUTHYROID
15	30	3.00	16.70	1.20	0.30	6.50	17.33	1.40	7.40	EUTHYROID
16	28	6.80	14.90	1.10	0.30	5.75	16.15	2.15	14.00	EUTHYROID
17	27	6.00	20.00	1.00	10.00	6.23	18.35	1.08	6.13	EUTHYROID
18	24	2.90	12.90	0.45	21.00	4.68	15.98	1.16	15.00	EUTHYROID
19	22	5.20	10.20	1.40	90.00	5.28	18.20	1.36	91.00	EUTHYROID
20	22	6.60	12.50	0.23	1.90	5.33	17.25	0.67	216.05	EUTHYROID
21	30	3.60	10.30	0.94	0.90	4.75	17.00	1.07	7.43	EUTHYROID
22	24	4.10	14.00	1.00	18.90	4.33	14.78	1.33	12.98	EUTHYROID
23	31	6.50	22.50	0.47	0.70	4.60	16.78	0.32	2.63	EUTHYROID
24	27	3.00	16.80	1.20	0.40	6.60	19.85	1.58	26.78	EUTHYROID

NORMAL VALUES OF OUR LABORATORY; Anti-M = 0-50 IU/ml, ST4 = 9.4-25 pmol/L, ST3 = 3-8.5 pmol/L, s-TSH = 0.32-4.1 μIU/ml

Tablo II. Charactheristics of 4 Patients, Who Developed PPT

PATIENT NR	AGE	DURING PREGNANCY MEAN VALUES ANTI-M	ANTI-Tg	PPT MONTH	PPT WAS DETECTED ST3	ST4	s-TSH	ANTI-M	ANTI-Tg	CLINICAL STATUS
3	31	13.90	38.0	6	7.1	14.4	**0.17	*136	136	EUTHYROID
5	24	*440.10	87.1	3	5.1	16.7	*0.21	*1512	217.1	EUTHYROID
10	25	*178.00	28.0	6	9.5	15.8	**0.10	*100	1.4	EUTHYROID
20	22	1.90	1.9	6	5.2	#26.5	**0.21	*233	10.1	EUTHYROID

STANDART VALUES: Anti-M = 0-50 IU/ml
ST4 = 9.4-25 pmol/L
ST3 = 3-8.5 pmol/L
s-TSH = 0.32-4.1 μIU/ml
Anti-Tg = 0-50 IU/ml

phase never occurs or is not recognized because of the mildness of the symptoms (1, 8, 10, 14, 16). The transient nature of the PPT and the mildness of the symptom, make the diagnosis difficult in many cases.

Although the anti-M antibody titers were high in 7 of our 24 cases during postpartum period, PPTD was detected in only four of them with an elevation in FT4 level in one case and suppression of s-TSH levels in all four cases, postpartum anti-Tg antibody titers were also high in two of these PPTD cases.

These results seem to be consistent with the reports,about the weak correlation between anti-Tg antibody titers, and PPTD deveopment (1, 4), and strong correlation with anti-M antibody titers and PPTD occurrence (2, 3, 7, 8, 10, 11, 14, 15, 16, 17).

Although I131 uptake of the thyroid gland was not performed,because of pregnancy and lactation in our cases, the spontaneous normalization of the FT4 and s-TSH levels, and the absence of clinical findings of thyrotoxicosis in the women, who were diagnosed as subclinical thyrotoxicosis according o the laboratory evaluation, led us rule out the diagnosis of Graves Disease, which can also be seen during the postpartum period.

Our observations are also consistent with the reported common asymptomatic clinical course of PPT (1, 8, 14, 16).

The subclinic thyrotoxic phase, was not followed by the hypothyroid phase, in our patients. This hypothyroid period might have been missed by us because of the three month intervals between the visits, but another possibility is that, hypothyroid phase never developed.

In the present study, we have found a 29.1 % anti-M antibody positivity, a 16.6 % anti Tg positivity and a 16.6 % prevalance of PPTD, as subclinic thyrotoxicosis during the postpartum period in our cases. Although 16.6 % prevalance of PPTD, in our patients, seems to be very important, absence of the prominent thyrotoxic signs in the women, occurence of the thyrotoxic phase with only the supression of the s-TSH level except one patient who had slightly elevated FT4 level and moreover never occurrence of the hypothyroid phase as mentioned above, do not indicate the necessity of evaluating all women for PPTD at postpartum period. On the other hand, it is hard to explain the reasons of findings, although subclinical, such a high prevalance of PPTD in our study. Genetic and environmental factors could play a role in this result, as suggested by others (3, 4, 12). Excess iodine intake as a environmental factor, was emphasized to be an important causal factor for the high prevalance of PPTD (1, 12, 15). However although a few, these were authors who proposed higher occurrence rate of PPTD in iodine deficency areas (7). Ankara region where this present study was performed, is an average low iodine intake area in Turkey, and as we did not compare the regions where the iodine intake was higher or lower than Ankara, it was impossible to evaluate the contributions of the iodine intake to our results.

Another point in our study, which must be stressed, was the development of subclinic thyrotoxicosis together with the elevations of the anti-M antibody titers in two patients (cases 3 and 20) in whom the anti-M antibody titers were within normal range during their pregnancies. As known, the common opinion is, the occurrence of postpartum tyroiditis, with a higher rate, in patients who have elevated anti-M antibody titers during pregnancy.

In conclusion, although we found a 16.6 % prevalence of PPTD as subclinical thyrotoxicosis in our study, the absence of the clinical signs and never occurrence of even of subclinic hypothyroidism phase, we are of the opinion that only the women, who have high anti-M antibody titers during pregnancy and who show the clinical signs of thyroid dysfunction at postpartum period, should be evaluated with the thyroid function tests. However to have better conviction, the number of the patients studied,must be increased.

In addition, as the women who had a diagnosis of PPT carry a higher risk of developing PPTD in their subsequent postpartum periods, these women must also be evaluated for the possibility of development of PPTD.

REFERENCES

1. Amino N: Postpartum thyroid disease. In: BB Bercu and DI Shulman (ed) Advances in Perinatal Thyroidology, Plenum Press, New York, 1991: p 167-10.
2. Funig HYM, Koloğlu M, Collins K, John R, Richards CJ Hall R, McGregor AM, Postpartum thyroid dysfunction in mid glamorgan. British Medical Journal 1988; 296-241-244.
3. Gernstein HC, How common is postpartum thyroiditis? A methodologic overview of the literature. Arch Intern Med 1990; 150: 1397-1400.
4. Glinoer D, Riahi M, Grün JP, Kinthaert J, Risk of subclinic hypothyroidism in pregnant women with asymptomatic autoimmune thyroid disorders. Journal of Clinical Endocrinology and Metabolism 1994; 79: 197-204.
5. Koloğlu M, Fung HYM, Darke C, Richards CJ, Hal R, McGregor AM: Postpartum thyroid dysfunction and HLA status. Eur J Clin Invest 1990; 20-56-60.
6. Koloğlu S, Koloğlu LB, Başkal N, Koloğlu M: Autoimmune Thyroid dysfunctions of postpartum period in Turkey. Balkan Contribution of Endocrinology and Metabolism 1985; I. Vol: 249-263.
7. Kompe O, Jansson R, Karlsson A.: Effect of L-Thyroxine and Iodine on the development of autoimmune postpartum thyroiditis. Journal of Clinica Endocrinology and Metabolism 1990; 76: 1014-1018.
8. Larsen PR, Ingbar S: The thyroid gland In: Wilson JD and Foster DW (ed) Textbook of Endocrinology, WB Saunders Company, Pennsylvania, 1992; p 357-487.
9. Livolsi V: Postpartum thyroiditis, The pathology slowly unraves. American Journal of Clinical Pathology 1993; 100-193-195.
10. Nurrow GN: Thyroid dysfunction in recently pregnant: Postpartum thyroiditis. Thyroid 1994; 4: 363-365.
11. Othman S, Phillips DI, Parkes AB, Richard CJ, Harris B, Fung H, Darke C, John R, Hall R, Lazarus JH: A log-term folow-up of postpartum thyroiditis. Clinical Endocrinology 1990; 32: 559-564.
12. Rajatanavin R, Chailurkit L, Tirarungsikul K, Chlayodeja W, Jittivanich U, Puapradit W: Postpartum thyroid dysfunction in Bangkok: A geographical variation in the prevalence. Acta Endocrinologica 1990; 122.2: 283-287.
13. Robertson HEW: Lassitude, coldness and hair changes following pregnancy and their response to thyroid extract. Br Med J 1948 (suppl); 2275-76.
14. Roti e, Emerson C: Clinical Review 29: Postpartum thyroiditis. Journal of Clinical Endocrinology and Metabolism 1992; 74: 3-5.
15. Salomon BL, Fein HG- Smallridge RC: Usefulness of antimicrosomal antibody titers in the diagnosis and treatment of postpartum thyroiditis. Journa of Family Practice 1993; 36: 177-182.
16. Singer P: Thyroidits, In: Greenspan FS (ed) The medical Clinics of North America, Thyroid Diseases, WB Saunders Company, Philadelphia, 1991; p 61-77.
17. Wemeau JL, Lerlerc L, Cappoen JP, Dewailly D, Leroy R, Decoulx M, Lefebvre J, Postpartum thyroiditis, 31 cases, Revue Medicine Interne 1989; 10: 107-111.

JOURNAL OF ANKARA MEDICAL SCHOOL Vol 18, No 2, 1996 79-81

PERIPHERAL NEUROPATHY IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE*

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SUMMARY

The aim of this study was to determine the effect of chronic respiratory insufficiency of peripheral sensory and motor nerve conductions. One hundred twenty six patients with chronic obstructive pulmonary disease (COPD) and 86 healty volunteers have been investigated neurologically and neurophysiologicaly. These patients had no obvious causes of peripheral neuropathy (PNP). Mean PaO_2 was 68.1 ± 15.8 mmHg, mean $PaCO_2$ 41.4 ± 7.5 mmHg, mean FEV1, 1.8 ± 0.6 L,and mean FEV1/VC 59.9 ± 15.7 %. Thirty-fourpatients (27 %) had detectable and subclinical PNP, when compared with the control group, a statisticaly significant slowing of peripheral sensory and peroneal nerve motor conduction velocity was noted ($p<0.05$).

Key Words: *COPD, peripheral, neuropathy.*

While the effects of chronic respiratory insufficiency on the CNS are well known, the influence of this condition of the peripheral nervous system has been the subject investigations only in 1980's. The first report concerning the peripheral neuropathy in patients with COPD was published in 1968, and in this study, of the 8 patients reported with COPD, 7 had peripheral neuropathy (1). Sebsequenty, other clinical studies have demonstrated an increased occurence of PNP in patients with COPD (4,6). However the prevalence and responsible factors for PNP in COPD are still under discussion. The current study was designed to reveal the incidence of peripheral neuropathy in patients with COPD.

MATERIALS AND METHODS

This stuy was carried out on 126 out-patients with COPD who were referred to the Chest Disease Department of Selçuk University Hospital. 111 patients were men and 25 were women. Mean age was 60.2±8.4 years. The mean values of spirometric parameters of the patients were as follows: Pao_2 68.1±15.8 mmHg, $PaCO_2$ 41.4 ± 7.5 mHg, FEV1 1.18 ± 0.6 L, and FEV1/VC 59.9 ± 15.7 %.

The patients had to meet the following criteria: no history or evidence of diabetes mellitus, neoplasm, severe malnutrition, renal failure, neurotoxic drug use, peripheral vascular disease and alcholism. Healthy 59 male and, 27 female people with mean age 59.3 ± 5.3 years were assigned to the control group.

After taking of history, patients were questioned about symptoms suggestive of peripheral neuropathy, such as paresthesia and weakness. They all underwent a complete neurological examination. motor and sensory deficits were documented as "present" or "not present". Deep tendon reflex abnormalities of the arms and legs were recorded.

Nerve conduction studies were done unilateraly. Motor velocity in the median, ulnar and peroneal nerves, orthodromic sensory velocity in the median, ulnar and peroneal nerves, orthodromic sensory velocity in the median and ulnar nerves, and antidromic sensory velocity in the sural nerve were tested. Surface electrodes were used in the study of sensory nerve conduction. Concentric needle electrodes were inserted in the abductor pollicis brevis, abductor digiti quinti, extensor digitorum

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brevis and median, ulnar and peroneal nerves were stimulated respectively for recording M responses. For electromyographic studies, a neuropact-4 device was employed.

The studies were done in a room with a temperature of 22-23°C. The conduction velocity values of control group and those of the patients with COPD were compared using the unpaired t test. A p value < 0.05 was considered statistically significant.

RESULTS

Of the 126 patients with COPD, clinical and subclinical PNP was present in 34 (27 %) patients. The patient group, when compared with the control group had a statistically significant slowing of sensory nerve conduction velocities in median, ulnar and sural nerves ($p<0.05$) (Table I).

The peroneal and median nerves motor distal latencies were significantly longer than the control group's peroneal and median nerves ($p<0.05$). However, no significant differences were found between the motor conduction velocities of peroneal and median nerves compared to the control group's values ($p>0.05$) (Table II).

DISCUSSION

The etiology of neuropathy occuring in association with chronic obstructive pulmonary disease (COPD) is not clear. There have been only several reports of PNP in patients with COPD in which prevalence rates based on clinical findings varied between 7 % and 80 % (1). On the basis of electrophysiological studies, the prevalence of PNP have been reported in 85 % of COPD patients(4). Currently, there is a consensus which suggests that COPD should be considered as a cause of PNP (1,4-6).

The lowest prevalence of PNP has been reported in a study consisted of 1561 patients. In this study, 20% of the patiets had clinically detectable and 4 % had subclinical PNP(7). Prevalence of PNP in our patients is in agreement with this study. In a recent study from our country, the abnormalities in electromyographic findings suggestive of nerve conduction impairment have been demonstrated in 36 % of 44 patients(8). A higher prevalence of PNP in COPD patients reported in previous studies may be based in part of methodologic differences.

The mechanism of high risk of neuropathy occuring in association with COPD isnot clear, how ever, there are several hypotheses. These hypotheses have been supported by a number of experimental studies that have demonstrated susceptibility of the peripheral nerve to acute and chronic hypoxemia(2).

Table 1. Sensory conduction velocities of the patients and control group (mean±SE).

	Median	Ulnar	Sural
Control Group	49.3±0.7	43.8±0.4	48.2±0.5
Patients Group	43.6±0.5	42.6±1.6	37.3±1.8
p value	<0.05	<0.05	<0.05

Table 2. Motor conduction velocities and distal latencies of the patients and control group (mean ± SE).

	Median		Peroneal	
	DL*	MCV**	DL	MCV
Control Group	3.31±0.1	53.8±0.5	4.6±0.1	48.6±0.5
Patients Group	4.66±1.0	53.5±0.4	5.8±0.1	44.6±0.1
p value	<0.05	>0.05	<0.05	>0.05

* DL = Distal latency, ** MCV = Motor Conduction Velocities.

Smoking and malnutrition are other possiblerisk factors in the pathogenesis of COPD-associated peripheral neuropathies. Tobacco smoke contains three potentially neurotoxic substances, nicotine, hydrocyanic acid and carbon monoxide(3).

In a histological study, Brambilla et al. demonstrated nonspecific nerve lesions,muscular atrophy, thickening of the basement membrane of vasa nervorum and endothelial proliferation in COPD patients with PNP. Therefore endoneural hypoxia may be one of the mechanisms responsible for alternations of peripheral nerve function in COPD(8).

In conclusion, PNP should be considered as a frequent complication of respiratory failure in patients with COPD. Our results show that the further investigations which will elucidate the possible factors causing PNP are needed.

