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(Histopathologic Study)

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Pitfalls of Internal Mammary Artery (IMA) Dissection:
Steal From a Large First Branch and Successful Coil Occlusion

A Case of Hair Casts with Scanning Electron Microscopic Findings

A Case With Takayasu's Arteritis and Celiac Sprue

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EFFECTS OF CIGARETTE SMOKE EXPOSURE ON SPERMATOGENESIS IN RAT

Serdar Yardımcı* • Ali Atan** • Hakkı Taştan*** • Yusuf Kalender**** • Suna Kalender*** •
Kadirhan Sunguroğlu***** • Mustafa Cihat Avunduk*****

SUMMARY

In this study, rats in experimental group were exposed to smoke-air mixture (1/9 volume) 2 hours/day, consecutively 60 days. Control animals exposed to room air. Initial and 60th day plasma levels of testosterone, follicle stimulating hormone and luteinizing hormone were estimated by radioimmunoassay in both groups. Testes were examined by light and transmission electron microscopy at the 60th day of the exposure. Light microscopic findings showed that spermatogenic cell density and amount of mitotic forms in seminiferous tubules of smoke-exposed rats were lower than that of the controls. Electron microscopic examination revealed that spermatogonial cells of smoke-exposed rats had vacuolized and enlarged nuclei. Additionally, large amount of morphologically abnormal and immature sperms were detected in the lumen of seminiferous tubules of smoke-exposed rats. No histopathological abnormalities were seen in air-exposed control rats. At the 60th day of the exposure, mean plasma levels of testosterone and follicle stimulating hormone of smoke exposed rats were significantly lower than the latter values of control group ($p < 0.05$). Our data showed that long-term cigarette smoke inhalation had adverse effects on spermatogenic cell morphology and sperm production. It was demonstrated that smoke exposure caused formation of morphologically abnormal sperms. It was suggested that direct toxic effects of smoking on spermatogenic cells and decreased plasma levels of testosterone, follicle stimulating hormone and/or possible dysfunction of ultrastructurally abnormal Sertoli cells induced by long-term smoke exposure can play important role in decrease of spermatogenic cell population and formation of abnormal sperms in testes.

Key Words: Smoking, spermatogenesis, testosterone, electron microscopy, rat.

Many clinical studies have shown that long-term heavy smoking can cause the decrease in the total number of sperms and their motility (1-4). Some investigators also reported that the incidence of morphologically abnormal sperms in semen was higher in smokers than non-smokers (5,6). Recently, it was postulated that the incidence of abnormal sperms appeared to be correlated with the number of cigarettes smoked per day (7). In an earlier study, it was reported that chronic smoking was associated with various degrees of testicular atrophy in humans (8). It was demonstrated that systemic injections of nicotine which is a major physioactive substance in cigarette smoke, also reduced the reproductive capacity of male rats (8). It was found that the ratio of acrosomal region to the surface area of the sperms' head were low in smokers (9). They sug-

gested that these structural changes could be associated with the decreased sperm fertilizing capacity of smokers.

Qualitative and quantitative analyses of semen have revealed that smoking can affect sperm production adversely, but few testicular investigations have been performed about the effects of smoking on spermatogenesis in humans because of the ethic reasons and various difficulties (6,8,10). Additionally, many detrimental factors in humans such as aging, nutritional disorders, radiation damage, hot injury, alcohol consumption, etc. which can cause conflicting results have been noted in smoking related spermatological studies (7,8,10). It is believed that the assessment of the effects of smoking on male reproductive potential is difficult, because the plethora of environmental factors

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encountered in daily life could confound the detection of smoking-induced changes in semen parameters (11).

The aim of our study was to investigate the effects of smoke exposure on spermatogenesis and levels of sex hormones in animal models. For this purpose, testes of smoke-exposed rats were examined histopathologically by light and transmission electron microscopy and levels of plasma testosterone, follicle stimulating hormone (FSH) and luteinizing hormone (LH) were determined by radioimmunoassay.

MATERIALS AND METHODS

Animals

Male Wistar rats (weighing 200-250g) were randomly divided into experimental and control groups. All rats were housed in stainless steel wire cages except the period of smoke exposure and were fed on standard rat pellets and tap water ad libitum. Twelve rats in experimental group were exposed to cigarette smoke by using continuous exposure system 2 hours/day, 7 days/week for 60 days. Control rats (n:15) were restrained in an identical system but only exposed to room air.

Smoke Generation And Exposure

Smoke exposure system consisted of three glass chambers, pumps and fans. Centrifugal fans were attached to all chambers of the smoking machine for obtaining smoke-air mixture homogeneously. One pump was used to push air through the burning cigarette into the rate of 5.2 L/minute. By removing of the filter, each cigarette was smoked approximately for 10 minutes.

Plasma Obtaining Procedure

Before and after the exposures to smoke, blood samples were taken between 13 p.m. and 14 p.m. by intracardiac puncture under ether anesthesia and anticoagulated with heparin. Plasma was obtained by centrifugation of the blood samples at 4000 rpm for 15 minutes.

Hormone Assays

Initial and 60th day plasma levels of testosterone, FSH and LH were measured in both groups. The hormones' levels were determined by radioimmunoassay (Diagnostic Product Cooperation kits, USA).

Preparation Of Tissue Samples

All rats were sacrificed under high ether anesthesia following the last exposure and testes were removed. One testis was fixed in 10 % formaldehyde and the other one in 2.5 % gluteraldehyde. For light microscopic examination, the samples were dehydrated in ethanol, cleared in xylene, embedded in paraffin and 5 micron sections were prepared from several blocks of testes tissues. All sections were stained with hematoxylin-eosin and photographed by photomicroscope (Nikon optiphot Tip:115).

For electron microscopic examination of the tissues, primer fixation was made in 2.5% gluteraldehyde for 3 hours at 4 °C. Materials were washed with sodium phosphate buffer pH:7.4 for 2 hours at 4 °C and post-fixed in 1% OsO₄ containing sodium phosphate buffer solution pH: 7.4 for 1 hour at 4 °C. Tissue samples were washed with the same buffer solution for 3 hours at 4 °C and dehydrated in gradual alcohol and propylene oxide. Tissues were embedded in Araldite CY212 (12). Thin sections were prepared from several blocks by using ultramicrotome (Reichert OM U3) and then transferred to 300 mesh grids stained with 2% uranylacetate and lead citrate (13). Following these procedures, the sections were viewed and photographed by electron microscope (Jeol 100 CX II Model) at 80 kW.

Statistical Analysis

The results are expressed as mean + standard error of mean. Wilcoxon matched-pairs signed ranks test and Mann-Whitney U test were used for statistical analysis. Probability (p) values < 0.05 were considered statistically significant.

RESULTS

Light microscopic findings showed that spermatogenic cell density of seminiferous tubules of smoke-exposed rats were lower than that of the controls. Additionally, seminiferous tubules of smoke-exposed rats included a little amount of spermatogonial cells in mitotic division process compared to control animals (Figure 1a, b).

Electron microscopic examination revealed that spermatogoniums had normal shape in control animals (Figure 2a). Some spermatogoniums of the smoke-exposed rats had vacuolized and enlarged nuclei (Figure 2b). In air-exposed control rats, the large number of sperms had normal shape and tail

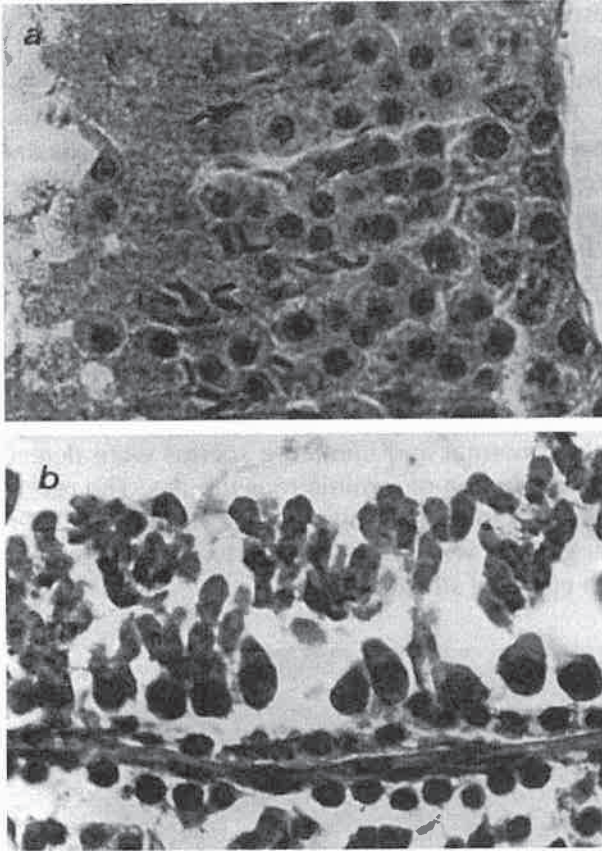


Figure 1. a The testis section of sham-exposed control group at 60th day. b Spermatogenic cell population of smoke-exposed group at 60th day (HE, x1000).

structure (Figure 3a). In the smoke-exposed group, large amount of morphologically abnormal and immature sperms were detected in the lumen of seminiferous tubules. Cytoplasm of these sperms had many vacuoles (Figure 3b). The tail lengths of them were shortened. The large lysosomal complexes and many vacuoles were often seen in the cytoplasm of Sertoli cells in smoke-exposed rats but not in control animals (Figure 2b).