REFERENCES

1. Appenzeller O, Parks RD, McGee J. Peripheral neuropathy in diseases of the resipiratordy tract. Am J Med 11:873-880, 1968.
2. Birismar T. Potential clamp analysis of the effect of anoxia on the nodal function of rat peripheral nerve fibers. Acta Physiol Scand 112:495-496, 1981.
3. Brambilla C, Paramelle B. Vila A, et al. Peripheral neuropathies and chronic obstructive pulmonary disease (COPD). Electrophysiological and histopathological study. Am Rev. Respir Dis 133:A-62, 1986.
4. Faden A, Mendoze e, Flynn F. Subclinical neuropathy associated with chronic obstructive pulmonary disease, possible pathophysiologic role of smoking. Arch Neurol 38: 639-642, 1981.
5. Moore N, Lerebours G. Senant J, et al. Peripheral neuropothy in chronic obstructive lung disease. Lancet 2:1311, 1985.
6. Narayan M, Ferranti R. Nerve conduction impairment in patients with respiratory insufficiency and severe chronic hypoxemia. Arch Phys Med Rehabil; 59: 188-192, 1978.
7. Nawak D, Brüch M, Arnaud F, et al. Peripheral neuropathies in patients with chronic obstructive pulmonary disease: A multicenter prevalance study. Lung 168: 43-51, 1990.
8. Sipahioğlu B. Kızıltan M, Hacıhekimoğlu A, Erk M,. KOAH ve nöropati, Solunum; 19:960-966, 1995.

JOURNAL OF ANKARA MEDICAL SCHOOL Vol 18, No 2, 1996 83–86

HISTOPATHOLOGICAL EVALUATION OF BIOPSY MATERIALS OF PATIENTS WITH CHRONIC RENAL FAILURE OBTAINED DURING ARTERIO-VENOUS FISTULA FORMATION

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SUMMARY

In this study, we evaluated that whether vascular structures which obtained during arterio-venous (A-V) fistula operation can give some clues about the primary renal pathology and metabolic status, and also can make any contribution for the success of A-V fistula. Twenty-six patients with chronic renal failure were included to the study. Hematocrit, blood urea nitrogen, serum creatinine, glucose, total calcium, inorganic phosphore, uric acid, total lipid, cholesterol, triglyceride and parathormon levels were measured. During the arterio-venous fistula operation a biopsy was taken from the artery and vein, and histopathologicaly examined under light microscopy.

Examination of biopsy materials revealed thrombus in vein wall in three patients, hyalinization in one and early-stage atherosclerosis in one patient. Primary renal pathology was chronic glomerulonephritis and amyloidosis in two patiets with thrombus. Arterio-venous fistula was failed in five patients. Three of these patients had normo-or hypotensive and two had hypertensive. The biopsy materials were abnormal in four of these patients.

In conclusion, biopsy materials which obtained during A-V fistula operation can give some clues about metabolic status of the patients, but can not contribute to the primary diagnosis.

Key Words: *Arterio-venous fistula, chronic renal failure, vascular structures.*

Currently there are problems in the diagnosis of the primary cause in end-stage renal disease (ESRD). By knowing the primary cause of the renal disease some additional treatment modalities could be applied for further treatment of these patients (1.13). In most of the cases renal biopsy could not be done, and therefore additional diagnostic modalities are utilized. In Turkey, rectal biopsy is often made to determine the cases with amyloidosis that is thought to be common. Another problem in the ESRD patients is the construction of a suitable vascular access for hemodialysis (HD) therapy. It is important for the patient to lead a good quality of life and for the length of hospital stay. The hospitalization period is usually prolonged due to complications seen after vascular interventions (6, 16).

Before constructing a vascular access for HD inadequate evaluation of vessels may be one of the major reason for arterio-venous (A-V) access failure. Especially it is important to examine the venous system by Doppler ultrasonography (3).

In this study we tried to determine whether vascular structures could give some clues about the primary renal pathology and metabolic status of the patient sand can make any contribution for the success of A-V fistula.

PATIENTS and METHODS

In this study a total of 26 patients, 14 female and 12 male, who applied to Ankara University Faculty of Medicine, İbn-i Sina Hospital, Department of Nephrology in 1992, with the diagnosis of ESRD, were analyzed. The mean age was 26.9±5.5 years (range 16-64). History and physical examination of

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these patients were carefully recorded. For each patient, hematocrit, blood urea nitrogen, serum creatinine, glucose, total calcium, inorganic phosphore, uric acid, total lipid, total cholesterol and triglyceride levels as well as serum parathormon (PTH) level were measured. None of these patients were given dialysis treatment for the last three month. Knowledge about the clinical status of the patients is presented in Table I.

Table I. Clinical features of the patients.

Age (year)	26.9 ± 5.5 (16-64)
Sex (F/M)	14/12
Primary Diagnosis	
ChronicGlomerulonephritis	8 (30.7 %)
Chronic Pyelonephritis	5 (19.2 %)
Amyloidosis	5 (19.2 %)
Polycystic Kidney Disease	2 (7.7 %)
Unknown	5 (23.0 %)

Surgical Technique

The region called snuff-box of the hand was entered,and end-to-side anastomosis between superficial branch of radial artery and a branch of radial artery and a branch of cephalic vein was performed by using continuous 7/0 prolene suture. During anastomosis procedure a biopsy was taken from the artery and vein, and histopathologically examined under light microscopy.

FINDINGS

Seventeen of 26 patients had blood pressure above the normal range, and in the remaining nine the blood pressure was either normal or below. Mean blood pressures were 155.1 ± 1.2/9.82 ± 1.1 mmHg. Laboratory findings are summarized in Table II.

Table II. Laboratory fimdings of the patients.

Hematocrit (%)	20.4 ± 2.9
BUN (mg/dl)	116.6 ± 17.3
Creatinine (mg/dl)	11.71 ± 2.46
Glucose (mg/dl)	107.5 ± 8.7
Total Calcium (md/dl)	7.99 ± 0.61
Inorganic Phosphore (mg/dl)	7.07 ± 1.09
Uric acid (mg/dl)	7.03 ± 1.66
Total Lipid (mg/dl)	897.3 ± 98.1
Triglyceride (mg/dl)	164.3 ± 31.9
Parathormon (ng/dl)	127.6 ± 63.4

Histopathological examination of the biopsy specimens revealed thrombus in vein wall in three patients (Figure 1), hyalinization in one (Figure 2) and early-stage atherosclerosis in one patient. Two of the three patients with thrombus in vein wall had chronic glomerulonephritis and amyloidosis afterwards. In the remaining the primary diagnosis was obscure.

FIGURE 1: The organized thrombus in vein wall x 100.

FIGURE 2: Hypocellular hyalinized appearance in vascular wall x 100.

In five patients A-V fistula failed, and their clinical findings are given in Table III. The access was non-functional in two of 17 hypertensive cases (11.1 %)and in three of 9 normotensive or hypotensive patients (33.3 %).Two of the three cases with a tendency to hypotension had amyloidosis.

The patient with early-stage atherosclerosis was a 31 year old female, and had chronic pyelonephritis. After ten months HD therapy, renal transplantation from living related donor was performed and a triple immunosuppressive therapy including prednisone, azathioprine and cyclosporine were started. Three years after the transplantation due to chronic rejection, an A-V access performed and HD therapy restarted.

Table III. Clinical and pathological features in patients who had A-V fistula failed.

No	Age	Sex	Primary Diagnosis	Blood Pressure	Histopathologic Finding
1	52	M	CGN	170/90	Thrombus
2	28	M	Amyloidosis	90/60	Hyalinization
3	53	F	Unknown	90/60	Thrombus
4	19	M	CPN	150/105	Normal
5	63	M	Amyloidosis	90/60	Thrombus

CGN: Chronic glomerulonephritis, CPN: Chronic pyelonephritis

DISCUSSION

In chronic renal failure, other organs and tissues as well as vasculer structures are significantly affected. Predominant pathological findings are accelerated atherosclerosis and calcification in the vessel wall (2,5). We observed atherosclerosis in a female patient who was 21 year old. When her age and sex are considered, early development of atherosclerosis can be explained by her clinical picture mentioned previously. As known in renal failure serum total lipid and triglyceride levels are increased (8). There is a defect in cholesterol transport system, and LDH degradation is decreased (9). Glucose containing fluids used during HD may provoke atherosclerosis by causing hyperlipidemia. Acetate used during HD had also been shown to increase cholesterol and trygliceride synthesis (7, 15). Apart from all these factors, hypertension that is seen nearly 85 % of patients may be another contributing factor in the development of atherosclerosis. It is well known that in renal transplant recipients risk of atherosclerosis in increased. One of the main reasons is hypercholesterolemia that is seen within six months after the transplantation. Here,steroids play an important role, too (12).

Another histophathological findings is thesoft tissue calcification. But we did not observe it. In CRF, calcification of small subcutaneous arteries and arterioles is not infrequent (4, 11, 14). But calibre of vessels used in A-V access formation is usually larger and, it should be kept in mind that in advanced hyperparathyroidism and calcium-phosphorus imbalance we may still observe calcifications. Including five patients with renal amyloidosis, when biopsies from vein and arteries were examined no positive result was obtained.

On the other hand, success rate of A-V access in CRF is greatly influenced by the status of venous system. Thrombosis is the leading cause for failure. In our study, all A-V fistulas were failed when thrombosis was present. For that reason to obtain a high rate of success preoperative carefulevaluation of vascular structures, especially the venous system, is essential.

In conclusion, biopsy specimens from arteries and veins give some clues about the metabolic status of the patient. However, histopathological examination of this kind of biopsy specimens from medium-sized vessels is far from contributing to the primary diagnosis.

REFERENCES

1. Advisory Committee to the Renal Transplant Registry: Renal transplantation in congenital and metabolic diseases. JAMA 232: 148-153, 1975.
2. Bagdade JD: Chronic renal failure and atherogenesis: Serum factors stimulate the proliferation of human arterial smooth muscle cells. Atherosclerosis 34: 243-248, 1979.
3. Buselmeier TJ, Rynasiewicz JJ, Howard RJ, et al: Fistulisation of shunt vasculature: A unique approach to fistula development. Br Med J2: 933-938, 1977.
4. Chan YL, Mathony JF, Turner JJ, et al: The vascular lesions associated with skin necros in in renal disease. Br J Dermatol 109: 85-95, 1983.

5. Ejerblad S, Ericsson JLE, Ericsson J: Arterial lesions of the radial artery in uremic patients. Acta Chir Scand 145: 415-428, 1979.
6. Fedman HI, Held PJ, Hutchinson JT, et al: Hemodialysis vascular access morbidity in the United States. Kidney Int 43: 1091-1096, 1993.
7. Gonen B, Goldberg AP, Harter HR, et al: Abnormal cell-interactive properties of low-density lipoproteins isolated from patients with chronic renal failure. Metabolism 34: 10-14, 1985.
8. Hass LB, Wahl PW, Sherrad DJ: A longitudinal study of lipid abnormalities in renal failure. Nephron 33: 145-150, 1983.
9. Hsia SL, Perez GD, Mendez AJ, et al: Defect in cholesterol transport in patients receiving maintenance hemodialysis. J. Lab Clin Med 106: 53-61, 1985.
10. Ibes IS, Alferey AC, Huffer WE, et al: Arterial calcification and pathology in uremic patients undergoing dialysis. Am J Med 66: 790-796, 1979.
11. Janigan DT, Morris J, Hirsch D: Acute skin and fat necrosis during sepsis in a patient with chronic renal failure and subcutaneous arterial calcification. Am J Kidney Dis 6: 643-646, 1992.
12. Kasiske L, Umen AJ: Persistent hyperlipidemia in renal transplant patients. Medicine 66: 309-312, 1987.
13. Karakuer H, Grauman JS, Mc Mullan MR, et al: The recent U.S. experience in the treatment of end-stage renal disease and transplantation. N. Engl J Med 308: 1558-1563, 1983.
14. Meema HE, Oreopoulas DM: Morphology, progression of arterial and periarterial calcifications in patients with end-stage renal disease. Radiology 158: 671-677, 1986.
15. Morris RJ, Srikantaiah MV, Davidson WD: Effect of uremia on incorporation of acetate into rat plasma and tissue lipids. Metabolism 29: 311-316, 1980.
16. Palder SB, Kirkman RL, Whittemore AD, et al: Vascular access for hemodialysis. Ann Surg 202: 235-239, 1985.

JOURNAL OF ANKARA MEDICAL SCHOOL Vol 18, No 2, 1996 87-91

CLASSIC EXTRAPLEURAL TRANSSTERNAL THYMECTOMY VERSUS MAXIMAL THYMECTOMY FOR MYASTHENIA GRAVIS: Review of 213 Cases.

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Rıza Doğan**** • Ahmet Yüksel Bozer**

SUMMARY

A retrospective anaysis of the records of 213 patients with myasthenia gravis (81 males and 132 females, mean age 32 ± 11 years) who underwent thymectomy through median sternotomy from 1980 to 1993, were performed. The patients were divided into two groups according to surgical procedures (classic extrapleural transsternal thymectomy and maximal thymectomy), these two were divided again into two subgroups according to presence or absence of thymoma. The early mortality rate was 2.8 % (6 patients). Mean follow-up time was 6.7 ± 3.1 years, ranging from 1 years to 14 years. Clinical staging was determined preoperatively and postoperatively at 1 year and at last follow-up using Oosterhuis classification. We conclude that our results support the recommendation for maximal thymectomy in the treatment of patients without thymoma can be performed safely in patients with thymoma.

Key Words: *Myasthenia gravis, tymoma, thymectomy, maxial thymectomy.*

Myasthenia gravis (MG), remains a potentialy debilitating and life threatening disease despite progress in therapy(1). The benefit of thymectomy as part of the treatent of myasthenia gravis has been demonstrated since the initial observations of Blalock and associates in 1939(2) It is not possible to separate the relative importance of the surgical and the medical treatment, but the combined program, has considerable benefit and constituts a safe and effective regimen for the treatment of myasthenia gravis (1, 10, 13, 18). This report reviews the clinical course of 213 patients with myasthenia gravis treated with maximal thymectoy (MT) or classic extrapleural transsternal thymectomy (CETT) or standard thymectomy through median sternotomy.

MATERIALS AND METHODS

The records of all patients operated on for myasthenia gravis in Hacettepe University, Faculty of Medicine, Thoracic and Cardiovascular Surgery Department, between January 1980 and June 1993, were studied retrospectively. All patients were followed from 1 years to 14 years (mean 6.7 ± 3.1 years). Routine clinic and laboratory studies were carried out at varying intervas during follow-up.

Eary death was defined as death within 30 days of operation or death before discharge from the hospital.

Patients: 213 consecutive patients (81 males and 132 females) ranging in age from 9 to 71 years (mean age 32 ± 11 years) underwent tyhmectomy. Duration of symtoms prior to thymectomy ranged from 3 months to 6 years (mean 21 months ± 8 months). At the time of initia evaluation a variety of presenting sings and symptoms were noted. The majority of patients had dyspnea (86.9 %), weakness (79.8 %), fatigue (78.8 %) and diplopia (17.8 %) as a presenting symptom. Precise diagnosis were estabished with clinical features response to edrophonium chloride, electrophysiologic studies, mediastinal CT and demonstration of circulatory antibodies. Associated disordes were as follows: Diabetes mellitus in 8 patients, coronary artery disease in 5 patients, rheumatoid artritis in 4 patients,

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Table 1. Details the early mortality for combination of description of groups and clinical staging using Oosterhuis classification.

Preoperative Stage	Ia	Ib	IIa	IIb
Stage 0-	-	-	-	
Stage 1-	-	-	-	
Stage 229	4	28	2	
Stage 348 (1)	4	44	3	
Stage 421	5(1)	15(1)	3	
Stage 53(1)	1	2(1)	1(1)	

Numbers in parantheses are number of early mortality.

Table 2. Hazard ratio estimation for predictive factors for early mortality and detoriation of disease by Cox proportinal hazard models.

Predictive factors (**)	OR	CL	P value (**)
Age			< 0.05
<50 years	1.0		
>50 years	1.5	3.2-6.8	
Sex			> 0.05
Female	1.0		
Male	0.9	0.6-1.1	
Associated Disease			< 0.01
No	1.0		
Yes	6.1	4.8-7.2	
Preoperativestaging			< 0.01
<3	1.0		
>4	5.8	4.9-6.7	
Presence of thymoma			> 0.05
No	1.0		
Yes	1.0	0.8-1.1	
Duration of symtoms			> 0.05
< 1 years	1.0		
> 1 years	1.3	0.9-2.1	
Therapy with CS's			< 0.05
Yes	1.0		
No	4.7	3.1-6.9	

Abbreviations: OR: Odds ratio, CL: Confidence limits.

euthyroid goitre in 3 patients, lung carcinoma in 2 patients (Eaton Lambert phenomena were not diagnosed) renal failure in 1 patient and angiofollicular lymph node hyperplasia (Castleman disease) in 1 patient. There were two patients with solitary thymic cyst among patients with thymoma.