Table 1 presents the mean plasma levels of testosterone, FSH and LH of control and smoke-exposed rats. The initial values of the smoke-exposed group did not significantly differ from the levels of control group. In smoke-exposed group, mean plasma testosterone level decreased significantly after the exposure. No significant changes in plasma testosterone levels were observed in control group after the air exposure. Mean plasma levels FSH and LH of two groups did not change significantly after the exposures.

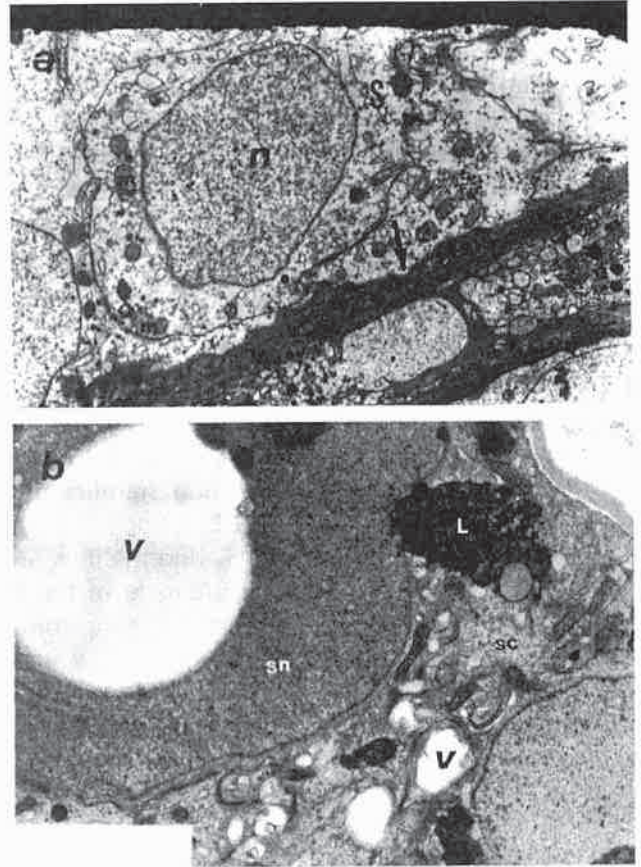


Figure 2. a Electron micrograph of the normal spermatogonium in control animals at 60th day of the sham exposure. Basal lamina (→), spermatogonium (s), nucleus (n), mitochondria (m) (x 5250). b Spermatogonium from rats exposed to cigarette smoke at 60th day. Vacuolization (v) in spermatogonium nucleus (sn), lysosomal complexes (L) and vacuoles (v) in the cytoplasm of Sertoli cells (sc) (x 10000).

The latter plasma levels of testosterone and FSH of smoke-exposed group were significantly lower than latter values of control group ($p < 0.05$), but mean LH level of smoke-exposed group did not differ significantly from the control group at the 60th day.

DISCUSSION

Spermatological studies have generally been concentrated on the density, motility and morphology of smokers' sperms to determine the association between smoking and spermatogenesis (1,6,7,11). Although spermatological studies in humans, comparing smokers to non-smokers, have shown a decrease in density and motility of sperms (2,5,7), these results are not consistent with all the previous

studies regarding the effect of smoking on sperm quantity (10,11,14). Some investigators also presumed that decrease in sperm density and motility of smokers may be attributed to smoking induced toxic effects in spermatogenic cells (4,5,15). The results reported by Hoidas et al. were not consistent with the mentioned findings (10).

Although in some studies, it has been suggested that smoking had no harmful effect on sperm quality (10,11), nowadays, most of the authors agree on the deleterious effect of smoking (2-4,7-9,16). It was reported that sperm density, motility and amount of abnormal sperms of smokers did not statistically differ from that of the non-smokers (11). Evans et al. revealed that semen of smokers had significantly great percentage of abnormal forms of sperms (5). They suggested that the sperm abnormalities in smokers may be due to genetic damage of these cells as a consequence of exposure to toxic compounds of tobacco smoke. In a recent study, it was demonstrated that smokers had a lower ratio of acrosomal region to the total surface of the sperm (6). It was suggested that smoking caused alteration of sperm cytoskeleton and the formation of morphologically abnormal sperms.

Up-to-date, few cytological studies were performed to investigate the effects of smoking on spermatogenic cell morphology in testes (6). Many deleterious factors in humans such as environmental pollution, nutritional disorders, alcohol consumption, radiation damage and hot injury influence on sperm quality and quantity, adversely (4,11). It is considered that potential confounders mentioned above can be eliminated in animal models. In this

present study, the effect of long-term smoke exposure on spermatogenesis and levels of plasma sex hormones were investigated in rats.

The light microscopic findings of this study showed that number of the spermatogenic cells and mitotically active forms were lower in smoke-exposed rats than control rats. Recently, Viczian et al. has reported that smoking caused inhibition of mitotic activity of spermatocytes in animals (6).

Electron microscopic examination of smoke-exposed group indicated that some spermatogonial cells had vacuolized and enlarged nucleus. In smoke-exposed group, large amount of morphologically abnormal and immature sperms were detected in the lumen of seminiferous tubules. The results of this and other previous studies showed that spermatogenesis was affected negatively by the long-term cigarette smoking in rats.

Table 1. The mean plasma levels of testosterone, FSH and LH of control (n:15) and smoke-exposed (n:15) groups before and after the exposures (mean + SE). The initial values of both groups were compared with their latter values. (NS: not significant)

		Before exposure	After exposure	Statistical significance
Testosterone (pg/ml)	Control	17.9 + 1.5	15.8 + 1.4	NS
	Smoke-exposed group	18.9 + 1.4	10.7 + 1.4	p<0.05
FSH (mU/L)	Control	35.7 + 6.8	36.9 + 2.7	NS
	Smoke-exposed group	35.4 + 4.3	27.7 + 1.2	NS
LH (mU/L)	Control	3.5 + 0.9	3.5 + 1.2	NS
	Smoke-exposed group	5.4 + 1.8	1.9+0.3	NS

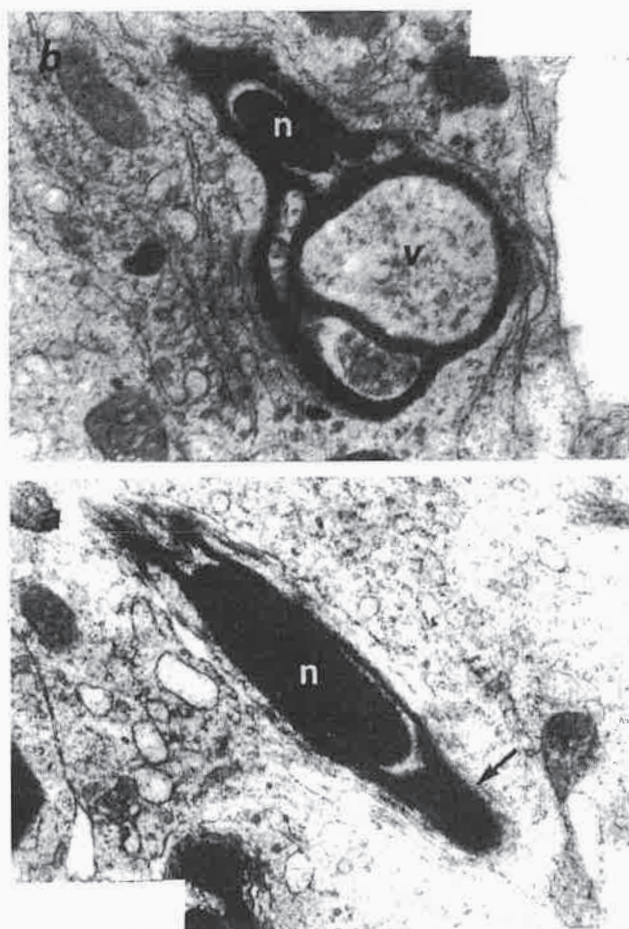


Figure 3. a Electron micrograph of the sperm from animals subjected to sham exposure nucleus (n), achrosome (→), (x 14000). b Electron micrograph of morphologically abnormal sperm in smoke-exposed rats nucleus (n), vacuolization (v) in cytoplasm of sperm (x 24000).

Nowadays, the pathophysiological basis of smoking induced impaired spermatogenesis remains unknown (4). Biochemical studies showed that tobacco smoke contains various toxic, irritant and mutagenic compounds such as nicotine, oxygen free radicals, pesticides, aromatic hydrocarbons (benzene derivatives) and some trace elements such as cadmium, lead, iron etc. (4,17,18). It was considered that structural changes of spermatogenic cells in smokers could be related with toxic compounds in tobacco smoke (15,16). Nicotine, which is the major physioactive substance in cigarette smoke, is highly toxic alkaloid (1,8). Riesenfeld et al. reported that reproductive capacity of rats was greatly reduced by nicotine injections (8). Larson et al. demonstrated that chronic nicotine administration or smoke exposure caused testicular atrophy and degeneration in various degrees (8).