All patients had been treated medically prior to thymectomy. Anticholinesterase drugs were used in all patients preoperatively and were contiud during early postoperative periods. Corticosteroids (CS's) were used prior to opeation 128 patients. Preoperative treatment with CS's was similar in all patients and consisted of initial high dose daiy prednisone (1-1, 5 mg/kg/d) and then slowly tapered for 1-1,5 years to the lowest dose that maintained best control of symptoms. Postoperatively, CS's were discontinued when possible (according to clinical status).

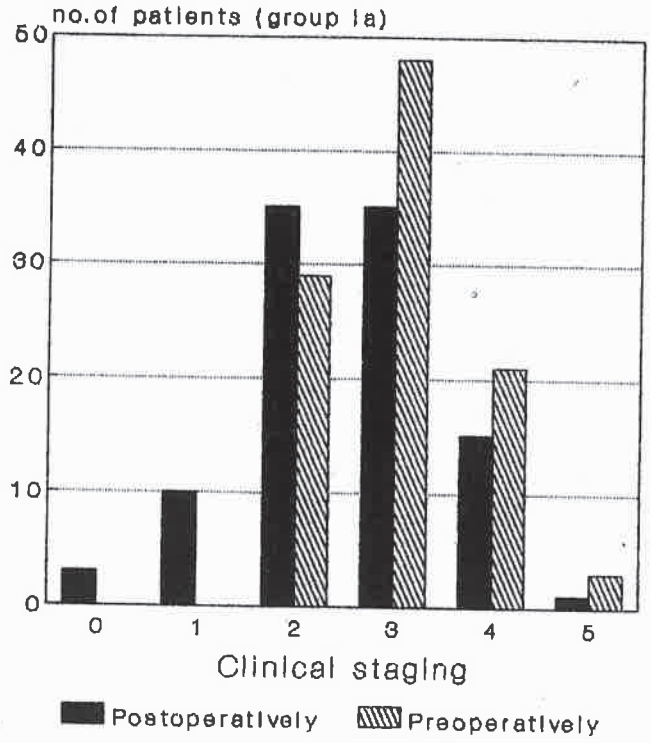
Patients with symptomatic generalized myasthenia gravis were selected for operations. Symptoms were severe and disabling in many patients and, in some, were progressive despite increasing amounts of medication. Tracheostomy had been performed in 7 patlets for respiratory failure prior to operation. Five of these were in cholinergic crisis and all of them were treated with plasmaphoresis. If a tracheostomy is in place at the time of operation the tracheostomy wound is packed and the patients lungs are ventilated by an oral endotracheal tube.

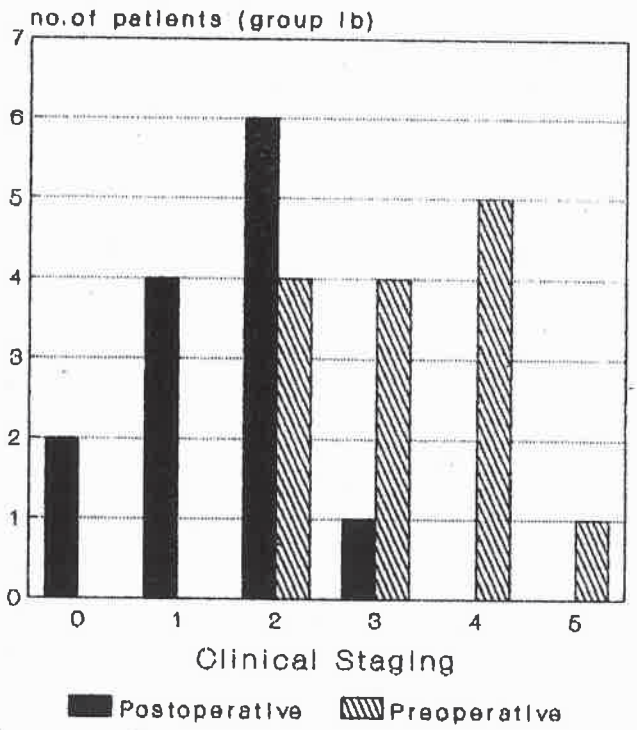
The patients were divided into two groups and these two were divided again into two subgroups. Classic extrapleural transsternal thymectomy (CETT) was performed in 115 patients (54%) (Group I) who cosisted 101 patients (47.4 %) without thymoma (Group Ia) and 154 patients (6.6 %) with thymoma (Group Ib). Maximal thymectomy (MT) was performed in 98 patients (46 %) (Group I) who consisted of 89 patients (42 %) without thymoma (Group IIa) and 9 patients (6 %) with thymoma (Group IIb).

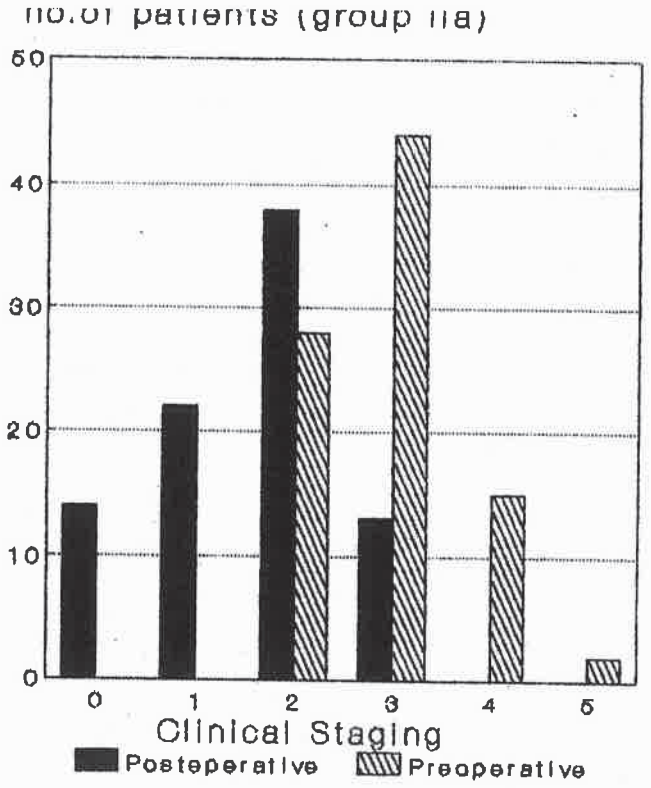
Surgical Procedure : Following median sternotomy and exposure anterior mediastinum, entire thymus including cervical stalks was dissected and completely excides with mediastinal fat and soft tissues for CETT.

In addition, the mediastinal plevra is incised bilaterally just beneath the sterum from the level of the thoracic inlet to the diaphragm for MT. An end block dissection from diaphragm to innominate vein and from hilum to hilum was performed. All including both mediastinal pleural sheets is excised. Both techniques were used according to surgeon's preference.

Most of patients were extubated either in the operating room or in the early postoperative period. Postoperatively 121patients needed prolonged mechanical ventilatory support for repiratory failure. Seven of them had tracheostoy prior to operation.







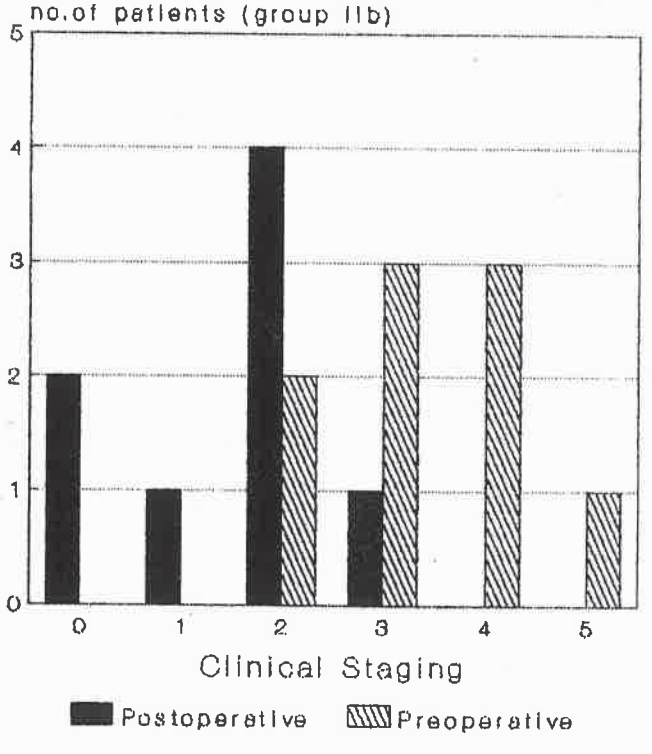


Fig I, a, b, c and d: Preoperative and postoperative clinical staging according to Oosterhuis at 1 year.

Patients discharged from the hospital were followed-up at 3 moths intervals during the first postoperative year. Thereafter, they were seen at least once a year. Routine clinic studies were carried out during follow-up. Medical records of 28 patients were lost two or more years after operation.

The clinical stages were graded preoperatively, postoperatively at 1 year and at last follow-up using Oosterhuis classification (14); stage 0: remission, no medication; stage 1: minimal signs and symptoms; stage 2: mildly disabled; stage 3: moderately disabled; stage 4 : severely disabled and stage 5 respiratory support needed. We rarely saw relapses (6 patients) and they were treated with anticholinesterase drugs. Only one patient required CS therapy.

The primary outcome measures investigated were early and late mortality at any time after operation. Comparison of group characteristic was done by the student's t test and the x^2 test. All descriptive statistics are expressed as mean ± standart error for continious data, probability ($p < 0.05$) was interpreted as evidence of a significant difference between groups (two-tailed test).

Risk factors were analyzed by means of the Cox proportional hazard method(3). Acturial survival was calculated with the Kaplan Meier method (8).

RESULTS

There were 6 early deaths (2.8 %). No significant difference between groups ($p > 0.05$). The causes of early deaths were as follows: Respiratory failure (prolonged ventilatory support) in 2 patients, mediastinitis in 2 patients, cerebrovascular attack in 1 patient and acute myocardial infarction in 1 patients. Predictive factors for early mortality are older age ($p<0.05$), preoperative poor condition ($p<0.01$) and presence of associated disease especially coronary artery disease ($p<0.01$). Details of the early mortality for combination of distribution of groups and clinical staging are listed in Table I.

Postoperative non fatal complications consisted of atelectasis in 14 patients (6.8 %), respiratory failure in 12 patients (5.8 %) pneumonia in 6 patients (2.9 %), bleeding and reexploration in 5 patients (2.4 %), mediastinitis in 4 patients (1.9 %) and phrenic nerve injury in 2 patients (1 %) Mediastinitis and pneumonia were seen in patient who were receiving CS's.

Pre and postoperative 1 year clinical stagings according to the Oosterhuis were shown in Fig Ia, b, c,and d. Thymectomy appear to offer the best prognosis for groups Ib, IIa, IIb patients.

During the median follow-up 6.7±3.1 years, there were 8 late deaths among remaining 207 patients. All of dthem died from unrelated causes. Acturial survival of the patients at 1 year and 5 years was 100 % respectively in all patients.

Hazard ratio estimation for predictive factors for early mortality and detoriation of disease by Cox proportional hazard models are shown in table II. No significant difference was found between patients with or without thymoma ($p>0.05$) for early mortality.

DISCUSSION

Although the relationship between thymus gland and myasthenia gravis is still not clear, it has been recognized for many years, that thymectomy can bring about remission or improvement of disease (4, 11, 15).

Stepwise Cox proportional hazard analysis revealed age at operation presence of associated disease, preoperative staging and CS's therapy as the most significant determinant factors of early mortality and improvement of disease in the present study. Our findings are similar to that of some investigators, but others have demonstrated no correlation between age, preoperative stage are clinical results (5, 6, 12, 17).

In our study, the age range of patients was 9 years to 71 years. We believe that the older age alone is not a contraindication for operation. The possible mechanism of the mortality and/or morbidity is not only related to age, but also related to associated disorders.

In our institution, thymectomy is undertaken for all patients with thymoma and those patients with generalized myasthenia gravis. Although, generally the ocular type is treated in a conservative manner for prolognged period.(9).

From a surgical point of view, a variety incisions may be used for thymectomy(16). The median sternotomy incision provides excellent exposure and we recommend transsternal approach for al cases.

According to our study, the excision of the thymic and mediastinal fat and soft tissue is adequate for patients with thymoma. There were two local recurrences,one of them was in group Ib and

the other was in group IIb. Although, the optimum resection remains contraversial either in patient with or without thymoma(7), in view of clinical improvement, MT have become out first choice of treatmet the management of patients without thymoma. Optimal results are to be found with MT in these patients.

Another interesting observation in our study is that duration of disease has no independent influence on outcome. Some authors have reported that shorter duration of disease is associated with more favorable results after thymectomy(1). Early thymectomy in myasthenia gravis is still contraversial. We also recommend eary operation, because it plays a major role in the treatment of myasthenia gravis. However stepwise logistic regression analysis showed that preoperative CS's therapy is independently and significantly predictive of mortality and morbidity and, to our opinon, it should be used preoperatively.

Although result of operation alone may not be evident for months, our study showed that status at 1 year postoperatively is strongy associated with long-term outcome.

In conclusion, thymectomy was found to be benefical to all patients with myasthenia gravis and improvement of the clinical status was achived in most of the patients after a years the operation. Our results, support the recommendation for MT in the treatment of patients without thymoma.

REFERENCES

1. Beghi E, Antozzi C, Batocchi AP, et al: Prognosis of myasthenia gravis: a multicenter follow-up study of 844 patients. J Neurol Sci 106:213-220, 1991.
2. Blalock A, Mason MF, Morgan HJ, Riven SS: Myasthenia gravis and tumors of the thymic region: report of a case in which the tumor was removed Ann Surg 110:544-561, 1939.
3. Cox DR: Regression models and life tables. J R Stat Soc 34: 187-220, 1972.
4. Durelli L, Maggi G, Casadio C, et al: Searching for prognostic factors at the time of thymectomy for myasthenia gravis. Ann NY Acad Sci 681: 556-560, 1993.
5. Evoli A, Batocchi AP, Provenzano C, Ricci E, Tonali P: Thymectomy in the treatment of myasthenia gravis: report of 247 patients. J Neurol 235: 272-276, 1988.
6. First WH, Trirumalai S, Doehring CB, et al: Thymectomy for the myasthenia gravis patient: factors influencing outcome. Ann Thorac Surg 57: 334-338, 1994.
7. Jaretzki A, Wolff M: Maximal thymectomy for myasthenia gravis. J. Thorac Cardiovasc Surg 96: 711-716, 1988.
8. Kaplan EL, Meier P: Nonparametric estimation from incomplete observation. J. Am Stat Assos 53: 457-481, 1958.
9. Lanska DJ: Indications for thymectomy in myasthenia gravis. Neurology 40: 1828-1928, 1990.
10. Maggi G, Cassadio C, Cavalo A, et al: Thymectomy in myasthenia gravis: Results of 662 cases operated upon in 15 years. Eur J Cardiothorac Surg 3: 504-511, 1989.
11. Marano E, Pagano G, Persico G, et al: Thymectomy for myasthenia gravis: Predictive factors and long-term evaluation. Acta Neurol Napoli 15(4): 277-288, 1993.
12. Mulder DG, Graves M, Hermann C: Thymectomy for myasthenia gravis: recent observation and comparisons with post experience. Ann Thorac Surg 48: 551-555, 1989.
13. Olanow CW, Wechser AS, Sirotkin-Roses M, et al: Thymectomy as primary therapy in myasthenia gravis. Ann NY Acad Sci 505: 595-600, 1987.
14. Oosterhuis HJGH: The natural course of myasthenia gravis: a longterm folow-up study. J Neurol Neurosurg Pschiatry 52:1121-1127, 1989.
15. Osterman PO: Current treatment of myasthenia gravis. Prog Brain Res 84: 151-161, 1990.
16. Otto TJ, Strugalska H: Surgicaltreatment for myasthenia gravis. Thorax 42: 199-204, 1987.
17. Papatestas A, Genkins G, Kornfeld P, et al: Effects of thymectomy in myasthenia gravis. Ann Surg 206: 79-88, 1987.
18. Perlo VP, Poskanzer DC,Schwab RS, et al: Myasthenia gravis: evaluation of treatment in 1355 patients. Neurology 16:431-439, 1966.

JOURNAL OF ANKARA MEDICAL SCHOOL Vol 18, No 2, 1996 93–95

LYMPHANGIOMA OF THE HEAD AND NECK

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SUMMARY

Lymphangioma usually presents in infacy or early childhood as compressible masses and remains a complex entity in term of its developmentand management. Twelve patients whith lymphangioma received surgical thrapy at Hacettepe University Medical Faculty. In 3 patients more than one operation is required to control the disease. Athough many different treatment modalities have been recommended in the literature, surgical excision remains the treatment of chocie.

Key Words: *Lymphangioma, neck, surgery, tumor.*

Cystic hygroma and lymphangiomas are lymphatic malformations caused by blockade of primordial lymph channels in embryologic life (8.9). Cystic hygroma was first defined by Redenbacher (1) in 1828 as 'Ranula congenita'. These lympahatic originated lesions have been classified as neoplasm or hamartoma, but today they are generally considered as congenital developmental obnormalities (6, 10).

Lymphangiomas are mostly localized in head and neck area and especially in the cervical region. They are also seen in axillary and pectoral regions, mediastinum, abdomen thigh and arm. Most common inital symptom is painless lump. Sudden increase in size due to infections and bleeding and sometimes spontaneous regression may be seen. In this article, patients with head and neck lymphangioma who admitted to our clinic are presented and their surgical results are discussed.

MATERIAL and METHOD

Twelve cases of head and neck lymphangioma or cystic hygroma were admitted to the Department of Otolaryngology-Head and Necek Surgery in Hacettepe University Medical Faculty between 1974 and 1992. Cutaneous lymphangioma cases were not considered.

There were seven male and five female patients aged between 1.5 and 32 years. Mean age was 11.1 years. They were admitted to the hospital 5 to 96 months after the onset of their symptoms. Mean duration was 37.4 months. Five of the patients had a lump at birth.

Nine patients presented with a neck mass, 7 of these patients had the mass on the left side, 2 on the right side. Two patients had lesions in tongue and one in right parotid region. One patient had respira-

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tory distress beside neck mass. This patient underwent surgery three times in other medical centers and tracheotomy was performed because of the respiratory distress.

RESULTS

Total excision of the mass was performed in 6 patients and partial excision in the 3 patients with neck masses. A second stage excision was performed to these three patients with advanced lesions. In two patients internal jugular vein and in one patient external carotid artery were ligated. One temporary facial nerve paralysis, one hypoglossus nerve paralysis and one temporary. Horner syndrome were observed. One patient had wound infection postoperatively.

In the patient who had been operated three times in other centers, a tracheotomy was performed because of respiratory distress and only a partial resection could have been done because of the extension of the mass into the mediastinum. Respiratory distress disappeared but recurrence occured 6 months later.

Partial glossectomy was performed in two cases with lymphangioma in tongue. Aspiration, and articulation problem were seen in one patient with a large mass. A partial parotidectomy was performed in the patient with a mass in the right parotid region without any complication. There was no mortality in any of the cases.

Nine of the twelve patients were followed in the postoperative period. In three cases there were recurrences in 6 months (% 33.3). Two of the recurrences were in the neck and one in tongue and they were all in the original locations. All of them were reoperated and the disease was taken under controll in two cases. However, in the third patient only subtotal resection was done, because of the mediastinal involvement (11.1 %).

Postoperative follow–up period ranges between 1.5 and 10 years (mean 44.5 months) in patients. All of the patients were free of tumor except one in whom subtotal excision was performed.

DISCUSSION

Lymphangioma and cystic hygroma are rare entities. There is no sex predominance (6). Cervical region is the most common sight for lymphangiomas(11). Lymphatic system is more dense and complex in left cervical region so lymphangioma is commonly seen on the left side. In our cases 58 % of masses were on the left side.

Most of the cases are found in newborn or in young pediatric age oruop. Eighty to ninety percent of cases are diagnosed in the first 2-5 years of lie. Adult cases are also seen. Fourty-one percent our cases had a history of lump at birth. In congenital cases, diagnosis is not difficult. CT or MRI is helpful for surgery, to investigate the mediastinal extension or relationship of lesion with larynx, esophagus and common carotid artery.

Lymphangiomas are classified under three groups according to Landing and Farber (7):

1. Lymphangioma simplex : Capillary like thin walled lymphatic channels are seen.
2. Cavernous lymphangioma: Dilated lymphatic channels are seen.
3. Cystic hygroma : Large multiloculated cysts are seen.

Mostly these three forms are seen together. Bill and Sumner (2) believe that there is no histopathologic difference between these groups, but according to these authors lymphangioma is formed in dense tissues like the tongue and cystic hygroma is formed in loose tissues like the neck.

Spontaneous regression has been reported in these lesions (3), but delayed surgery will cause the enlargement of lesion, and excision will be more difficult. Aspiration, sclerosing agent injection and radiotherapy are alternative methods. Aspiration is the initialy applied method but recollection may be seen, and complete aspiration is not possible in multicystic lesions. Sclerosing agent injection is reported by many authos (3, 4) but it has many complications. Radiation therapy is reported to be successful as a primary treatment modality(5).

We believe that surgery is to be the most reliable treatment modality. In our cases results of surgery are quite successful, especially when total excision could be performed. Other treatment methods may be helpful in inoperable cases or may be given as an adjuvant treatment.

REFERENCES

1. Barrand KG, Freean NV: Massive infiltrating cystic hygroma of the neck in infancy. Arch Dis Childhood. 48: 523, 1973.
2. Bill AH, Sumner DS: A unified concept of lymphangioma and cystic hygroma. Surg Gynecol Obstet. 120: 79, 1965.
3. Bromhead IW: Cystic hygroma of the neck. Br J Plast Surg. 17: 225, 1964.
4. Crawford BS, Vivakananthan MB: The treatment of giant cystic hygroma of the neck. Br J Plast Surg. 26:69, 1973.
5. Figi FA: Radium in the treatment of multilocular lymph cysts of the neck in children. Am J Roentgenol. 21: 473, 1929.
6. Kennedy TL: Cystic hygroma-lymphangioma a rare and still unclear entity. Laryngoscope. 99:1, 1989.
7. Landing BH, Farber S: Tumors of the cardiovascular system. In: atlas of tumor pathology. Washington D.C. Armed Institute of Pathology, 1956.
8. Ricciardelli EJ, Richarson MA: Cervicofacial cystic hygroma. Arch Otolaryngol Head Neck Surg. 117: 546, 1991.
9. Sabin FR: On the origin of the lymphatic system from the veins, and the development of the lymph hearts and thoracic duct in the pig. Am J Anat 1:367, 1902.
10. Takato T, Fukuda O, Ohhara Y: Hamartoma of the tongue: Two case reports. Plastic and Reconstuctive Surgery 2: 258, 1985.
11. Ward GE, Hendrick JW, Chambers RG: cystic hygroma of the neck. West J Surg Obstet Gynecol 58:41, 1950.

JOURNAL OF ANKARA MEDICAL SCHOOL Vol 18, No 2, 1996 97–100

CLAM SIGMOIDOCYSTOPLASTY IN NEUROGENIC BLADDER DYSFUNCTION

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SUMMARY

Bladder augmentation with clam enterocystoplasty has been used successfuly in the treatment of patients with neurogenic bladder dysfunction refractory to conservative treatment. A total of 40 patients with high pressure, poor compliant neurogenic bladder who were refractory to conservative management underwent clam sigmoidocystoplasty. The mean follow-up time was 27.2 months (range 13-44 months). Mean bladder capacity increased from 127 (65-164) to 365 (300-413) ml. Mean filling pressure decreased from 99 (70-125)to 19.5 (15-30) cmH20. Thirty-eight of the 40 patients (95 %) were totaly continent day and night. Thirty-four patients performed clean intermittent self catheterization (CISC) every 4-6 hours and 4 patients voided spontaneously. In two patients the operation had failed probably due to sigmoidal patch ischemia and they required additional anticholinergic medication. Four patients who were on CISC had episodes of febrile urinary tract infectios as they had stopped CISC and tried to void by valsalva or suprapubic tapping. No other serious complications were encountered. We conclude that clam sigmoidocystoplasty is a suitable surgical procedure for the management of patients with a refractory neurogenic bladder.

Key Words: *Bladder augmentation, Clam sigmoidocystoplasty, neurogenic bladder.*

Bladder augmentation with bowel was first described by Miculicz almost a century ago (18) and widely used in the treatment of tuberculosis of bladder,interstitial cystitis and bladder carcinomas (2, 7, 10). Until early 1980s, patients with neurogenic bladder dysfunction were considered inappropriate candidates for augmentation cystoplasty (22). It is after the advent of clean intermittent self catheterization (CICS) that this procedure has gained widespread acceptance for the management of high pressure, poor compliant neurogenic bladders refractory to conservative therapies (16, 17, 19).

Choices of tissue to provide both increased capacity and compliance of the bladder include ileum, ileocecal segment, sigmoid colon and stomach (10, 15, 17, 23). Although some authors believe that the segment used for augmentation does not really influence the outcome (13, 22), many others prefer a certain bowel segment mainly based on anatomic adventages (21, 24).

Athough there is a general consensus about using a detubularized intestinal segment (10, 23) bladder wall resection in neurogenic bladder dysfunction is stil controversial (7). Much has been written about the results of clam enterocystoplasty procedure since it was first described by Bramble in 1982 (1) for the treatmet of primary detrusor instability. Since than there have been many reports indicating that it is an effective procedure in neurogenic bladders when the bladder is not too severely fibrotic (3, 5, 12).

We present our experience with clam sigmoidocystoplasty in 40 patients with high pressure, poor compliant neurogenic bladder dysfunction.

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MATERIALS AND METHODS

From October 1991 to June 1994, 29 men and 11 women with hyperreflex or hypertonic neurogenic bladder dysfunction underwent clam augmentation sigmoidocystoplasty. The mean age was 26.1 years (range 5-50 years). The etiology of the neurogenic bladder dysfunction in our patients are shown in Table I. Spinal cord trauma in 31 patients was the leading cause.

Table 1. Etiology of the neurogenic bladder dysfunction in 40 patients.

Etiology	No. of patients
Spinal cord trauma	31
Menigocele	4
Spina bifida	2
Herniated intervertebral disk	1
Mutiple sclerosis	1
Transvers myelitis	1
Total	40

All patients were previously failed with anticholinergic pharmacotherapy and intermittent catheterization. None of the patients underwent surgical procedure before a minimum conservativetherapy of 12 months.

Preperative evaluation of the upper and lower urinary tract included intravenous urography, water cystometrography with simultaneous abdominal pressure monitoring and surface sphincter electromyography with anal plug, voiding (spontaneous or with suprapubic tapping) cystourethrography, voiding transrectal ultrasonography and urethrocystoscopy.

Patients with a ceratinine clerance rate less than 40 ml/minute and those who were unwilling or not having the ability to perform unassisted intermittent self-catheterization were not accepted as suitable candidates for augmentation sigmoidocystoplasty.

The operation technique performed for bladder preparation was as Bramble described (1) with the modification of a sagittal plane bivalving of bladder instead of a coronal plane incision and the detubularized sigmoid patch was sutured to the bladder in 2 layers with uninterrupted absorbable sutures. In 6 patients with bilateral and in 3 patients with unilateral high grade vesicoureteral reflux, submucosal ureteral reimplantation was done at the tenia of the sigmoid colon. For urine drainage 2 Foley catheters were inserted into the reservoir,one through urethra and the other through an abdominal stab wound. In those cases whom we had performed ureteral reimplantation, rat-tail catheters were used instead of Foley catheter(s) so that no other stents were necessitated for ureteral splinting. We performed no other simultaneous additional procedure regarding sphincteric activity. The abdominal tube was removed on the 10th day, postoperatively. On the 15th postoperative day, if no leakage was seen on the cystogram, the urethral catheter was removed. Following the catheter removal, patients were observed for 3 to 4 additional days. The patients were discharged on CISC every two hours and were urodynamically evaluated every month for three months and then every three months for 12 months postoperatively. CISC intervals were decided according to the cystometric studies.

RESULTS

Average follow-up was 27.2 months (range 13-44 montshs). Urethral catheters were removed at a median of 18.6 days (range 14-34 days).

Postoperatively, mean bladder capacity was found to be 365 ml (range 300 to 413 ml) and the bladder compliance was good (Table II). All patients had a detrussor pressure less than 30cmH20 at 300 ml bladder volume. Pre and post-operative bladder capacities and filling pressures are shown in Table II.

By 3 months postoperatively 38 of the 40 patients (95 %) were totally continent day and night. Thirty-four patients with detrusor sphincter dyssynergia (DSD) performenced CISC every 4-6 hours and

Table 2. Pre and postoperative urodynamic findings.

	Preop.mean (range)	Postop.mean (range)
Cystometric bladder capacity (ml)	127(65-164)	365(300-413)
Mean maximum detrusor pres. (cmH20)	99(70-125)	19.5 (15-30)

4 patients voided spontaneously. Additional procedures were needed in 4 patients: Two had transurethral prostate resection due to prostatic enlargement, and the other two had bladder neck incision due to posterior ledge. In two patients the operation had faied (5 %) probably due to sigmoidal patch ischemia. However, they are doing well with oxybutinin hydrochloride, 5 mg orally 3 times daiy and CISC 4 times dailyl.

During follow-up, 4 patients who were on CISC had tried to void by valsalva or suprapubic tapping by the advisement of some other physicians, and they had episodes of febrile urinary tract infections. After appropriate antibiotic therapy and restarting to use CISC, they became asymptomatic. No other serious complications were encountered.

DISCUSSION

The goal of therapy for most patients with a hyperreflexic or low compliant neurogenic bladder has been to abolish the unstable detrussor contractions and lower detrussor pressure. In those cases refractory to conservative management, enterocystoplasty is usually effective in providing these aims(5). Compromised emptying is often accomplished through intermittent catheterization, as was necessary in 36 of our patients.

In an augmentation cystoplasty procedure some technical aspects are still contraversial. Whether the diseased bladder wall should be removed, which bowel segment should be chosen and in which shape the bowel segment be reconstructed are the three main factors of utmost importance. Several authors have recommended that the bladder should be subtotally resected in all cases in which enterocystoplasty was indicated (6, 24). On the other hand experience with the Clam technique since 1982 has shown that it is an easy procedure to perform and it comsiderably reduces the magnitude of the surgery. As many reports in the literature (2, 7, 22) our results have strongly supported that in patients with a poorly compliant bladder with grossly normal appearance there is no need for bladder resection, and clam procedure should be the procedure of choice.

Almost all segments of the bowel and stomach have been used in cystoplasty procedures. Each segment has its enthusiants and opponents and some have found widespread acceptance (7,9, 20). Several studies suggest that it is not the origin of the bowel segment but it is the shape of the segment which influence the outcome of the procedure (7, 15). Most reports note that using detubularised segments of bowel are more effective than tubular segments in preventing synchronized circular contractions with their resultant pressure increase and providing better storage (10, 23). We have used detubularized sigmoid patch and this has resulted in a very high success rate in our series.

Metabolic acidosis with subsequent bone demineralisation and osteoporosis (14), intestinal bacterial harboring (3), maligant transformation of intestinal mucosa and voiding difficulties due to mucus production (5) considerably limit the use of enterocystoplasties in several cases. In our series during an average follow-up period of 27.2 months we have not yet met any significant complications. Almost all patients had persistent or temporary pyuria but only 4 had symptomatic urinary infection with febrile attacks and all these had not used CISC as it was instructed. We have not administered any medical treatment for asymptomatic urinary tract infection unless urine culture yielded preudomonas, proteus or klebsiela. In the first half of the cases emptying difficulty by CICS due to mucus plugs was really a serious poblem. However, in the last 20 patients we routinely administered ranitidine as George et al. described (4) and observed an obvious descrease of mucus production. We have not seen significant electrolyte disturbances and spontaneous perforation during the follow-up. At the moment it is not possible to assess the likelihood of tumor formation.