Some previous studies showed that nicotine diminished plasma testosterone levels of rats in vivo and also inhibited androgen biosynthesis in cultured rat testicular cells (19-21). Testosterone is necessary for spermatogenesis and it plays an important role in germ cell maturation process. Therefore decreased testosterone production may be a causal factor in reduction in spermatogenic cell number (21). In some studies, it was shown that plasma testosterone levels of male smokers were lower than non-smokers. It was suggested that decreased plasma testosterone levels may adversely affect spermatogenesis (1,21). However Klaiber et al. did not confirm that smokers had lower serum testosterone concentrations than non-smokers (22).

Hormone assays of the present study indicated that the mean plasma testosterone level decreased in smoke-exposed rats but not in air-exposed controls. The latter plasma levels of FSH and LH of smoke-exposed group did not change significantly

after the exposures. When compared the latter values of air-exposed controls to latter values of smoke-exposed rats, the levels of testosterone and FSH (but not LH level) were found significantly lower in smoke-exposed rats. Our data were similar to the results of Mittler et al. who reported that chronic smoke inhalation reduced serum testosterone levels in dogs (23).

In this study, it was also seen that cytoplasm of Sertoli cells included large lysosomal complexes and many vacuoles in smoke-exposed rats but not in control animals. It is known that Sertoli cells facilitate the late stages of spermatid maturation. Therefore, it is possible that the cytostructural changes in Sertoli cells affect adversely normal spermatogenesis by causing impairment of Sertoli cell functions.

In conclusion, our histopathological findings showed that long-term cigarette smoke inhalation had deleterious effects on the spermatogenic cell morphology and sperm production. It was demonstrated that smoke exposure caused formation of morphologically abnormal sperms. It was considered that direct toxic effects of smoking on spermatogenic cells and decrease in plasma levels of testosterone, FSH and/or possible dysfunction of ultrastructurally abnormal Sertoli cells induced by long-term smoke exposure can play important role in decrease of spermatogenic cell population of testes and formation of abnormal sperms. Further experimental studies are needed to determine the mechanism of ultrastructural changes in testes and hormonal alteration in plasma induced by smoke exposure

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WIKTOR STENT IMPLANTATION: INITIAL SUCCESS AND LONG-TERM FOLLOW-UP

Ender Semiz • Oktay Sancaktar • Selim Yalçınkaya • H. Ege • Necmi Değer

SUMMARY

Wiktor stent is a balloon-expandable tantalum coil stent with high radiopacity. From April 1995 to April 1996, we implanted 56 Wiktor stents in 46 lesions (LAD: 23, RCA: 16, Cx: 7) in 42 patients (average age 53±10 years). Revascularization indications were acute myocardial infarction (AMI) (45 %), unstable (31 %) and stable (24 %) angina pectoris. All interventions were planned procedures except one. Stented vessels had an average diameter of 3.14±0.27 mm and 7 % of the vessels were less than 3 mm in diameter. Deployment of the stents was successful in all cases. Average percent diameter stenosis was reduced from 84 % to 6 % following stenting. Neither major cardiac event (death, CABG, AMI) nor subacute occlusion was encountered during the hospitalization period and 1 month follow-up. After discharge, ticlopidine and aspirin were given to all cases for 1 month and infinitely, respectively. Mean hospitalization period was 1.5 day. The restenosis rate was 25 % in 40 of the 42 patients who were symptomatic at long-term follow-up or completely event free for 8 months. Restenotic lesions were redilated successfully in 8 patients.

Conclusions The results of this study indicate the Wiktor stent to be implanted with a high procedural success rate with no major cardiac event. Besides, angiographic outcome with an acceptable rate of restenosis at 8 month follow-up, clinical and radionuclide imaging follow-up for a period of 18 months is favorable.

Key words: Coronary stents, Wiktor stent, angioplasty, restenosis.

In recent years, coronary stenting has been developed to overcome the difficulty in dilating certain types of lesions, abrupt vessel closure, and late stenosis. Randomized STRESS and BENESTENT trials clearly demonstrated improved clinical outcomes (1) and reduced angiographic restenosis (1, 2) when compared with conventional balloon angioplasty (BA) for elective single-vessel coronary revascularization.

Types of delivery systems, composition and configuration of stents allow to distinguish them. Despite all coronary stent currently being evaluated are metallic, each has different degrees of radiopacity and radial compliance. Wiktor stent (Medtronic Inc., Minneapolis, MN), originally designed by Dominik Wiktor, is a balloon-expandable tantalum coil stent with advantages of its radiopacity and flexibility (3). This study reports the procedural results

together with clinical and angiographic outcome at 8 month follow up. Clinical and radionuclide imaging follow-up every 5 month for a period of 18 months has also been reported.

METHODS

Study patients

Between April 1995 and April 1996, 56 Wiktor stents were implanted in 46 lesions in 42 patients (1.33 stent per patient) at Akdeniz University School of Medicine, Antalya, Turkey. The average age was 53±10 years (range 38 to 72), and 35 cases (83 %) were male. Indications for revascularization were acute myocardial infarction (AMI) (45 %), unstable (31 %) and stable (24 %) angina pectoris. Patient characteristics are outlined in Table 1.

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Table 1 Patient characteristics

	N	%
Patients	42	-
Men	35	83
Age (years)	53±10	(range 38-72)
Stable angina pectoris	10	24
Unstable angina pectoris	13	31
Acute MI	19	45
Prior BA	6	14
Prior MI	7	17
Prior CABG	2	5
Coronary risk factors		
Smoking history	34	81
Diabetes	6	14
Cholesterol ≥ 200 mg/dl	25	60
Hypertension	16	38
Family history	23	55

MI= Myocardial infarction; BA= Balloon angioplasty;
CABG= Coronary artery bypass grafting.

Coronary stents

The Wiktor balloon-expandable intracoronary stent was used in this study. It consists of a single strand of radiopaque tantalum wire wrapped around an angioplasty balloon in a U-shaped configuration (coil stent) which offers marked flexibility and thus conformability with the vessel curvature. 0.014 inch coronary guidewire is used to deliver the stent balloon system via an 8-Fr. guiding catheter.

The current prototype of the Wiktor stent measures 16 mm in length, which is the major limitation.

Stent implantation protocol

All of the patients had a >70 % stenosis in their native vessels. Coronary flow distal to the lesion was classified before the procedure according to the Thrombolysis in Myocardial Infarction Trial (TIMI) criteria (4). Except one, all were planned procedures. The study protocol was approved by the Committee for Clinical Investigation at Akdeniz University School of Medicine and written informed consent was obtained from all patients.

Patients were premedicated with aspirin (300 mg/day) and ticlopidine (250 mg bid) for 48 hours before implantation. BA and stent implantation were performed by the femoral approach using 8 French catheters. 56 stents were implanted in 46 lesions in 42 patients. High-pressure inflations (mean 15±2 atm, range 13-22 atm) were used to optimize stent expansion (Swiss Kiss) after initial deployment of the stent.

Table 2 Angiographical data

	N	%
Lesions stented	46	-
LAD	23	50
RCA	16	35
CX	7	15
Lesion morphology (*)		
Type A	5	11
Type B1	11	24
Type B2	24	52
Type C	6	13
% diameter stenosis		
TIMI flow before stent		
TIMI 0	1	2
TIMI 1	3	7
TIMI 2	2	4
TIMI 3	40	87
Type of dissection before stent		
Type A	4	9
Type B	6	13
Type C	1	2
Type D	0	0
Type E	1	2
Type F	0	0
Thrombus before stent	22	48
Reference vessel diameter		
< 3.0 mm	3	7
≥ 3.0 mm	43	93
Number of diseased vessels		
1 vessel disease	37	88
2 vessel disease	5	12
3 vessel disease	0	0

LAD= Left anterior descending artery; RCA= Right coronary artery.
CX=Circumflex artery, TIMI= Thrombolysis in Myocardial Infarction.
(*)Modified AHA / ACC lesion classification.

Study end points

Acute or subacute stent thrombosis, repeat intervention, coronary artery bypass surgery (CABG), AMI, or death were the primary clinical end points of the study. Procedural success was defined as successful deployment of the stent in the absence of an adverse cardiac event. A < 10 % residual diameter stenosis following final deployment of the stent was used to define angiographic success. Subacute thrombosis was defined as a stent thrombosis within 30 days of deployment. Restenosis was defined as having a > 50 % stenosis on angiograms at 8 month follow-up. Angina and/or ischemia in radionuclide imaging studies have also been investigated every 5 month for a mean period of 18 month (range 14-22 months) follow-up.

Results

Angiographic lesion characteristics are listed in Table 2. Of 46 lesions, 24 lesions were in the left anterior descending coronary arteries, 16 were in the

right coronary arteries, and the remaining 7 were in the left circumflex coronary arteries. 65 % of the lesions before BA were type B2 and C according to the American Heart Association / American College of Cardiology (AHA/ACC) Task Force criteria (5). Angiographic appearance of intracoronary thrombus was present in 48 % of the lesions (22/46). Average diameter of the vessels stented was 3.14 ± 0.27 mm (range 2.7-3.9 mm) and 7 % of the vessels were less than 3 mm in diameter. Angiographic success as defined by < 10 % residual diameter stenosis was achieved in all of the cases (42 of 42). Average percent diameter stenosis was reduced from 84 % to 6 % after stenting. High-pressure inflation was performed in all stent with an average pressure of 15 ± 2 atm (range 13-22 atm). No acute occlusion or major cardiac event (AMI, CABG, death) occurred in hospital before discharge. Blood transfusion was required in two patients. Pseudoaneurysm formation at the femoral puncture site was repaired surgically. They were discharged after a mean period of 1.5 day. Procedural results are summarized in Table 3.