Although the results of enterocystoplasties are most satisfactorial in bladder augmentation, and clam sigmoidocystoplastyis found to be a safe and efficient technique in this study, they are in fact not completely ideal bladder replacements due to several potential risks. In selected cases ureterocystoplasty(11) and seromuscular colocystoplasty lined with urothelium(8) have recently been reported as alternative bladder augmentation choices. Also the clinical outecome of neurostimulator implanation on recent reports has been extremely encouraging. However, more studies with more patients and longer folow-up periods are requested for proper evaluation of the efficacy of these new techniques and enterocystoplasty is stil the standard treatment for the hyperreflexic or hypertonic neurogenic bladder unresponsive to anticolinergics.

REFERENCES

1. Bramble, F.J.: The treatment of adult enuresis and urge incontinence by enterocystoplasty. Br J Urol. 54: 693-696, 1982.
2. Dounis, A., Abel, B.J., and Gow, J.G.: Cecocystoplasty for bladder augmentation, J Urol. 123:164-167, 1980.
3. Fenn, N., Conn, I.G., German, K.a., Stephenson, T.P.: Complications of clam enterocystoplasty with particular reference to urinary tract infection. Br J Urol. 69:366-368, 1992.
4. George, V.K., Gee, J.M., Worthley, M.I., Stott, M., Gashes, C.G.C., Ashken, M.H.: The effect of ranitidine on urine mucus concentration in patients with enterocystoplasty. Br.J.Urol., 70:30-32, 1992.
5. George, V.K., Russell, G.L., Shutt, A., Gaches, C.G.C., Ashken, M.H.: Clam, ileocystoplasty. Br J Uro. 68:487-489, 1991.
6. Gil-Vernet, J.M., Jr.: The ileocolonic segment in urologic surgery. J Urol. 94:418-422, 1965.
7. Goldwesser, B., Webster, G.D.: Augmentation and substitution enterocystoplasty. J Urol. 135:215-224, 1986.
8. Gonzales, R., Buson, H., Reid, C., Reinerberg, Y.: Seromuscular colocystoplasty lined with urothelium: experience with 16 patients. Urology, 45: 124-129, 1995.
9. Hautmann, R.E., Egghart, G., Frohneberg, D., Miller, K.: The ileal neobladder. J Urol., 139:39-42, 1988.
10. Hendren, W.H., Hendren, R.B.: Bladder augmentation: experience with 129 children and young adults. J Urol. 144:445-453, 1990.
11. Hitchcock, R.J.I., Duffy, P.G., Malone, P.S.: Ureterocysto plasty: the bladder augmentation of choice. Br.J Urol. 73:575-579,1994.
12. Holgersen, K.B., Kirkeby, L.T., Nordling, J.: Clam ileocystoplasty. Scand J Urol. 28:55-58, 1994.
13. Kerr, W.K., Gale, G.L., Peterson, K.S.S.: Reconstrictive surgery for genitourinary tuberculosis J Urol. 101:254-257, 1969.
14. Koch, M.O., McDougal, J.S., Hall, M.C., Hill, D.E., Braren, H.V., Donofrio, M.N.: Long-term metabolic effects of urinary diversion: a comparsion of myelomeningocele patients managed by clean intermittent catheterization and urinary diversion. J Urol. 147:1343-1347, 1992.
15. Light, J.K., Engelmann, U.H.: Reconstruction of the lower urinary tract: observations on bowel dynamics and the artificial urinary sphincter. J Urol. 133:594-599, 1985.
16. Linder,A., Leach, G.E., Raz, S.: Augmentation cystoplasty in the treatment of neurogenic bladder dysfunction. J Urol. 129:491-494, 1983.
17. Luangkhot, R., Peng, B.C.H., Blaivas, J.G.: Ileocystoplasty for the management of refractory neurogenic bladder: surgical technique and urodynamic findings. J Urol. 145:1340-1344, 1991.
18. Miculicz, J.: Zur operation der augeborenen Blasenspalte. Zentrabl. Chir., 26:641-645, 1899.
19. Raezer, D.M., Evans, R.J., Shrom, S.H.: Augmentation ileocystoplasty in neuropathic bladder. Urology, 25:26-29, 1985.
20. Reddy, P.K., Lange, P.H., Fraley, E.E.: Bladder replacement after cystoprostatectomy: efforts to achieve total continence. J Urol. 138:495-499, 1987.
21. Sidi, A.A., Reinberg, Y., Gonzales, R.: Influence of instestinal segment and configuration on the outcome of augmentation enterocystoplasty. J Urol. 136:1201-1204, 1986.
22. Smith, R.B., van Cangh, P., Skinner, D.G, Kaufman, J.J., Goodwin, W.E.: Augmentation enterocystoplasty a critical review. J Urol. 118:35-38, 1977.
23. Tammela, T.L.J., Lindell, O.I., Viitanen, J.K., Hellström, P.A., Kontturi,M.J., Lukkarinen, O.A.: Functional and urodynamic characteristics of bladder substitution with detubularised right colonic segment. J Uro. 67:298-302, 1991.
24. Zimman,L., Libertino, J.a.: Tchnique of augmentation cecocystoplasty Surg Clin North Am, 60:703-711, 1980.

JOURNAL OF ANKARA MEDICAL SCHOOL Vol 18, No 2, 1996 101–102

FUNCTIONAL ENDOSCOPIC SINUS SURGERY IN ADULTS

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SUMMARY

Functional Endoscopic Sinus Surgery (FESS) which has a long history in ENT surgery,became very popular in the last decade all over the world. Long term results of the large series have been appearing in the literature. Results of 208 adult patients operated using Messkerlinker technique in our clinic without any major complications are presented. Success rate of this surgery in the patients with sinus disease and nasal polyposis were found as % 80 and % 86, respectively, during 2 years of follow-up. Our results are comparable with the world literature.

Key Words: *Sinus surgery, Adults.*

Functional Endoscopic Sinus Surgery (FESS) which has a long history in ENT-Head and Neck Surgery, became very popular during the last decade all over the world. FESS's ability to cure the paranasal sinus disease functionally and eradicate the etiopathogenesis of the infection with minimal surgical trauma, made it major technique in paransal sinus surgery. Long term results of the large series have been appearing in literature recently (1, 2). Results of 208 patients, without any major complications which are comparable with literature are presented.

MATERIAL AND METHOD

From May 1990 to December 1993, 28 patients with chronic sinusits and/or nasal polyposis underwent FESS, Messerklinger's technique following medical treatment failure in 2nd ENT clinic of Ankara Numune State Hospital.

Follow-up period varied from 3 to 34 months (median 24 months). In the postoperative period antibiotics, antihistaminics and decongestants were prescribed for 10 days. In postoperative endoscopic care cruts in the operation cavity was removed on the 3th and 7th days after surgery. Endoscopic controls were undertaken on the second and sixth week.

In the patients with a prior history of allergy or with polyposis, topical corticorteroids and systemic antihistaminics were prescribed on the second week following surgery.

FINDINGS

Preoperative symptoms and their frequencies are summarized in Table I. The distrubution of pathology to sinuses as diagnosed by CT and endoscopic examination is also shown in Table II. A total of 208 patients underwent 329 surgical procedures (87 unilateral, 121 bilateral). The ages of patients varied between 19 and 65 (mean 42 years). There were 112 male and 96 female.

The distribution of the operations performed in 208 patients are summarized in Table III. Of the 186 patients folowed 20 months, 152 (% 82) were asymptomatic, 34 (19 of them had previous operations) stated that their preoperative symptom complaints remained unchanged. Of 118 patients with nasal polyposis, 101 (% 85) were asymptomatic 12 months following surgery.

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DISCUSSION

Recently, FESS as a surgical therapeutic technique, has been performed more fruquently in sinonasal disease. Though there are promising progress in this subject, there are difficulties in appraising and comparing the surgical results of sinonasal disease. Staging of this disease which is a dynamic process is hard and there is no widely accepted classification in literature. Because of this lack of universal classification, comparing results from differents centers may not be possible every time. In the literature, the success of this procedure is stated as the patients being as asymptomatic postoperatively. Rice (1) showed that in a series of 100 patients after a single surgical procedure, 83% of the patients stayed as asymptomatic in the postoperative 2nd year. Levine (2) gave a success rate of 88.3% in a series of 154 patients with nasal polyposis that undergone FESS and a rate of 80.2 %. In the present study, success rate of FESS was found 82 % for the all patients, this ratio is 85 % for the patients suffering from polyposis.

FESS which has potential serious and fatal complications must be performed by well educated surgeons, after a carefully designed course based on a very good theoretic knowledge. Levine (2)presented 8.3 % minor and 8.7 % major complication rate in 250 operations. Stankiewicz (5) presented 7 major, 19 minor complications in 90 patients. Stammberger (6) on the other handstated except 2 CSF leakage there are no major complications in his series of 4000 patients. In our series, in which 329 procedures were performed in 208 patients 62 minor and no major complications were noted. Complications in our surgica procedures are presented in Table IV.

This study shows that the results of FESS for sinonasal disease is comparable with the literature and quite promising in our population. We believe that we shall give better reliable results with larger numbers of cases with longer periods of folow-up in the future.

Table I. Preoperative Symptoms.

	%
Headache	95
Stuffy Nose	64
Anterior Nasal Discharge	20
Posterior Nasal Discharge	40

Table II. Pathologic Involvement of the Paranasal Sinuses on CT.

	%
Maxillary Sinus	56
Anterior Ethmoid	78
Posterior Ethmoid	28
Frontal Sinus	24
Sphenoid Sinus	11

Table III. Distribution of the Operations Perfomed in 208 patients.

	No.of Cases
Infindubulotomy	14
Infindubulotomy and Meatal Antrostomy	175
Posterior Ethmoidectomy	78
Sphenoidectomy	32
Total	329

Table IV. Complications of the Surgery.

	No.of Cases
Bleeding	15
PeriorbitalEchimosis	8
Injury of Lamina Paprycea	6
Snechia	27
Abnormal Bleeding Lead to Ceasing of the Surgery	6

REFERENCES

1. Levine HL et al. Functional endoscopic sinus surgery: Evaluation surgery and follow-up of 250 patients. Laryngoscope. 1990;> 100-79-84.
2. Messerklinger W. Endoskopische diagnose und chirurgie der rezidiverenden sinusitis. In: Krajina Z, ed. Advences in nose and sinus surgery; Zagreb Univ., Publ. 1985.
3. Rice DH et al. Endoscopic sinus surgery: Result at 2 year follow-up. Otolaryngol Head Neck Surg. 1989; 101:476-479.
4. Stammberger H. Functional endoscopic sinus surgery: Eur Arch Otolaryngol 1990; 247:63-76.
5. Stankiewicz JA et al. Complication in Endoscopic intranasal Ethmoidectomy: An update. Laryngoscope 1989; 99: 686-690.
6. Turgut S et al. Functional Endoscopic Surgery Congress Volum II, pp. 562-631. 1993.

JOURNAL OF ANKARA MEDICAL SCHOOL Vol 18, No 2, 1996 103–105

THE INVERTED PAPILLOMA OF THE NOSE AND PARANASAL SINUSES

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SUMMARY

In erted papillomas are rare lesions of nose and paranasal sinuses. Eight patients with inverted papilloma who were treated in the Department of Otolaryngology-Head and Neck Surgery at Hacettepe University Medical Faculty were presented. All patients were treated surgically. The tumor was excised in four patients with Caldwel-Luc and ethmoidectomy approach, and in the others with lateral rhinotomy (in one patient Wilson incision was also added) approach. Patients' symptoms, treatment and presence of concomitant malignancy were analyzed and discussed.

Key Words: *Nose, sinus, surgery, tumor.*

Inverted papilomas which arise from the lining membranes of the nose and paranasal sinuses are relatively unfamiliar lesions which have been reported in the literature under variety of titles. These lesions are true neoplasms of the noese and paranasal sinuses. It is often benign but malignancy can occur in 1 % to 53 % of cases. It is a rare growth, comprising between 0.5 % and 4.0 % of all primary nasal tumors. The etiology remains uncertain. Clinical behavior is marked by aggressiveness and tendency of recurrence (4, 5, 11).

Eight patients who were treated between 1970 and 1994 in the Department of Otolaryngology-Head and neck Surgery at Hacettepe University Medical Faculty were presented with a review of the literature.

MATERIAL AND METHOD

In the Department of Otolaryngology-Head and Neck Surgery at Hacettepe University Medical Faculty,the records from 1970 to 1992 were reviewed and 8 cases of inverted papilloma were identified. The patients who were not followed up, were not taken into consideration. Patients were assessed for presenting symptoms, treatment and pathologic findings. Concomitant malignancy was sought.

The eight cases were consisted of eight men over 45 years of age. These patients were seen with the complaints of bloody rhinorrea (two patients), nasal obstruction (six patients), epistaxis (three patients). One patient had epidermoid carcinoma with inverted papiloma at the surgical specimen. One patient developed malignancy during his follow-up.

All of the patients underwent nasal polipectomies several times before admission to our clinic.

RESULTS

Al of the patients were treated surgicaly. Four patients underwent surgery by Caldwell-Luc and ethmoidectomy and tumor excision from the nasal cavity and maxilary sinus. The tumor was excised in 4 patients with lateral rhinotomy (in one patient Wilson incision was also added) approach.

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Three patients were tumor free in the follow-up. Three patients have developed recurrence in a period of 2 months to one year. Two patients with malignancy were treated with partial maxilla resection, radiotherapy and chemotherapy. Follow up period ranged from 2 to 24 years.

DISCUSSION

Schneiderian papiloma, commonly caled inverted papiloma has more than 25 synonyms (1,8). Among these are epithelial papilloma, transitional cell papilloma, squamous papilloma and papilary adenoma.

The macroscopic appearence is that of an irregular, velvety lesion, red, pale pink or gray in color and polypoid in form. The characteristic microscopic feature of this tumor is the increase in thickness of the covering epithelium with extensive invagination into the underlying stroma(11).

An association between inverted papilloma and carcinoma is reasonably established. Published literature quotes overall incidence rates as ranging widely from 1.7 % to 53 % (4). A total 1.147 cases of inverted papilloma has been reported (6). In our series 2 of the 8 patients were shown to have malignancy. The question is that whether carcinoma develops de novo or true transformation occurs from inverted papiloma to squamous cell circinoma. Fechner (2) reviewed 300 cases of inverted papilomas and found only three cases (1 %) which appeared to have undergone malignant transformation. Lempertico, et al (3) in contrast, found 14 out of 170 cases (8.2 %). Our cases support the idea of malignant transformation. Another source of confusion is the difficulty in separating synchronous from metachoronous lesions. Most lesions are histologically bening, some show foci of carcinoma while others are virtually total squamous cel carcinoma with only small areas of papilloma. Carcinoma should be ruled out in the management of inverted papilloma.

Proposed etiologies for inverted papiloma have included allergies, chronic sinusitis, airborne pollutants and viral inducations (5, 8). However it is not clear whether these are the causes or the results of the disease. HPV have been proposed to play some partin the etiology of inverted papilloma (7, 12).

The most common physical finding is a unilateral polypoid mass causing nasal obstruction. Patients are often treated for various lengths of time for sinusitis or various rhinitises, allergic or non allergic. After a varying period of poor treatment response, these patients are referred to various specialties for assessment. All of our patients underwent nasal polypectomies before admission to our clinic.

Preoperative CT scanning has an important part in the therapy. It shows the extension of the lesion accurately and helps the surgeon in the management of the lesion.

Treatment of choice is surgery (4, 5). Medical therapy is only adjunct to clear specific complications such as sinusitis. Radiotherapy is used only for those cases with associated malignancy after surgery. It is evident that biopsy is mandatory to arrive at a histologic diagnosis but often the clinical suspicion is not there and as mentioned,most often the surgery first performed is polypectomy.

Lawson et al (4) reports recurrence rates ranging from 6 % to as high as 78 %. He divided the surgical treatment used in eight published series into limited and radical excisions. Limited excision resulted in recurrence between 41 % and 78 % of cases whereas more extensive surgery reduced this rate to an average of 13 %. Lateral rhinotomy approach (to have exposure) and extensive surgery is advised in the cases that have extension to the maxillary sinus in the manageent of inverted papilloma in the literature (1, 4, 5, 8, 9, 10). Patient cooperation and treatment compliance can be a significant problem. Often the diagnostic biopsy procedure will relieve the patient's complaints and it is difficult to get the patient to return for review. It is only the risk of associated malignancy possible transformation that convinces the patient of considering radical surgery. We advise conservative surgery for selected group of patients. Our criteria are as :

1. No previous nasal surgery.
2. Radiographic evidence that the lesion was limited to the nasal cavity with minimal extension into the ethmoid labrynth or to the antrum.
3. Experienced surgeon.
4. Close follow-up.