All patients were given ticlopidine and aspirin following the procedure for 1 month and infinitely, respectively. Subacute occlusion was not encountered during 1 month follow-up.

Following the initial intervention, clinical information during the follow-up period of 8 months was obtained in all patients. Information was obtained directly by interview in 31 (74 %), by telephone in

11 (26 %). Except two patients with acute myocardial infarction, all patients remained event free for a period of 8 months. Event free survival was 95 %. Symptomatic patients at long-term follow-up or patients who completed their event free period of 8 months underwent control coronary angiography. The restenosis rate was 25 % (10/40) in 40 of the 42 (95 %) patients. Target vessel revascularization (TVR) was performed successfully in 8 patients (20 %) without any major cardiac event.

After a mean period of 18 months (range 14-22 months), clinical follow-up information, obtained directly by interview in 35 (83 %), by telephone in 7 (17 %), was available in 42 of 42 patients (100 %). Angina class at the 18th month follow-up, with 91 % of patients remaining angina-free, has been shown in Table 4. 38 of the 42 patients (90 %) were asymptomatic during this period of time. No ischemia in any of these patients was detected in the radionuclide imaging studies performed every 5 month during this period of 18 month. Clinical endpoints at 8 and 18 months are outlined in Table 5.

Discussion

Abrupt vessel closure during conventional BA and restenosis during follow-up are the main problems to compromise its overall efficacy (6-11). Acute closure is associated with significant morbidity and mortality, which is thought to be result of a combination of factors such as dissection, spasm and thrombus formation. It occurs in 2 to 10 % of cases. Smooth muscle cell proliferation at the site of dilation causes extensive neointimal thickening and late restenosis, in 20 to 40 % of cases, occurs, which may necessitate repeat BA or CABG (12, 13).

Intracoronary stent implantation has been developed to overcome the two major limitations of BA. A number of different stent are available at present with their specific designs, compositions and delivery systems (14-17). The Wiktor stent is a balloon-expandable stent made of a single, loose tantalum

Table 3. Procedural and post-procedural characteristics

	N	%
Indication for stenting		
Elective	41	89
Restenosis following prior BA	5	11
Suboptimal result	0	0
Bail-out	1	2
Successful implant		
Major cardiac event		
Death	0	0
Acute MI	0	0
Urgent CABG	0	0
Acute/ subacute closure	0	0
Reference segment		
3.0 mm	31	67
3.5 mm	14	31
4.0 mm	1	2
Number of stents / patients	56/42	-
Single stent	31	74.3
2 stents	9	21
3 stents an over	2	5
Blood transfusion	2	5
Surgical repair	1	2

BA= Balloon angioplasty, MI= Acute myocardial infarction; CABG= Coronary artery bypass grafting.

Table 4. Functional class 18 months after intervention

	N=42	%
CCS Functional Class		
No angina	38	91
I	2	5
II	1	2
III	1	2
IV	0	0

CCS= Canadian Cardiovascular Society.

Table 5. Clinical end points at 8 and 18 months

	N	%
8 month follow-up		
Control angiography	40/42	98
Restenosis	10/40	25
TVR	8/40	20
Q Wave MI	1/42	2
Non-Q Wave MI	1/42	2
CABG	0	0
Death	0	0
CVA	0	0
18 month follow-up		
Number of patients	42/42	100
rePTCA (*)	0	0
Q Wave MI	1/42	2
Non-Q WaveMI	1/42	2
CABG	0	0
Death	0	0
CVA	0	0
Any event at 18 month follow-up	10/42	24

TVR=Target vessel revascularization; MI= Myocardial infarction; CABG= Coronary artery bypass grafting; CVA= Cerebrovascular accident (*) rePTCA performed between 9th and 18th month follow-up.

wire 0.125 mm in diameter and has a helical coil structure. The potential for corrosion and stress fracture is minimized by its sinusoidal helix design. Low-metallic surface area (8.8 %) in combination with its design and electrochemical properties of tantalum may protect against thrombus formation. High radiopacity is its another characteristic.

The success rate of elective implantation of all types of intracoronary stents differs between 95 to 100 %. Initial experience with elective Wiktor stent implantation in humans with restenosis following BA revealed a thrombosis rate of 10 % in acute or subacute phase of implantation (17). Following coronary stenting, adding ticlopidine (250 mg bid) to postprocedural treatment with aspirin and low-molecular weight heparin. French investigators (18, 19) observed a reduction in the incidence of subacute

thrombosis from 10.4 % (145 patients) to 1.3 % (237 patients who received 1 month of subcutaneous low molecular weight heparin), 1.7 % (523 patients who received 2 weeks of heparin) and 1.8 % (491 patients who received 1 week of heparin). Full antiplatelet therapy (ticlopidine and aspirin) without additional subcutaneous heparin but with high-pressure BA has become routine clinical practice at present. In our study, we also used just ticlopidine and aspirin both for 48 hours before implantation and for 1 month and indefinitely following the procedure., respectively. Swiss-Kiss was performed in all lesions thought to have suboptimal result. There was no acute or subacute closure.

In contrast to the favorable results observed with the Palmaz-Schatz stent (Benestent I, Stress I, and Start) (1, 2, 20, 21) restenosis trials, primary Wiktor stenting of the right coronary artery in a pilot study did not reveal a clinical or angiographic advantage over conventional BA with 6 month restenosis rates of 47.5 % and 35 %, respectively (22). European Wiktor Stent Study Group reported a > 50 % arterial diameter narrowing of 27 % in patients with threatened or acute closure complicating BA (23). The incidence of restenosis greater than 50 % diameter stenosis for the Wiktor stent was reported to be 30 % (17, 24), that seems to be higher than ours. Our results at 8 month follow-up with a restenosis rate of 25 % demonstrate an acceptable rate of stent restenosis compared with the results of the other studies above.

The present study shows the Wiktor stent to be implanted in coronary arteries electively with a high rate of angiographic success without any major cardiac event. Angiographic outcome at 8 month follow-up is acceptable. 38 of 42 patients (91 %) were asymptomatic during a mean period of 18 month. Radionuclide imaging studies with exercise stress testing done every 5 month also revealed no ischemia during this follow-up period.

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SIGNIFICANCE OF SMOKING IN PATIENTS RECEIVING THROMBOLYTIC THERAPY FOR ACUTE MYOCARDIAL INFARCTION

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SUMMARY

Background: Cigarette smoking is associated with increased coronary morbidity and mortality, which has multiple deleterious effect on atherogenesis, thrombosis and arrhythmogenesis. But some investigators have noted that hospital mortality after acute myocardial infarction is lower in patients who smoke than nonsmokers. To evaluate the initial and 6 months later association of smoking and thrombolytic therapy, we analyzed the results of streptokinase complications in acute myocardial infarction.

Method and Result: This study involved 205 patients. Patients were divided into three groups: group 1 - non smoker 43 patients (those patients who never smoked 30 men, 13 women); group 2 - ex smoker 71 patients (those who quit smoking > 1 month before infarction, 66 men, 5 women); group 3 - active smoker 91 patients, 83 men and 8 women. Patients admitted to the hospital in the first 6 hours of Myocardial Infarction (MI) and received 1.500.000 units of streptokinase as intravenous route. During in patient follow up rhythm and conduction disturbances, shock, congestive heart failure and death in patients with acute myocardial infarction is merely established. Coronary angiography (CAG) is performed after 6 ± 2 weeks to the 61 patients who still have angina. In the first 6 months follow - up reinfarction and mortality rate was much more in the nonsmoker ones ($p < 0.001$)

Conclusion: Smoking patients who received thrombolytic therapy after acute myocardial infarction have significantly worse progression in hospital but after 6 months death and reinfarction was established more in nonsmokers than smokers. But Diabetes Mellitus ($p < 0.05$), hypercholesterolemia ($p < 0.05$) and family history percentage ($p < 0.001$) was high in nonsmokers. Under these circumstances smoking must be absolutely stopped .

Keywords: Acute Myocardial Infarction, smoking, thrombolytic therapy.

The most firmly established risk factors for Coronary Artery Disease (CAD) are hypercholesterolemia, hypertension, Diabetes Mellitus (DM) and cigarette smoking. Cigarette smoking is associated with a higher incidence of Myocardial Infarction (MI) and death from CAD (1-6). Hammond and et al had shown that the most 50 % reduction in CAD risk is established 1 year after quitting (7). Doll and et al declared that at 45 years of age CAD risk among heavy smokers was 15 times than that of nonsmokers (8).

Despite the fact that smoking is a well established risk factor for the development of CAD, some investigators have noted that among hospitalized patients with Acute Myocardial Infarction (AMI), smokers appear to have a better prognosis than nonsmokers (9-13). To evaluate the association of

smoking with mortality during hospitalization after thrombolytic therapy an 6 months afterwards, we analyzed the results of streptokinase trial.

MATERIALS AND METHODS

The study population consisted of 205 patients (178 men, 27 women) with AMI who received streptokinase. These patients were followed up for 6 months after AMI.