Our patient group was also treated according to the principles that was put forward above. The patients with extensive lesions were treated with extensive surgery but with organ preservation. When the lesions were restricted to nasal cavity our surgery was conservative and we did not have recurrence in this group of patients.

In conclusion, we advise a high degree of suspicion in polyps of the nose, and agree with the literature in the treatment of inverted papilloma to go as radical as the patient's situation permits and to add radiotherapy as an adjunt in associated malignancy.

REFERENCES

1. Calcaterra TC, Thompson JW, Paplia EE: Inverting Papilloma of the nose and paranasal sinuses. Laryngoscope 90: 53-60, 1980.
2. Fechner RE, Alford DO: Interted papilloma and squamous carcinomas. Arch Otolaryngol 88:73-78, 1968.
3. Lampertico P, Russel WO, Mac Comb WS, et al: Squamous papilloma of the upper respiratory epithelium. Arch Pathol Lab Med 7:293-302, 1963.
4. Lawson W, Le Benger J, Som P, et al: Interved papilloma; an analysis of 87 cases. Laryngoscope 99: 1117-1124, 1989.
5. Myers EN, Schramm VL Jr, Barness EL: Management of inverted papiloma the nose and paranasal sinuses. Laryngoscope 91: 2071-2084, 1981.
6. Pelausa EO, Fortier MAC: Schnederian papilloma of the nose and paranasal sinuses. The University of Ottowa experience. J. Otolaryngol 21:9-15, 1992.
7. Respler DS, Jahn A, Peter A: Isolation and characterization of papilloma virus DNA from nasal inverting (Schnederian) papillomas. Ann Otol Rhinol Laryngol 96:170-173, 1987.
8. Segal K, Atar E, Mov C, et al: Inverting papilloma of the nose and paranasal sinuses. Laryngoscope 96: 394-398, 1986.
9. Smith O, Gullane PJ: Inverting papilloma of the nose: analysis of 48 patients J Otolaryngol 16:154-156, 1987.
10. Suh KW, Facer GW, Devine KD, et al: Inverting papiloma of the nose and paranasal sinuses. Laryngoscope 87:34-46, 1977.
11. Vrabec DP: Inverted schnederian papilloma; a clinical and pathological study. Laryngoscope 85:186-220, 1975.
12. Weber RS, Shillitoe EJ, Robbins KT, et al: Prevalence of humon papilloma virus in nverted nasal papillomas. Arch Otolaryngol Head Neck Surg 114:23-26, 1988.

JOURNAL OF ANKARA MEDICAL SCHOOL Vol 18, No 2, 1996 107–109

THE DEVELOPMENT OF SUBACUTE GRANULOMATOUS THYROIDITIS DURING LITHIUM TREATMENT

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SUMMARY

During lithium treatment various anatomic and/or functional abnormalities of the thyroid can develop. This to our knowledge, is the second reported case of subacute granulomatous thyroiditis developing a patient receiving lithium treatment. The case, a 34 year old female patient, had been an lithium treatment for schizophrenia since 1989 when she was referred to us for a goitre that was detected in September 1994. At referral, she had complaining of nervousness, dysphagia, pain in the neck that was aggravated by swalowing, excessive sweating, heat intolerance, increased appetite, weight loss. She had an upper respiratory track infection two weeks earlier. She had a grade II diffusely enlarged thyroid and also a thyroid nodule on the right. Her erythrocyte sedimentation rate was 40mm/h, and white blood cel count was 9500/mm^3. 131 I uptake by her thyroid was suppressed. She as normal evels of thyroid hormones and no thyroid antibodies. Fine needle aspiration of the thyroid and the cytological examination of the aspirated material confirmed the diagnosis of subacute granulamatous thyroiditis. She was followed monthly without lithium being stopped. No medication was presciribed for the subacute thyroiditis. She was still euthyroid at the fifth month. Her serum lithium level stayed within acceptable therapeutic levels all through follow-up. This case is a reminder that other forms of thyrotoxicosis, like subacute granulomatous thyroiditis, that are not caused directly by lithium can occur during lithium treatment.

Key Words: *Lithium, subacute granulomatous thyroiditis.*

Lithium carbonate has been used for the treatment of manic-depressive disorders since 1949(4). Lithium effects the function of the thyroid gland, which may resut in clinical as well as biochemical hypo or hyperthyroidism with or without goitre (3,5, 6, 7, 8, 9).

Here we present a case of subacute granulomatous thyroiditis developing in a patient while she was receiving treatment with lithium for schizophrenia.

CASE REPORT

A 34 year old female patient was referrded to our department with thyroid enlargement in September, 1994. She had been taking lithium for schizophrenia since 1989 (900 mg/day) and had been followed regularly. Her complaints were nervousness, dysphagia, characterized by pain in the neck during swallowing, excessive sweating, tremor of the hands, heat intolerance, dry mouth, weight loss in spite of increased appetite (two kg. in 15 days). She gave a history of upper respiratory tract infection two weeks earlier. Although the patient appeared clinicaly euthyroid, examination of her thyroid revealed a grade II diffuse enlargement (according to WHO criteria), and a hard, well circumscribed 2x2 cm. nodule in the lower part of the right lobe without any tenderness or pain. Other physical examination was normal. She had no family history of thyroid disease.

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Table. Hormonal and other laboratory findings of the patient.

	At the time of diagnosis	3 months later	5 months later
fT3 (53.4-7.2 pmol/L)	5.7	7.4	7.1
ft4 (11.0-24.0 pmol/L)	16.9	13.8	17.4
s-TSH (0.2-5.1 mIU/ml)	0.7	1.7	2.2
Anti-M (0-50 IU/ml)	10.2	4.0	1.7
White blood cell count (/mm³)	9500	7500	8500
Sedimentation (m/hr)	40	12	4
131 I Uptake 4 th hour 8 th hour	 8 24		 26 49

Her blood biochemistry was normal. The white blood cell count and ESR were 9500/mm3 and 40 mm/hr respectively. Hormonal and other laboratory findings of the patient are shown in the table. Thyroid scintigraphy with technetium 99 m pertechnetate (99 m Tc) revealed thyroid gland suppression, and the aspiration cytology, was diagnostic for subacute granulamatous thyroiditis. She continued the lithium medication she had being taking. no other drug was prescribed for her thyroid condition. When she was seen a month later, she had no complaints.

Lithium was continued and she was still euthyroid when she was seen again three months later.

Afer 5 months, the thyroid nodule regressed and the patients was had no complaints. Radioactive iodine uptake by the thyroid returned to normal and repeat thyroid scintigraphy with 99 m Tc revealed a diffuse hyperplastic gland. The serum lithium level was 0.87 mmol/L (therapeutic range: 0.5-1.5 mmol/L).

DISCUSSION

Lithium is concentrated in thyroid gland as much as 2.5-5 times its serum level (14). It inhibits the synthesis and metabolism of thyroid hormones at probably 5 different steps (3). The effects of lithium related to thyroid are related to:

1. The inhibition of iodide concentration mechanism.
2. The inhibition of iodination of tyrosine.
3. The inhibition thyroxin (T4) and triiodothyronine (T3) release.
4. The inhibition of peripheral conversion of T4 to T3.
5. The impairment of stimulation of the thyroid gland by the thyrotopin (TSH).

In animal experiments it is observed that the effects of lithium vary depending on whether it is used a short-term or a long-terms basis(2). Although on short-term usage it decreases capturing of iodine and hormone release(11), the main effect with chronic usage is that it inhibitis the release of thyroid hormones from the thyroid gland (1, 10).

Lithium treatment can cause hypothyroidism with or without goitre according to the above mentioned mechanisms. Thyrotoxicosis can aso occur during lithium treatment (1, 6,9).

Three mechanisms have been postulated for the pathogenesis of thyrotoxicosis during lithium treatment (5, 8, 19):

1. Lithium stimulation of the immune system; there is an increase in thyroid autoantibody levels with lithium usage.
2. Overcompensation against the supressive effects of lithium on thyroid hormone synthesis and release.
3. Patients with multinodular goitre or with subclinical autoimmune thyroid disease may develop thyrotoxicosis due to iodine as the iodine pool in the thyroid gland increases during lithium treatment.

Theoretically this could occur either as a result of immunological charge or via expansion of intathyroidal iodine. The exact mechanisms arenot understood and remain to be resolved.

This is the second reported case of subacute granulomatous thyroiditis developing during lithium trerapy (12). In our case the diagnosis of subacute thyroiditis has been confirmed by fine needle aspiration cytology. Moreover, the patients normal anti-M and Anti Tg titres also support the diagnosis. The frequent causes of the thyrotoxicosis occuring during lithium therapy are Graves Disease, multinodular toxic goitre and silent thyroiditis(5).

In conclusion, this case is a reminder that other forms of thyrotoxicosis, like subacute granulomatous thyroiditis, that are not caused directly by lithium can occurduring lithium treatment.

It appears that lithium, can precipitate goitre, hypothyroidism, or thyrotoxicosis in suspectible individuas. It seems likely that the exact manifestation of thyroid disease in an individual will depend on the prevailing nutritional iodine status,and the presence of underlying autonomous thyroid nodules or autoimmune thyroid disease.

REFERENCES

1. Barclay ML. Brownlie BE. Turner JG, Wells JE.: Lithium associated thyrotoxicosis: a report of 14 cases, with statistical analysis of incidence. Clin Endocrinol 1994; 40:759-64.
2. Berens SC, Bernstein RS, Robbins J, Wolff, J.: Antithyroid effects of lithium. J Clin Invest. 1970; 49: 1357-67.
3. Berenes SC, Wolff J.: The endocrine effets of lithium. In: Johnson FN, ed. Lithium research and therapy. London: Academic Press. 1975: 443-69.
4. Cade JFJ: Lithium salts in the treatment of psychotic excitement. Med J. August; 1949; 36:349-52.
5. Chow CC, Cockram C.S.: Thyroid disorders induced by lithium and amiodarone: an overview. Adverse Drug Reac. Acute Poisoning Rev 1990; 9(4) 207-222.
6. Cubit T.: Lithium and thyrotoxicosis. Lancet 1976x; I: 1247-8.
7. Edhag O, Swahn A, Wester P.O.: Hypothyroidism following lithium treatment. Acta Med Scand 1973;193:553-5.
8. Lazarus J.H.: Endocrine and metobolic effcts of lithium. New York: Plenum Medical 1986; 99-125.
9. Reus V.I, Gold P, Post R.: Lithium-induced thyrotoxicosis. Am J Psychiatry 1970; 136:724-5.
10. Sedval G, Johsson B, Petterson U, Levin K.: Effects of lithium salts on plasma PBI and uptake of 131 I in thyroid gland in man and rat. Life Sci 1968; 7:1257-64.
11. Singer I, Rotenberg D.: Mechanisms of lithium action. N engl J Med 1973; 289:254-60.
12. Sinnott MJ. McIntyre HD. Pond SM.: Granulomatous thyroiditis and lithium therapy. Aus NZJ Med. 1992; 22(1):84.
13. Transbol I, Cristiansen C, Baastrup P.C.: Endocrine effects of lithium. Hypothyroidism, it's prevalence in longterm treated patients. Acta endocrino 1978; 87:759-67.
14. Wolff J.: Lithium interactions with the thyroid gland. In: Cooper TB, Gershon S, Kleine NS, Schou M, eds. Lithium-controversies and unresolved issues. Princeton NJ.: Excerpta Medica 1979; 552-64.

JOURNAL OF ANKARA MEDICAL SCHOOL Vol 18, No 2, 1996 111–114

DISTAL ANTERIOR CEREBRAL ARTERY ANEURYSMS: ANALYSIS OF 6 CASES

Alper Baysefer • Abdurrahman Bakır • Serdar Kahraman • Erener Timurkaynak*

SUMMARY

We report six patients with distal anterior cerebral artery aneurysms (DACAA). All aneurysms were saccular. Of these, 5 patients had single aneurysms, one had two aneurysms. Five patients underwent direct surgery and four of these had excellent outcomes after surgery. One patient died from rebleeding without a possible surgery.

Key Words: *Distal anterior cerebral artery aneurysms, surgery.*

Distal anterior cerebral artery aneurysms (DACAA'S) comprise only 2.7 to 9.2 % of all intracranial aneurysms (8). These lesions are most commonly found near the gem of the corpus callosum at the point of origin of the callossomarginal artery (9).

We report six patients who had DACAA and describe the treatment of these aneurysms and the results that were achieved.

MATERIAL AND METHOD:

Onehundred twentyeight patients with cerebral aneurysms diagnosed at the Gülhane Military Medical Faculty from 1986 to 1994. Six patients had ruptured aneurysms of the distal anterior cerebral artery (DACA). There were 4 women and 2 men, ranging in age between 36 and 54 years. One patient had two aneurysms (Fig.1). Associated vascular anomalies were not seen in any of the patients.

Digital substraction angiography was carried out for 4 patients and two patients had it already performed at different medical centers. Computed tomography for 3 patients (Fig. 2) and magnetic resonance angiography for 2 patients were performed (Fig. 3).

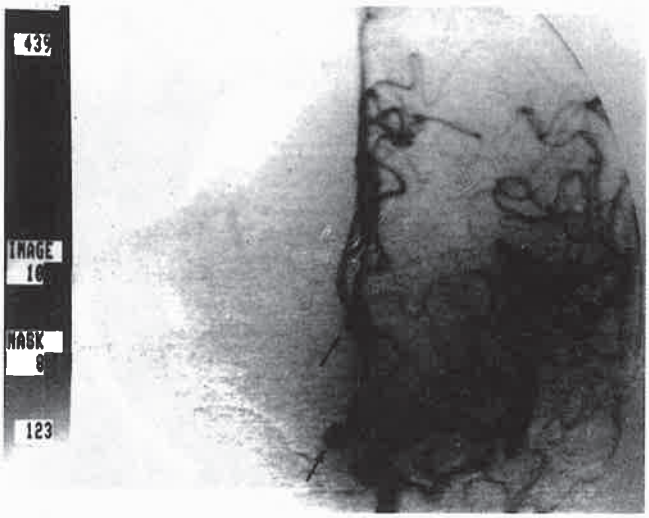

Fig. 1. Digitaly substraction angiography of left carotid artery (AP view) showing A3 and A co A aneurysms (arrows).

The aneurysms were located at two sites of the DACA. Five of the 6 had A3 location and one A2 location (Fig4,5). Five patients underwent direct surgery. Microsurgery using an operating microscope has been teh procedure used. DACAA's were exposed via an intehrhemispheric approach. In all surgically treated cases, the neck of the aneurysms were clipped with Yaşargil clips.

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Table I. The Surgical results Of The Distal Anterior Cerebral Aneurysms (1986-1994).

Number of cases	Sex, Age	Location*	Classification**	Size	Neuroradiology	Surgical Treatment	RESULT		
							Excellent	Good	Death
1	F, 42	Right A3	II a	Medium	Conventionel	Clip	+		
2	M, 48	Left A3	III b	Medium	Conventionel angiography	Clip		+	
3	F, 39	Left A2	I a	Medium	DSA	Clip	+		
4	M, 54	Riht A3	II a	Large	CT, DSA, MRA	Clip	+		
5	F, 36	Right A3 + ACoA	IIb	Medium	CT, DSA, MRA	Clip	+		
						TOTAL	4	1	-

* : Rhoton and Fisher's classification
** : Yaşargil's classification

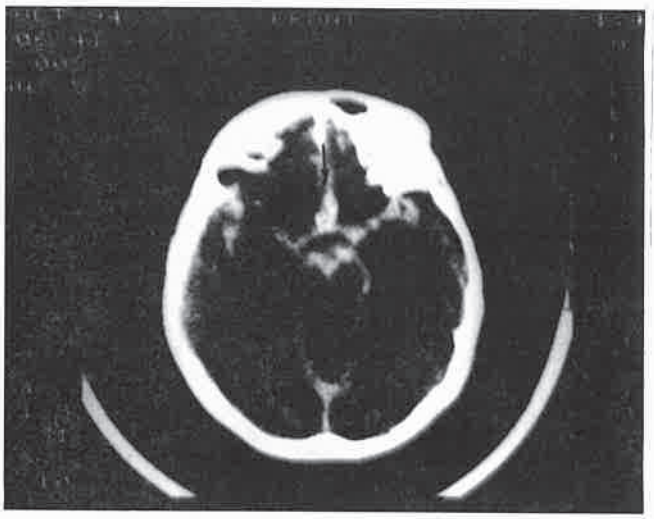

Fig. 2. Computed tomography demonstrating the high density areas (subarachnoid hemorhage).

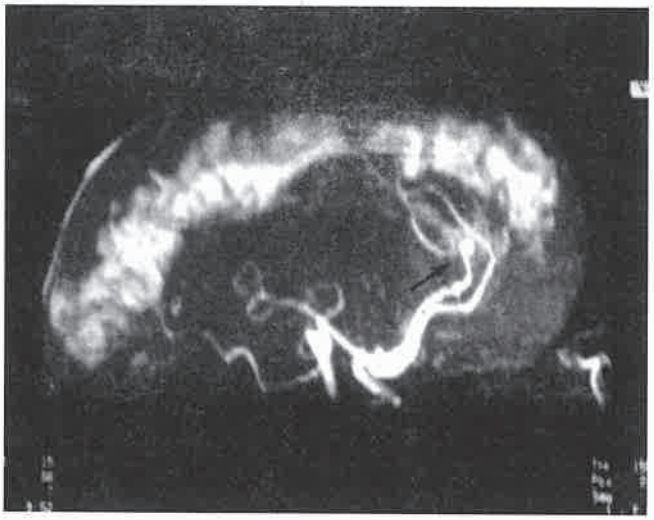

Fig. 3. Magnetic resonance angiography (lateralview) showing A3 aneurysm (arrow).

RESULTS

The surgical results are shown in table 1. One patient died from rebleeding (second) three days after admission to our department. The surgical results were excellent in 4 cases. I one case, preoperatively existing hemiparesis endured in early postoperative period but the deficit decreased with rehabilitation. At 4 months after surgery, the patient's neurological examination was normal.

DISCUSSION

The incidence of DACAA is rather low and neurosurgeons have less surgical experience with these aneurysms than the other locations. The frequency of this location of aneurysms has been varied between 2-9.2 percent in the priorly reported large series (7,8,11). In our series, this frequency is 4.7 percent with 6 cases.

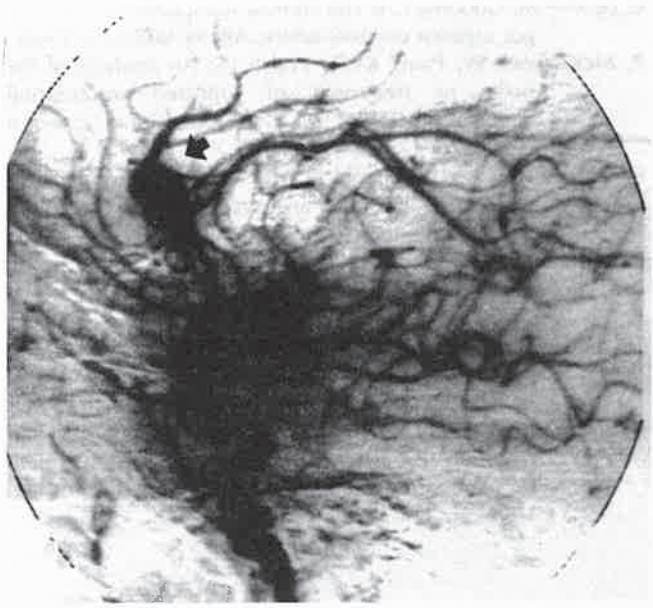

Fig. 4. Digital substraction angiography of left carotid artery (lateral view) showing a large A3 aneurysm (arrow).

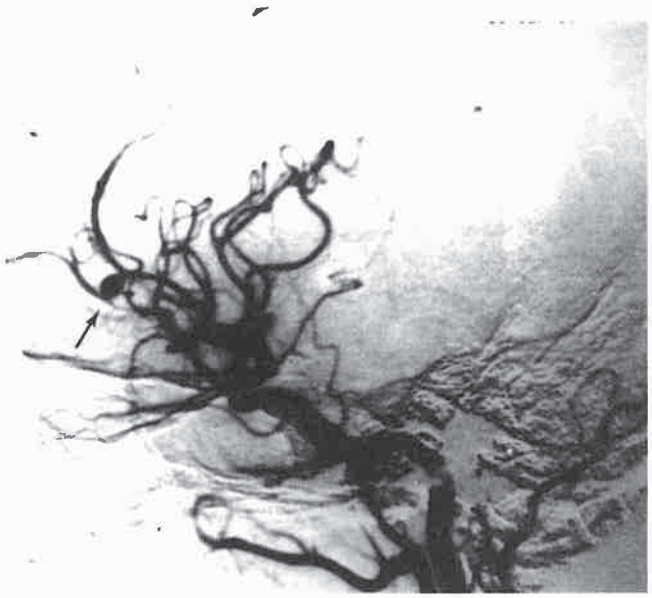

Fig. 5. Digital substraction angiography of left carotid artery (lateral view) howing A2 aneurysm (arrow).

The high incidence of multiple aneurysms in patients with DACAA's has been noted, amounting to 37.5 % of the total 325 cases in the 16 series (8). The most common location of the second aneurysm is middle cerebral artery (3,6,9). The second aneurysm was determined at anterior communicating artery in only a case of our series (16.6%).

Anterior cerebral artery (ACA) anomalies are often associated with DACAA's, including an azygous ACA, a bihemispheric ACA, triple ACA's (1,5,9). Among these anomalies, an azygous ACA is the most characteristic feature associated with these aneurysms. In angiographic studies, it was reported to be seen in 2-3.7 % (2,6). Vascular anomaly was not observed in our cases.

The anatomy of DACA consists some special problems in surgical treatment of the aneurysms of this site. Two surgical approaches to these lesions have been discussed. Subfrontal craniotomy has been recommended for aneurysms arising proximal to the DACA bifurcation and in the region below the genu of the corpus callosum (11). However, interhemisphheric approach in the aneurysms located proximally to genu of the corpus callosum is prefered (5,8). One potential problem with the interhemispheric approach is that, the DACAA, lying particularly just beneath the genu of the corpus callosum, may be encounteredbefore one establishes proximal control. Despite the narrow working space in this location, the neck of the aneurysm must be exposed with a cautious dissection. All our cases were operatedwith interhemispheric approach. DACAA's are frequently surrounded by densely scarred arachnoid, which made complete dissection difficult and enhanced the risk of intraoperative rupture. Recently, it appears that the development of microsurgical technique has decreased the incidence of intraoperative rupture of these aneurysms (4,10). Although an intraoperative rupture occured in case of our series, it was clipped properly and an excellent surgical result was observed.

The surgical results of the periorly reported series have bene statisfactory. The average surgical mortality rate has ranged from none to 22.2 % (8). Our surgical mortality rate ise 0 %.

Some authors have recommended delayed surgery to reduce postoperative mortality and morbidity (10). On the other hand, several authors have operated on patients with these aneurysms early after their subarachnoid hemorrhage and obtained good operative results (3,4), as we have supported.

As a result, we believe that an excellent surgical result dependes on patient's preoperative condition, using microsurgical methods, and early operation of the patient to minimalize rebleeding.

REFERENCES

1. Baptista AG; Studies of the arteries of the brain: II. The anterior cerebral artery: Some anatomic features and their clinical implications. Neurology (NY) 13:3825-835, 1963.
2. Huber P, Braun J, Hirschmann D, Agyeman JF, Incidence of berry aneurysms of the unpaired pericallosal artery: Angioraphic study. Neuroradiology 19:143-147, 1980.
3. Kawamura S, Suzuki A, Sayama I Yasui N, Ruptured aneurysm of the distal anterior cerebral artery [in Japanese; English abstr]. Jpn J Stroke (Tokyo) 10:298-305, 1988.
4. Kuwabara S, Ishikawa S, Andoh S, Matsumoto S, Sekimoto H, Uemura Y, Yamane K, Takahashi M; Aneurysms of the distal anterior cerebral artery [in Japanese; English abstr]. Neurol Med Chir (Tokyo) 24:580-590, 1984.
5. Laitinen L, Snellman A; Aneurysms of the pericallosal artery: A study of 14 cases verified angiographically and treated mainly by direct surgical attack. J Neurosurg 17:447-458, 1960.
6. Le May M, Gooding CA; The clinical signiticance of the azygos anterior cerebral artery. AJR ss: 602-610, 1960.
7. McKisscock W, Paine KWE, Walsh LS; An analysis of the ruslts of treatment of ruptured intracranial aneurysms: Report of 772 consecutive cases. J Neurosurg 17:762-766, 1960.
8. Ohno K, Monma S, Suzuki R, Masaoka H, Matsumisha Y, Hirakawa K; Saccular aneurysms of the distal anterior cerebral artery. Neurosurgery 27:907-913, 1990.
9. Perhlmutter D, Rhoton AL Jr; Microsurgical anatomy of the distal anterior cerebral artery. J Neurosurg 49:204-228, 1978.
10. Sindou M, Pelissou-Fuyotat I, Mertens P, Keravel Y, Athayde AA; Pericallosal aneurysms. Surg Neurol 30:434-440, 1988.
11. Yaşargil MG; Surgery of the intracranial aneurysms and results, in Microsurgery, Vol. II, Clinical COnsideration. Stutgart, Georg Thieme Verlag. 1984; pp 224-231.

JOURNAL OF ANKARA MEDICAL SCHOOL Vol 18, No 2, 1996 115–119

TWO CASES OF DIASTEMATOMYELIA WITH TWO DISTINCT LEVELS

Engin Gönül • Alper Baysefer • Serdar Kahraman • Ferruh Gezen*

SUMMARY

Two cases of diastematomyelia are presented. Diastematomyelia is a rare malformation of the spine. Our cases had two distinct levels of diastematomyelia. The spinal cord was divided at a single level in 96 % of the patients with diastematomyelia reported in the literature. The septum was located in the thoracic and the lumbar spine of both cases. MRI was very useful in definitive diagnosis and detection of associated abnormalities. The patients were undergone surgery and neurological condition was improved. Diagnoses and timing of surgery are discussed in this report.

Key Words: *Diastematomyelia, Split cord malformation*

With modern imaging techniques, various forms of spinal dysraphism are being diagnosed in children with increasing frequency (1,2,7,8). Traditional terms used to describe the two main forms of these rare malformations, diastematomyelia and diplomyelia. The new classification recommends the term splid cord malformation (SCM) for all double spinal cords (11). A type ISCM which is called diastematomyelia consist of two hemicords each contained within its own dural tube and separated by a dura-sheathed rigid osseocartilaginous median septum. A type II SCM which is called diplomyelia, consist of two hemicords housed in a single dural tube separated by a non rigid, fibrous median septum. Diastematomyelia is a primary embryological malformation involving division of variable length of the spinal cord into two hemicords of more or less equal caliber, and abnormalities of posterior elements or the vertebral bodies are usually present. The unified theory of embryogenesis proposed that all variant's type of SCMs have a common embryogenetic mechanism (11). Basic to this mechanism is the formation of adhesions between ecto and endoderm. Leading to an accessory neuroenteric canal around which condenses on endomesencyhmal tract that bisects the developing notochord and causes formation of two hemineural plates.

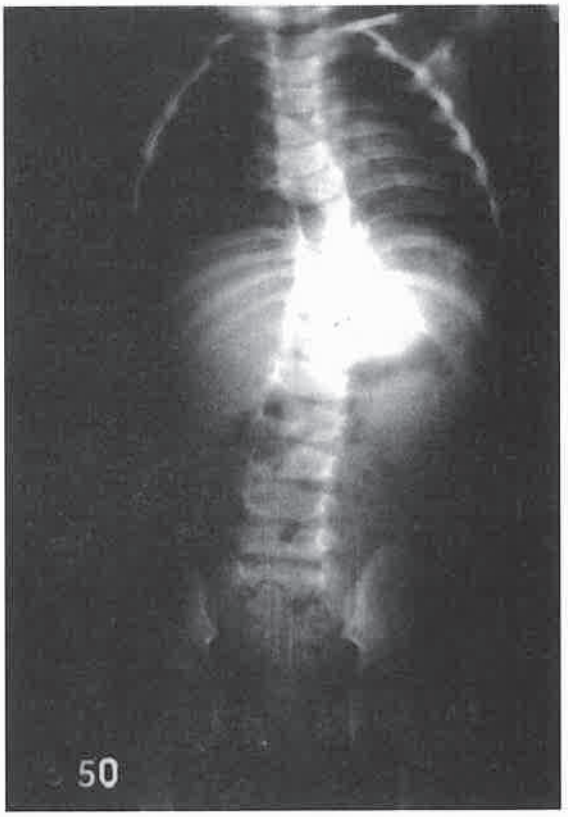

Fig. 1. The plain x-ray showing scoliosis.

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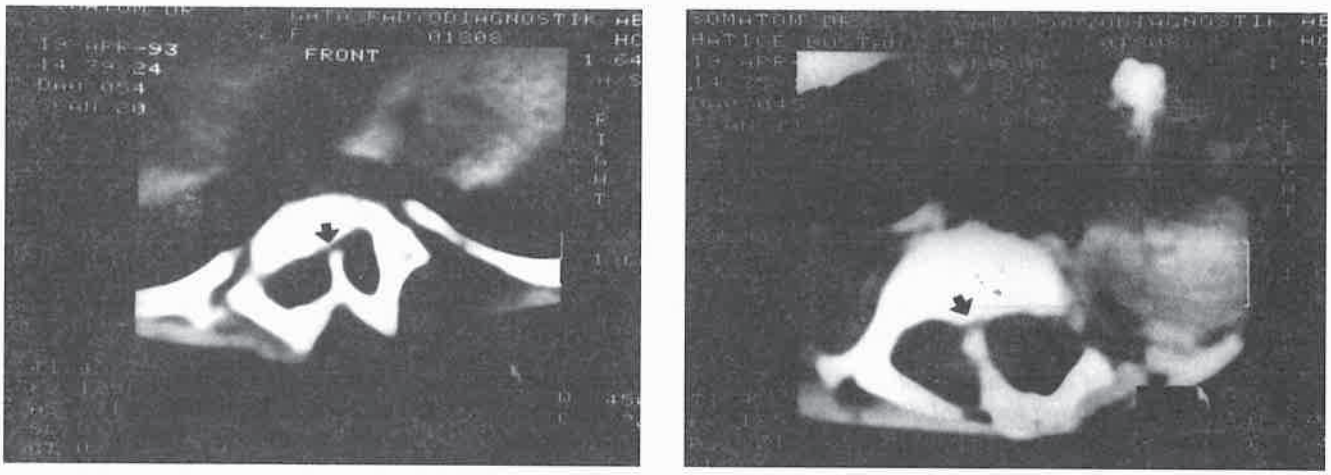

Fig. 2. a and b: CT-scan showing median bony septum at thoracal 10 and lumbar 2 (arrows).

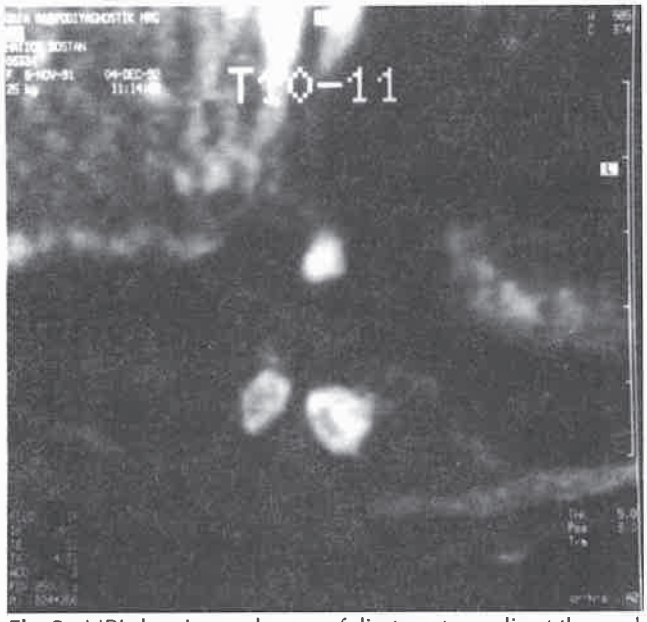

Fig. 3. MRI showing snake eye of diastematomyelia at thoracal 10.