In this study patients were divided into three groups. Group 1: 43 nonsmoker (30 men, 13 women, mean age: 58.13 ± 9.8 these patients had never smoked). Group 2: 71 ex smokers (66 men, 5 women, mean age : 55.98 ± 10.51 who quit smoking > 1 month before infarction). Group 3: 91 active smokers (82 men, 9 women, mean age: $54.1 \pm$

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9.8). The diagnosis of AMI was established by at least two criteria:

- 1) Characteristic chest pain
- 2) Electrocardiographic (ECG) changes with the evolution of Q waves (transmural infarction)
- 3) Characteristic elevations of serum Creatine Kinase (CK-MB) enzymes.

Non transmural infarction was diagnosed by typical ST segment and T wave changes accompanied by the CK-MB changes.

1.500.000 IV of streptokinase (STK) is given by infusion to the patients who are admitted to hospital in the first 6 hours of AMI. The clinical outcome analyzed in hospital were, reinfarction, ventricular and atrial dysrhythmias, conduction disturbances, stroke, hemorrhage, age, sex, shock, death, family history, previous MI and angina, DM, hypertension, hypercholesterolemia, congestive heart failure (CHF) according to Killip classification. CAG is performed to the 61 patients in the 6 ± 2 weeks after AMI, because they still had angina. CAG was performed via the femoral artery by Judkins method. We searched reinfarction and death after 6 months in all 3 groups.

Univariable comparisons of differences in baseline and outcome variables between the three groups

were done by chi square test analysis trends for categorical variables, Fisher exact test and test for two proportions from independent groups. Associations were regarded as significant if $p < 0.05$.

Results

205 patients were included in this study. The baseline characteristics of three groups differed significantly (table 1). Active smokers were young (mean age 54.1 ± 9.8 versus non smokers 58.13 ± 9.8) ($p < 0.05$). Mean age was 55.98 ± 10.5 in ex smokers. Most of the active smokers were men ($p < 0.01$). Active smokers had a higher rate of previous angina ($p < 0.05$) and CHF ($p < 0.05$) according to Killip class. Ex smokers had a higher rate of Killip 2 and 4 class ($p < 0.05$). Angina lasting more than 1 month was mostly found in active and ex smokers ($p < 0.01$). Anterior wall MI is found mostly in active smokers ($p < 0.01$). DM and hypercholesterolemia is found mostly in the patients who never smoked ($p < 0.05$) (table 2). Family history was also found more in group 1 patients ($p < 0.001$). During hospital follow-up ventricular tachycardia (VT) and ventricular fibrillation (VF) is found more in the active smokers comparing to nonsmokers ($p < 0.05$), and VF more in ex smokers ($p < 0.05$). Conduction dis-

Table 1. The patients baseline characteristics

Characteristic	Non smokers (n = 43)	p Value	Ex smokers (n = 71)	p Value	Active smokers (n = 91)	p Value
Men	30		66	$p < 0.01$	83	$P < 0.01$
Women	13		5		8	
Age	58.1 ± 9.8		55.9 ± 10.5		54.1 ± 9.8	$P < 0.05$
Hypertension	15		21	NS	23	NS
Diabetes Mellitus	6	$p < 0.05$	10	NS	3	NS
Hypercholesterolemia	5	$p < 0.05$	2	NS	2	NS
Family History	6	$p < 0.001$	3	NS	1	NS
Anterior wall infarction	20	NS	41	NS	64	$p < 0.01$
Inferior wall infarction	22	NS	30	NS	27	NS
Previous infarction	4	NS	14	NS	3	NS
Previous angina	27	NS	62	$p < 0.01$	74	$p < 0.05$
Angina < 1 month	23	NS	18	$p < 0.01$	25	$p < 0.01$
Angina > 1 month	4	NS	44	$p < 0.001$	49	$p < 0.001$
Killip class at entry						
Killip 1	1	NS	—		—	
Killip 2	1	NS	4		10	$p < 0.05$
Killip 3	2			13	$p < 0.05$	2
Killip 4	1	2			$p < 0.05$	

*NS : Not significant

Table 2. In hospital clinical outcome

	Non smokers p Value (n =42)	Ex smokers p Value (n = 71)	Active smokers Value (n = 91)	Value
VPS > 3 / min	7	9	25	NS
APS > 3 / min	-	3	3	3
Atrial fibrillation	-	1	6	NS
VT	1	13	11	p < 0.05
VF	1	6	13	p < 0.05
A - V Block 1.°	-	-	-	-
2.°	-	1	1	-
3.°	-	-	3	-
RBBB	1	1	1	-
LBBB	-	-	-	-
Shock	-	-	2	-
Reinfarction	3	13	12	NS
Hemorrhage	-	-	1 (Gingival bleeding)	-
Stroke	-	-	-	-
Deaths	-	3	2	-

turbance (3° Atrio - Ventricular block), shock and death is found more in active smokers. Though, we did not have sufficient number of patients for statistical analysis, analysing is not made for these complications.

In hospital follow-up reinfarction was more in ex smokers comparing to the nonsmokers (p < 0.05).

The CAG outcome is presented in table 3. There were no difference in 3 groups concerning number of vessels involved. After 6 months follow-up death was found more in nonsmokers comparing to active smokers (8 of 43 patients versus 2 of 89 patients) (p < 0.001). Reinfarction was also more in nonsmokers (9 of 43 patients versus 3 of 89) (p < 0.001). There were no difference in ex smokers and nonsmokers in death and reinfarction (p > 0.05).

Discussion

Many studies have shown that cigarette smoking is associated with a higher incidence of MI and

death from CAD (5, 7, 12-17). It is well known that smoking has influence on atherogenesis, thrombosis, vasomotion and arrhythmogenesis (18). Also accelerating the atherosclerotic process smoking is enhances platelet aggregation and thrombosis and lowers the baseline of fibrinolytic activity in vessels (19 - 21).

Moreover cigarette smoking damages endothelial cell lining, increases sympathetic discharge, lowers the threshold of ventricular fibrillation and has arrhythmogenic activity (20, 21, 22). But these findings have not been universal. Paradoxically, smoking is associated with better outcome during the hospital follow-up of AMI with and without thrombolytic therapy (2, 9, 13, 15). In our study we established that complications were observed more in the active smoking group in patients who had thrombolytic therapy for AMI. VT and VF were observed more in the active smokers comparing to nonsmokers (p < 0.05). In these patients sinus

Table 3. The CAG outcome

	Non smokers (n = 16)	Ex smokers (n = 23)	Active smokers (n = 22)
1 vessel disease	11	10 (p > 0.05)	13 (p > 0.05)
2 vessel disease	3	6 (p > 0.05)	6 (p > 0.05)
3 vessel disease	1	6 (p > 0.05)	2 (p > 0.05)
NO of lesions PTCA performed	10	15 (p > 0.05)	14 (p > 0.05)
Need for by-pass surgery	2	4 (p > 0.05)	2 (p > 0.05)

rhythm is achieved by cardioversion and defibrillation. Complete Atrio Ventricular Block is established mostly in active smokers. Shock and death are established mostly in nonsmokers. In active smokers CHF (Killip 2) is found mostly comparing to nonsmokers ($p < 0.05$).

Shock and CHF could be explained by the enlargement of necrosis. In our patients anterior wall MI is found mostly in active smokers comparing to nonsmokers ($p < 0.01$). Ex smokers are found intermediary group in the our tstudy. In this group, in hospital follow-up, CHF (Killip 3 and 4) and reinfarction is mostly established ($p < 0.05$). Anterior wall MI is not found statistically meaningful in this group but 41 of 71 patients had anterior wall MI. In the 6 months follow-up reinfarction and death were found much in nonsmokers ($p < 0.001$).

Kelly and et al (6) didn't find a difference in the rate of reinfarction between nonsmokers and smokers 1 month after AMI. In our study nonsmoker 43 patients were older comparing to the active smokers. However, risk factors, DM, hypercholesterolemia ($p < 0.05$) and family history is found more in this group ($p < 0.001$).

Consequently; Active smoking patients with AMI had more complications during hospital follow-up. In the first 6 month follow-up nonsmokers had a high incidence of reinfarction and death. But these patients had a high incidence of DM, hypercholesterolemia and family history. We do not recommend smoking to patients who have DM, hypercholesterolemia, family history and AMI.

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ACUTE SILICOSIS IN QUARTZ MILLERS

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SUMMARY

Quartz may cause silicosis in a relatively short course of time in heavily exposed workers. Twenty-three males with an average age of 27 ± 7.97 years (range 17-48) had worked in a quartz mill for an average of 11.6 ± 9.4 months (range 1-36). Spirometric tests, ^{67}Ga lung scintigraphy, fiberoptic bronchoscopy and bronchoalveolar lavage studies were performed. Posteroanterior chest radiographies of the workers were scored according to the ILO standard x-ray films. Workers were allocated into two groups according to the ^{67}Ga scan scores. Group I consisted of 8 workers who had a negative scan. Group II consisted of 15 subjects with a ^{67}Ga scan score of 6.8 ± 4.1 ($p < 0.0001$). The two groups also differed significantly by x-ray scores (0 v.s. 5.6 ± 4.1 , $p < 0.001$). The groups did not differ by age nor by smoking index. Group II had a significantly longer exposure time than Group I, but the post-exposure time did not differ significantly. Pulmonary functions of Group II were significantly worse than that of Group I. Percent of alveolar macrophages were significantly lower in Group II whereas percent of lymphocytes and granulocytes, namely the neutrophils, were significantly higher. Standard x-ray films and ^{67}Ga lung scans are the most valuable laboratory techniques in assessing silicosis and BAL may also be performed to highlight the active alveolitis in these patients.