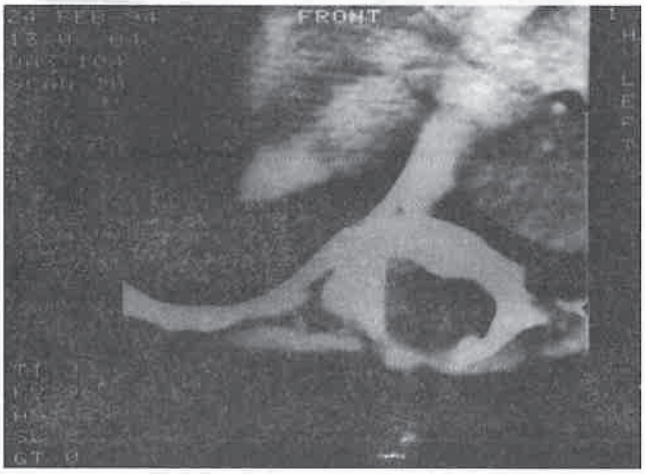

Fig. 4. CT-scan showing postoperative spinal cord at thoracal 10.

SUMMARY OF CASES

CASE I: A 3-year-old girl presented with congenital scoliosis, a worsening limb and, hypertrichosis and pigmentation in her back. She had no neurological abnormalities except the bilateral aschill clonus. Plain x-rays showed scoliosis, fusion abnormalities of vertebra at thoracal 9-10-11 and multilevel spina bifida at the lumbar spine (Fig. 1). Intervertebral disc space was narrowed characteristically at the thoracal 9-10-11. The transverse diameter of the vertebral bodies was widened. CT imaging showed bony spur at thoracal 10 and lumbar 2 (Fig. 2a and 2b). The spinal cord seemed to be divided into two halves at these levels such as snake eyes (Fig.3). MRI also showed same abnormalities associated with tethered cord at lumbar 4. At the first operation; she was explored through a posterior thoracic approach. Total laminectomy was performed on thoracal 10 and then the posterior longitudinal ligament was opened. The bony septum was separated from the dura by the operating microscope. The dura seemed very thin, so duraplasty performed with the cadauer dura greft. Replacement of the laminae was not performed. Control CT scan showed total removal of the bony spur at throacal 10 (Fig.4). From the first operation, 11 months later the second bony spur was removed at lumbar 2 level through a posterior approach. Laminectomy was not performed because that she had a spina bifida at the same level. Tethered cord was released. Control CT scan showed no bony spur. Neurological condition of the patient was improved.

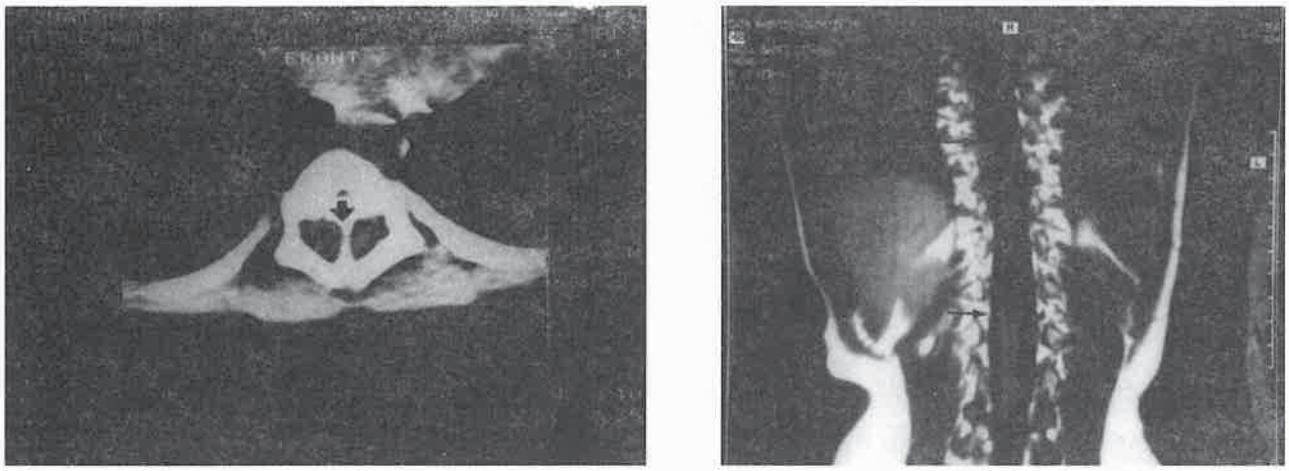

Fig. 5. a and b: CT-scan showing median bony septum at thoracal 8 (arrow).

CASE II: A 4-year-old boy presented with weakness of legs and late walking. Neurological examination revealed slight weakness of his legs. Plain x-ray showed slight scoliosis. He had bilateral pes equinavarus deformity; therefore he had been operated twice. CT scan showed bony spur at thoracal 8 and lumbar (Fig.5a and 5b). MRI supported these findings associated with tethered cord at lumbar 3 (Fig.6). The bony spur was resected at thoracal 8 through a posterior approach in the first operation. Total laminectomy was performed. Control MRI showed diastematomyelia at lumbar 1 level (Fig.7). Between the lumbar 1 and 2 vertebrae, there was a fibrous band. The dural tube divided into two parts and released after the excision of the fibrous band. Postoperative CT scan showed no diastematomyelic spur (Fig.8). Neurological condition of the patient was improved.

We prefered to the different stage for each level of diastematomyelia in our cases. Because of we think that the one stage operation for diastematomyelia with multiple level may be cause of spinal instabilization and may be heavy for child.

DISCUSSION

Diastematomyleia denotes an anomaly in which there is separation of a segment of the spinal cord into two hemicords. It often occurs with a bony, cartilaginous, or fibrous septum interposed between the two hemicords (4,5,67,11). The cord is normal above the level of the diastematomyelia, and usually reunits below the level of the split and again becomes normal. Because no true duplication of the cord occurs, each division represents an equal or unequal portion of one spinal cord. Our cases supported this view. A true duplication of the cord was defined as one containing two dorsal or two ventral horns and for corresponding nerve roots (11). Each member of the true duplicated cord was therefore considered a complete cord. In contrast, a cleft cord was thought to be one bisected by a midline spur, into two paired hemicords, each containing a single

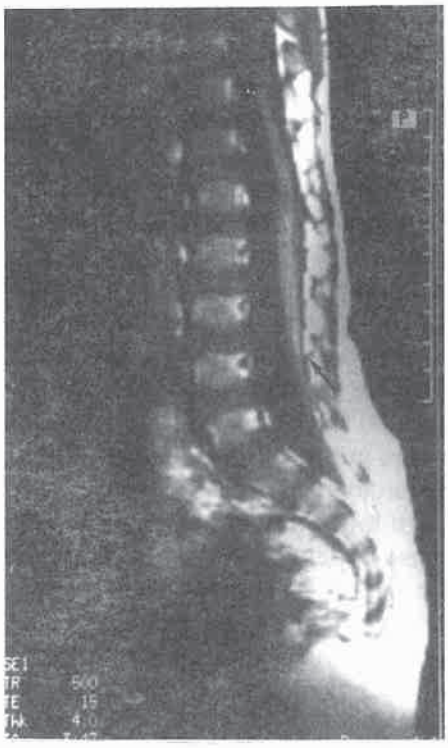

Fig. 6. MRI showing ethered cord at lumbar 3 (arrow'

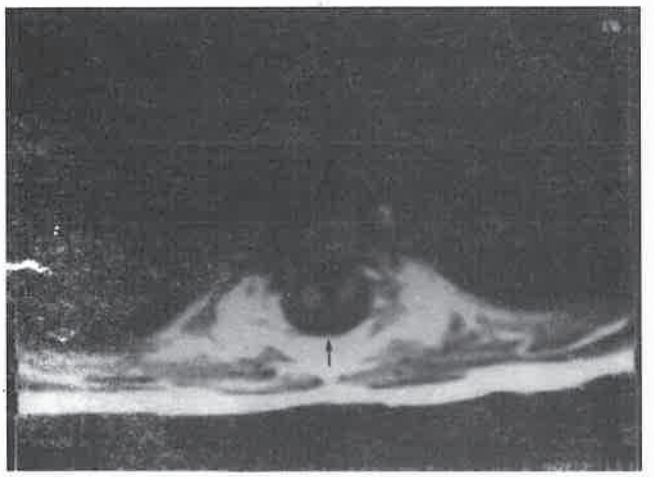

Fig. 7. MRI showjing diastematomyelia at lumbar 1 (arrow).

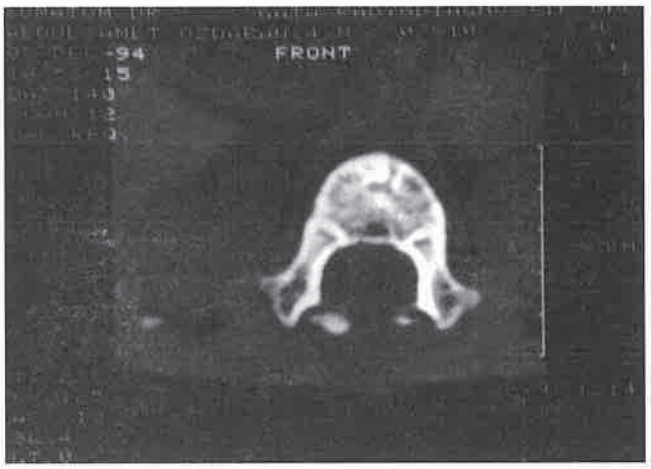

Fig. 8. Postoperative CT-scan showing total laminectomy and spinal cord at thoracal 8.

dorsal and ventral horn with corresponding dorsal and ventral roots. These two forms arise from different embryogenetic mechanisms. The presence of a midline bone spur suggests that diastematomyelia results from some form of mesodermal invasion of the neural tube, whereas diplomyelia is thought to arise from segmental origin (11).

One division of cord may be significantly smaller, and the roots hypoplastic. The smaller hemicord may correlate with symptomatic extremity (4). Our cases were not this type. The spinal cord was divided at a single level in 96% of the patients in the literature (4). There were rare separate divisions at two or even three distinct levels. Our cases had two distinct levels.

A relatively small percentage of these patients is without symptoms. The condition is discovered after the cutaneous findings or during incidental evalutaion of the spine (9). In 20 % to 60% of diastematomyelia patients, a collection of findings that involve the lower extremities, back, and trunk with an otherwise normal neurologic examination, has been termed the orthopedic syndrome (6,9). İn the other large group of patients, neurologic symptoms are predominant. The patients may manifest mixed upper and lower motor neuron signs. As many as 50 % of these patients also have scoliosis (4,9).

The septum is located in the cervical spine in 1 %, in the thoracic spine in 28 % , in the lumbar spine in 70% and, in the sacrum in 1% (4,13). Since diastematomyleia occurs in early development when the spinal cord and spine are of equal length, a penetrating septum tethers the cord and prevent cranial migration. Thus, a lumbar septum usually penetrates the distal spinal cord and is associated with a low conus. The septum is attached to both anterior and posterior vertebral elements alone in 11 % and, to the anterior elements alone in 21% (4). Abnormalities of the posterior elements are the most common skeletal defects, and a multiple level spina bifida, fusion of adjacent hemilaminae, or anomalous spinous processes are frequent (1,7). The intervertebral disc space is characteristically narrowed. The transverse diameter of the vertebral bodies is usually widened and anteroposterior diameter narrowed. Congenital scoliosis is frequently associated with the vertebral body abnormalities (1,4,8). Our cases had a tethered cord, fusion anomalies of the vertebrae, foot deformities, and congenital scoliosis. The bony spur was attached to the anterior elements. Symptoms and signs produced by the diastematomyleia are primarily due to traction by the septum. Diastematomyelia may be associated with myelomeningocele, epidermoid tumor, congenital dermal sinus, neuroenteric cyst, arachnoid cyst, lipoma or hydromyelia (2,3,4,8,12,14). Our cases were not associated with these abnormalities. Diastematomyelia occurs in females more often than in males, in ratio 3.5 to 1 of the reported cases (4,7). Cutaneous manifestations were presented in 77 % of the patients, with hypertrichosis in 50 % and hemangiomatous discoloration in 6 (%4,5,7,9). Twenty percent of the patients were asymptomatic and were evaluated because of cutaneous manifestation or an incidental radiological finding (4,5,7,8). One of our cases had a cutaneous finding.

Myelography and CT scanning using water soluble contrasts have been helpful in the evaluation of

diastematomyelia. MRI has several distinct advantages over CT,myelography: It is a nonivasive technique, can allow evaluation of an extensive area of the spine and displays the spinal cord structure directly (10,12). We recommend to use of combination of CT scan and MRI, because of it provides the best information about the anatomy of the spinal cord in relation the septum. MRI especially provides the best information about the soft tissues and associated abnormalities (1,2,7,8,10,14). MRI and CT imaging are sufficient for preoperative evaluation and managemenet of the diastematomyelia or split cord malformations .Operation should be advised for a symptomatic patient; particularly if a sphincter abnormality is present. Some authors believe that asymptomatic children and those with an apparently stable neuromusculoskeletal syndrome should have a prophylactic operation within the first two years of life (11). We should advise the operation only for symptomatic patients such as our cases. Previously we have an experience for single level diastematomyelia. We believe that the prophylactic operation may be harmful on stabilization of spine and neurological condition in asymptomatic patients. This asymptomatic patients were evaluted with an incidental radiological finding and cutaneous manifestation (4,5,7,8). The asymptomatic adult patients with diastematomyelia may have a back pain only without neurological deficit.

Postoperatively clinical assessment showed 53% to be in stable condition, and 45 % had some degree of improvement. Only 2 % were permanently worse after operation (11). Scoliosis may continue to progress after operation. Falure of postoperative improvment, or late deterioration may be due to incomplete removal of septum, failure to remove the central dural sleeve, failure to remedy another symptomatic abnormality at the operative level or a different level, or rarely a regrowth of the septum. Our cases are improved postoperatively.

REFERENCES

1. Bradford DS, Heithoff KB, Cohen M: Intraspinal abnormalities and congenital spine deformities: a radiographic and MRI study. J Pediatr Orthopaedics 11:36-41, 1991.
2. Breningstall GN, Marker SM, Tubman DE: Hydrosyringomyelia and diastematomyleia detected by MRI in myelomeningocele. Pediatr Ne urol 8:267-71, 1992.
3. Çobanoğlu S: Diastematomyelia: a report of two cases. Türk J Pediatr 31:89-94, 1989.
4. French BN: Diastematomyelia. Youmans Neurol Surg Vol 2:1192-1201, 1990.
5. Gower DJ, Curling OD, Kelly DL, Alexander E: Diastematomyelia: A 40 year experience. Pediatr Neurosci 14:90, 1988.
6. Guthkelch AN: Diastematomyelia with median septum. Brain 97:729, 1974.
7. Harwood-Nash DC, McHugh K: Diastematomyelia in 172 children: The impact of modern neuroradiology. Pediatr Neurosurg 16:247-261, 1990-91.
8. Hawnaur JM, Hughes D, Jenkins JPR, Bannister CM, Isherwood I: Investigation of children with suspected spinal dysraphism by magnetic resonance imaging. Eur J Pediatr Surg 1, Suppl 1: 18-19, 1991.
9. Humphreys RP, Hendrick EB, Hoffmann HJ: Diastematomyelia. Clin Neurosurg 30:436, 1983.
10. Özek MM, Pamir MN, Özer AF, Keleş GE, Erzen C: Correlation between computed tomography and magnetic resonance imaging in diastematomyelia. Eur J Radiol 13:209-214, 1991.
11. Pang D, Dias MS, Ahab-Barmada M: Split cord malformation: Part 1: A unified theory of embryogenesis for double spinal cord malformation. Neurosurgery 31:451-480, 1992.
12. Rabb CH, McComb JG, Raffel C, Kennedy JG: Spinal arachnoid cysts in the pediatric age group: an association with neural tube defects. J Neurosurg 77: 369-372, 1992.
13. Rawanduzy A, Murali R: Cervical spine diastematomyelia in adulthood. Neurosurgery 28:459-461, 1991.
14. Thron A, Schroth G: Magnetic resonance imaging of diastematomyelia. Neuroradiology 28:371, 1986.