Key words: Acute silicosis, bronchoalveolar lavage.

Quartz may cause silicosis in a relatively short course of time in heavily exposed workers. It is documented that silica-laden alveolar macrophages of such patients release pro-inflammatory mediators giving rise to an accumulation of inflammatory cells in the lungs (1, 2, 3). Dust burden of the alveolar macrophages in granite workers without radiologic proof of silicosis, decrease by retirement but they never restore the level of nonindustrial subjects (4). In the autopsied lungs of granite workers fibrotic lesions associated with cristalline silica were found without any radiologically detectable pulmonary disease (5). We studied 23 quartz millers with or without radiological evidence of silicosis

MATERIALS AND METHODS

Patients:

Twenty-three quartz millers with an average age of 27 ± 7.97 (range: 17-48 years) were studied. Fo-

urteen were smokers who smoked an average of 5.4 ± 7.6 pack-years cigarettes. Nine were non-smoker. They had no prior history of pulmonary disease. They had worked in the quartz mill for 11.6 ± 9.4 months (range: 1-36 months). All had quitted work for 1 to 9 years with a mean post-exposure time of 4.6 ± 2.1 years.

Working place:

Three mills with similar environment were in different provinces. Rock was cut into small pieces outdoors. Afterwards it was milled in a bad ventilated, small mill where no protection was available. Milled quartz was sent to glass factories. The workers spend half of their working hours outdoors and the other half in the mill. They worked for seven days a week and 12 hours a day. As a side product, three percent of talc was also produced.

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Control subjects:

Twenty subjects (14 females, 6 males, age 27.5 \pm 8.4) consisted the control group. One of them was normal and the others had allergic rhinitis. All were non-smokers. No lung pathology could be detected with clinical, radiological and laboratory (spinometric tests, FOB, BAL and the histologic and electron microscopic evaluation of the bronchial mucosa) evaluation.

Diagnosis of silicosis:

The diagnosis of silicosis was based on a history of prolonged and heavy exposure to silica and abnormal chest x-ray findings consistent with silicosis according to the ILO classification (1). The profusion of small opacities, either regular (p, q, r) or irregular (s, t, u) were scored from 0 to 10 (Table 1). Co-lasence (AX) and big opacities (A, B, C) were scored from 1 to 4 and added to the profusion score.

The index of ^{67}Ga lung uptake was obtained from the posterior scan. It was based on a 0 to 16 relative scale. The average background activity per pixel was estimated from a region in the abdomen below the kidneys. The activity obtained on the liver was scored as 16. Background activity was subtracted from the region of interest and global lung activity, so ^{67}Ga uptake was scored (1). Group I was consisted of eight workers who had a negative ^{67}Ga lung scan. In Group II there were fifteen of them who had an abnormal ^{67}Ga lung scan.

Pulmonary functions:

Forced vital capacity (FVC), forced expiratory flow volume in one second (FEV1) and maximum expiratory flow-volume curves were determined by the Gould pulmonary analysis apparatus. Single breath CO diffusion capacities (DLCO) were measured with Gould-2400 computerized spirometer. The tests were done twice and the best was expressed as the percent of predicted.

Blood gas analysis was also performed at rest and after a submaximal exercise on bicycle ergometer. Arterial blood was drawn into a heparinized syringe and analysed on ABL-330 blood gas analyzer.

Immune markers:

Erythrocyte sedimentation rate (ESR), immune globulins (IgG, IgA, IgM), serum proteins (albumin, α_1 , α_2 , β and γ globulins), rheumatoid factor (RF), antinuclear antibody (ANA) and anti-ds DNA were determined.

Bronchoalveolar lavage (BAL) analysis:

The patients underwent fiberoptic bronchoscopy and BAL was performed on the right middle lobe. A total of 100 ml of saline solution (0.9 percent NaCl) in five 20 ml aliquots was instilled and gently aspirated by syringe. The retrieved BAL was filtered through 3-4 layers of gauze. Recovered cells were smeared and stained with Giemsa stain where differential count was performed. Results were expressed as the percent of the total.

Statistical analysis:

The results were expressed as the mean \pm standard deviation (S.D.). The groups were compared with student's t-test. The relation between the radiologic and other findings was tested with Spearman's rank correlation.

RESULTS

The x-ray diffractometric analysis of the last product from one of the mills revealed 95 percent of α -quartz (Figure 1).

The two groups did not differ from each other in respect to age, smoking habits and the postexposure time whereas Group II had a significantly prolonged time of exposure ($p < 0.01$) (Table 2).

^{67}Ga scan score and x-ray score showed a close correlation ($r = 0.8$, $p < 0.05$). Patients with a negative ^{67}Ga scan had also a normal x-ray. On the other hand two patients with a normal x-ray film had an abnormal ^{67}Ga lung scan score. Among the patients with silicosis six of them had simple silicosis and six had complicated silicosis. X-ray and ^{67}Ga lung scan of a patient with complicated silicosis can be seen on Figure 2 and 3. On Table 3 X-ray and ^{67}Ga scan scores can be seen.

Table 1. ILO classification of x-ray findings in silicosis

0/-and 0/0	: 0	2/2	: 6
0/1	: 1	2/3	: 7
1/0	: 2	3/2	: 8
1/1	: 3	3/3	: 9
1/2	: 4	3/+	: 10
2/1	: 5		

Table 2. Demographic findings of patients with acute silicosis

	Group I (n: 8)	Group II (n: 15)	p
Age (years)	26.6 \pm 9.2	27.2 \pm 7.5	NS
Smoking index (pack-years)	4.2 \pm 6.9	6.1 \pm 8.0	NS
Time of exposure (months)	10.2 \pm 10.2	32.0 \pm 19.7	< 0.01
Postexposure time (years)	4.7 \pm 3.3	5.5 \pm 3.8	NS

NS: Not Significant

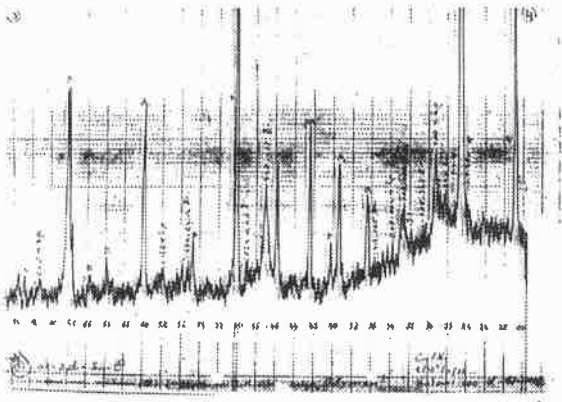


Figure 1. X-Ray diffractometric analysis.

Percent of predicted FVC, FEV1, DLCO and PaO2 after exercise was significantly lower in Group II (Table 4).

ESR, IgG, IgA, IgM levels were significantly higher in Group II than that of Group I. Among the serum proteins only α_2 was significantly higher in Group II whereas the level of the others did not differ (Table 5).

Rheumatoid factor (RF), antinuclear antibody (ANA) and anti-DNA antibody (anti-DNA) were also studied. RF and ANA were positive in a few subjects in Group II, one and three respectively (Table 6).

In the differential cell count of BAL proportion of alveolar macrophages, they were significantly increased in Group I when compared to Group II. An elevated proportion of lymphocytes was detected in Group II, compared to Group I. When compared to the control group, Group I had an elevated proportion of alveolar macrophages and a lower proportion of lymphocytes (Table 6). Proportion of

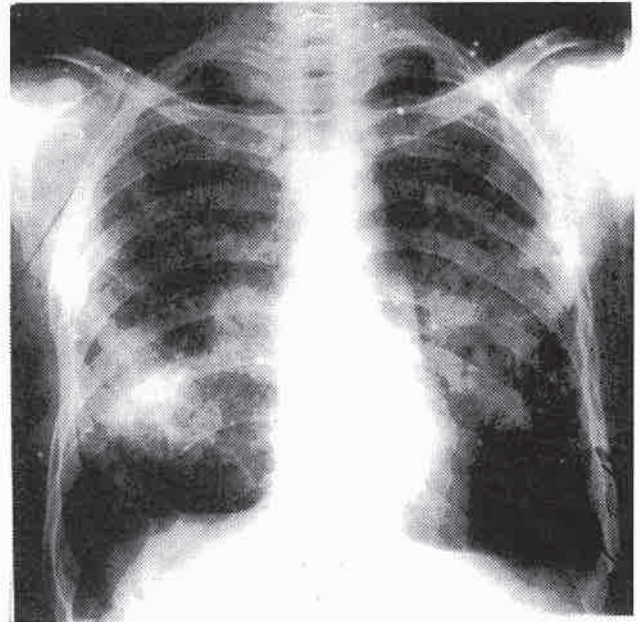


Figure 2. Chest x-ray of a patient with complicated silicosis.

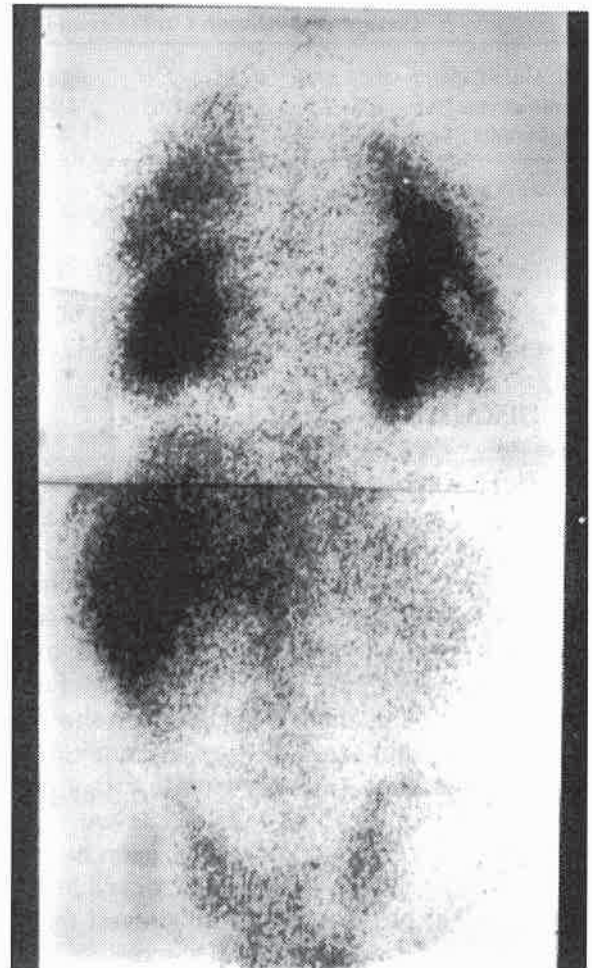


Figure 3. ⁶⁷Ga-lung scan of a patient.

Table 3. X-ray and ⁶⁷Ga scan findings of the patients

	Group I (n: 8)	Group II (n: 15)	p
X-ray score	0	5.6±4.1	<0.001
⁶⁷ Ga score	0	6.8±4.1	<0.0001

Table 4. Pulmonary functions of the study subjects

	Group I (n: 8)	Group II (n: 15)	p
FVC (% of pred.)	107.5±6.5	75.9±23.4	<0.001
FEV1 (% of pred.)	96.5±8.2	61.4±25.2	< 0.001
DLCO (% of pred.)	122.9±25.4	88.0±36.9	<0.05
PaO2 (at rest)	83.8±6.7	76.4±11.1	NS
PaO2 (exercise)	93.8±5.8	76.6±14.2	<0.05

Table 5. Immunologic findings of the study subjects

	Group I (n: 8)	Group II (n: 8)	p
ESR (mm/h)	4.0±3.96	27.3±21.2	<0.01
albumin	49.6±7.2	46.95±6.1	NS
a1 globulin	3.2±0.5	2.8±0.6	NS
a2 globulin	12.1±2.1	15.1±3.6	<0.05
b globulin	14.6±3.1	15.5±2.2	NS
g globulin	20.6±4.7	20.2±5.4	NS
IgG	1282.5±223.7	1743.8±577.2	<0.05
IgA	205.1±86.3	299.4±96.3	<0.05
IgM	152.5±38.5	168.1±64.1	NS

Table 6. Results of some of the immune markers.

	Group I (n: 11)	Group II (n: 10)
RF(+)	n: 0	n: 1
ANA (+)	n: 0	n: 3
anti-DNA (+)	n: 0	n: 0

Table 7. BAL findings of the study subjects

	Control (n: 20)	Group I (n: 8)	Group II (n: 12)
Alv. macro. (%)	89.1±8.5	95.7±2.9*	90.8±7.0**
Lymphocytes (%)	8.8±7.7	2.0±1.6*	4.3±5.6**
Neutrophils (%)	2.1±2.5	2.3±2.7	4.9±5.6

* p when compared to the control group < 0.05

** p when compared to Group I < 0.05

lymphocytes in BAL showed a weak but significant correlation with ^{67}Ga scan score ($r=0.431$, $p<0.05$).

DISCUSSION

The diagnosis of pneumoconiosis is based on the chest x-ray findings (1,6). However, air flow obstruction and emphysema of the lung is detected in some workers without any proof of pneumoconiosis on chest x-ray (6). This might be due to smoking but there does not exist any study to settle the question. In workers with a history of prolonged dust exposure, a subclinical alveolitis has been shown. This may also be implicated in the deterioration in pulmonary functions (7). Patients with radiologic evidence of silicosis had significantly lower values of FVC, FEV1, DLCO and PaO_2 after exercise.

^{67}Ga lung scan is a good indicator of inflammation of the tissue. Bisson et al. proved that ^{67}Ga scan scores of the patients with silicosis were as high as the patients with asbestosis or sarcoidosis. They

also found that ^{67}Ga scan score were closely correlated with the x-ray score of profusion of the silicotic nodules (8). Similarly, our patients with a positive ^{67}Ga lung scan had also x-ray findings consistent with silicosis.

In a postmortem study, fibrotic lesions associated with crystalline silica were found in the lungs of granite workers who lacked radiologic evidence of pneumoconiosis. These lesions were called the cryptic pulmonary lesions (5). Two of our study subjects with a normal chest x-ray had an abnormal ^{67}Ga lung scan. Thus, we suggest that ^{67}Ga lung scan may be a good method to detect these so called cryptic lesions.

Begin et al. documented an increase in ^{67}Ga scan score in close correlation with the increase in BAL cellularity even in the absence of radiologically detectable disease. They also showed an elevated ^{67}Ga uptake at sites of coalescence/conglomeration (1). Consistent with this finding, in the present study we found a weak but significant correlation between the proportion of lymphocytes in BAL and ^{67}Ga scan score.

Exposure to silica may cause changes in humoral or cellular immunity. Caplan's syndrome is the best known example of dust exposure and the changes in immune system of the workers (9). Doll et al. detected elevated levels of antinuclear antibody, rheumatoid factor and immunoglobulins (IgG and IgA). They postulated that silica induced the stimulation of B-lymphocytes and altered the surface antigenicity of macrophages giving rise to the immunologic changes in sandblasters (10). In good agreement with these results, we found a significant elevation of erythrocyte sedimentation rate, α_2 globulin, IgG and IgA in Group II. RF and ANA were positive in a limited number of patients.

Percent of alveolar macrophages of Group I was greater than that of control group and Group II. Percent of lymphocytes in BAL was lower in both groups, but significant only in Group I. Percent of neutrophils was greater in Group II when compared to control group, but not significant.

We previously studied BAL of retired coal workers who were chronically exposed to inorganic dust. We found a significantly lower proportion of lymphocytes when compared to the same control group. Coal workers with progressive massive fibrosis had proportionally higher neutrophils than that of control group. In subjects with simple pneumoconiosis the number of neutrophils per recovered ml of

BAL was significantly higher (11). In short, we found a lower proportion of lymphocytes and a slightly greater proportion of neutrophils in quartz millers and coal-workers.

Similarly, in their experimental study, Lugano and co-workers showed a neutrophilic inflammation around terminal bronchioli within one day of intratracheal silica injection in guinea pigs. After four days, the neutrophils were replaced by mononuclear cells. However, the neutrophils were significantly greater than that of controls at all time points. By day seven, the number of macrophages were elevated and small histiocyte granulomas were seen. They also showed that alveolar macrophages from experimental animals released chemotaxins for neutrophils (2).

Dauber et. al. studied the lungs of guinea pigs six months after intratracheal injection of silica. Bronchoalveolar cells obtained by standart lavage from experimental animals showed a threefold increase in the proportion of neutrophils. Multinucleated giant cells were also greater in these animals (3).

Sjöstrand et. al. studied the lung wall cells and lung cells recovered by whole lung lavage after 2 to 36 weeks after an exposure to aerolized cristobalite for eight days. In contrast to the beforementioned studies they documented a progressive increase in number of macrophages and lymphocytes. On the other hand, lavage cells increased in the first four weeks but they remained the same thereafter (12).

Christman et. al. studied 44 Vermont granite workers without evidence of silicosis. They did not found an alveolitis in these subjects (4). However, they detected an increased level of lymphocytes in

BAL of nine granite workers with 4 to 36 years of employment in industry but without evidence of silicosis (13).

Nugent et. al. detected an increased percent of lymphocytes in a sandblaster who had bilateral homogeneous and reticulonodular infiltrates on chest x-ray (14).

In simple silicosis, the lesions do not appear on chest x-ray until 20 years after the initial exposure. However, with a heavy exposure to respirable free silica particles, the lesions frequently appear as early as 4 to 8 years after first exposure. Enclosed and poorly protected workers developed visible disease in 6 to 9 months. Pulmonary alveolar proteinosis is a syndrome which is characterized by the accumulation of surfactant phospholipids and proteins in the alveolar spaces. Inorganic particulates and fibrogenic dusts are examples among diverse stimuli implicated as the cause of pulmonary alveolar proteinosis. In extreme cases of silica exposure, the intra-alveolar debris strongly resembles the lipoproteinaceous material of pulmonary alveolar proteinosis (15, 16). This may be the case in our patients. We did not observe an alveolitis in the BALs of the patients. Proteinaceous material accumulated in the alveoli may have decreased the inflammatory cells expected to be found in BAL.

Our study subjects are exposed to silica for quite a short time when compared to the ones in other human studies. Thus, the patients with silicosis have an acute form of the disease. The ones reported in the literature are chronically exposed to silica and developed the chronic form of the disease if they ever develop silicosis (17, 18).

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THYROID LESIONS IN PATIENTS WITH CHRONIC RENAL FAILURE UNDERGOING REGULAR HEMODIALYSIS: ASSESSMENT WITH ULTRASONOGRAPHY*

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Tülay Ölçer • Turhan Cumhur**

SUMMARY

It was aimed to determine the incidence of the thyroid lesions in hemodialysis patients. Thyroid glands of 25 hemodialysis patients (17 men, 8 women and aged 18-70) were examined with ultrasound utilizing a 7.5 MHz linear probe. Blood samples for TSH, fT3 and fT4 were obtained from the uremic patients just before the ultrasound examination. Thyroid glands of 10 (40%) uremic patients were normal ultrasonographically. Among 15 patients with thyroid abnormalities, 6 (24%) had diffuse hyperplasia and 9 (36%) had nodular disease. While the incidence of thyroid nodule was 36% in uremic patients, it was 9% in the control group. Among these two groups, the difference of nodule incidences was significant ($p<0.01$). There were no differences in age, sex, duration of hemodialysis and thyroid function between the patients with thyroid nodules and those without nodules. It is concluded that the incidence of thyroid nodule in uremic patients are higher than the normal subjects.

Key words : Chronic renal failure, hemodialysis, thyroid gland, ultrasonography.

Clinically unsuspected thyroid nodules are common findings during the course of parathyroid ultrasonography (US) of uremic patients with secondary hyperparathyroidism (1,2). The prevalence of the incidental nodules at the time of parathyroid operations is high as well (3). In one study, reported in 1974, it has been documented that, mean serum parathyroid hormone levels were lower in hyperthyroid and higher in hypothyroid patients (4).

The current study was undertaken to determine the frequency of abnormalities of the thyroid gland in dialysis patients assessed with ultrasonography. It was also aimed to establish whether there is a correlation between the nodular thyroid disease and age, sex, duration of hemodialysis (HD) and thyroid functions.

PATIENTS & METHODS

Twenty-five patients with chronic renal failure (CRF) who had been undergoing dialysis therapy for an average of 29 (1-65) months were included in

this study. (8 women and 17 men, ranging from 18 to 70 years of age with a mean \pm SD: 40 \pm 12 years).

The control group was selected from the volunteers who had no previous thyroid disease. Controls consisted of 14 women and 11 men with a mean age of 36 years (range:22-50 years).

A real-time scanner equipped with a 7.5 MHz linear transducer (Toshiba SSA-250; Tokyo) for small parts was used in all US examinations. Scans were obtained in the transverse and longitudinal planes, and the entire gland was imaged, including the isthmus with standard technique. The volume of each lobe was estimated, using standard geometric formula for ellipsoid volume: length X width X thickness X $\pi/6$. The volume of the whole thyroid gland was calculated from the sum of the each lobe (5).

Criterion for the diagnosis of a nodule was presence of any focal lesion that could be distinguished from the homogeneous thyroid parenchyma. Calcifications without mass lesions (vascular calcifications) and anechoic rounded lesions, 1-5 mm in di-

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ameter (dilated macro follicles) were not considered nodules and not taken into account during the evaluation. Nodules were, then classified into five groups according to their echogenicity: mixed, isoechoic, hypoechoic, hyperechoic and anechoic. Besides the echogenicity, number and size of the thyroid nodules were also noted.

Blood samples for TSH (thyroid-stimulating hormone), FT3 (free triiodothyronine) and FT4 (free thyroxine) were obtained from the uremic patients just before the ultrasonographic examination. Thyroid functions of controls with abnormal findings at US were also investigated further.

Dialysis patients with nodules and those without nodules were compared with Fisher's Exact test and Mann-Whitney U test. A P value less than 0.05 was considered statistically significant. To determine the statistical difference of the nodule incidences between the patients and the controls "the comparison of two independent proportions test" was used.

RESULTS

Laboratory findings: All FT3 and FT4 and serum TSH values were within the normal range. Blood testing yielded normal results in controls with abnormal sonographic findings.

US findings: Of 25 HD patients examined with US, thyroid glands of 10 patients (40%) were normal. The mean volume of the thyroid in these patients was 9.68 ± 2.68 ml. In the control group, 16 subjects had normal thyroid gland (64%). The mean thyroid gland volume of controls was 10.8 ± 2.13 ml.

Of 15 patients whose thyroid gland was found to be pathologic, 6 (24%) had diffuse hyperplasia. The mean thyroid volume of slightly and clearly enlarged glands were 17.9 ± 1.79 ml and 29.7 ± 0.59 ml respectively. In controls, 7 subjects (28%) had diffuse hyperplasia with a mean volume of 16.7 ± 1.84 ml.

Thyroid nodules were detected in 9 (36%) of the HD patients (Figure 1). The mean thyroid volume of the patients with nodules was 31.89 ± 52.24 ml. The nodule incidence was 8% in controls (2/25). The difference in nodule incidences between the controls and the patients was significant ($p < 0.01$). Our data suggested that no correlation was present between thyroid functions, age, sex, duration of dialysis and thyroid gland nodules (Table 1).

The nodules ranged in size from 2.5 to 50 mm in diameter. According to the echographic pattern,

Table 1. Characteristics of patients with/without thyroid nodules*

	Patients with thyroid nodules	Patients without thyroid nodules	P
No. of cases	9	16	>0.05
Age (Y)	40.55 ± 9.68	39.94 ± 14.22	>0.05
Sex (M:F)	6:3	11:5	>0.05
Duration of HD (mo.)	33.56 ± 22.41	26.38 ± 22.17	>0.05
TSH (mIU/ml)	1.01 ± 0.78	1.11 ± 1.08	>0.05
FT3(pg/ml)	3.91 ± 0.72	3.77 ± 0.37	>0.05
FT4(nq/ml)	1.22 ± 0.27	1.21 ± 0.23	>0.05

* Data are presented as mean values \pm standard deviation. HD: hemodialysis, TSH: thyroid stimulating hormone, FT3: free triiodothyronine, FT4: free thyroxine

hypoechoic nodules were the most common (62%). Multiple nodules were present in 7 (77%) patients and a solitary nodule was detected in 2 (22%) patients. Location was bilateral in 5 (55%) and unilateral (on the right) in 4 (44%) of the patients.

DISCUSSION

At present, gray-scale US is the first choice in the evaluation of the morphology of the thyroid gland although it is not capable of assessing thyroid function. It is considered to be the most sensitive method to detect asymptomatic thyroid nodules and to determine the features of these nodules in hyperparathyroidism (1,6). In our study, evaluating the thyroid gland by ultrasonography, the incidence of

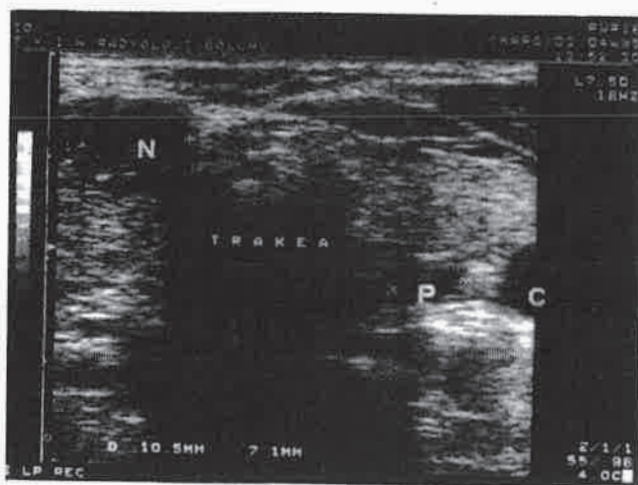


Figure 1. Transverse image of the thyroid gland demonstrates a 1 cm hypoechoic nodule (N) at the anterior of the right lobe in an uremic patient. Note also a parathyroid adenoma (P) adjacent to the posterior portion of the left lobe. C: Left carotid artery.

pathologic processes involving the thyroid of the uremic patients was found to be 60%. Ramirez reported the incidence of goitre as 58% in CRF (7). In another study, the mean thyroid volume was found to be significantly greater in patients with CRF (24 ml) than that of the controls (17 ml) (8).

Previous reports demonstrated that the prevalences of thyroid nodules in uremic patients were ranging from %41 to %64 (1,2,9,10). We found incidental thyroid nodules in 36% of HD patients. However, in the present study, there was no difference in TSH, FT3 and FT4 values between the patients with nodules and those without nodules. Our data also suggested that no correlation was present between thyroid function tests, age, sex, duration of dialysis and thyroid gland nodules. This result is com-

parable to the results reported by Miki and Hegedüs (2,8).

There are several studies that investigate the significance of the coexistence of lesions of the thyroid and parathyroid glands. Miki et al. speculated that parathormone might play a role in the development of thyroid nodules, because unsuspected thyroid nodules were found frequently in the uremic patients with secondary hyperparathyroidism (10). However, they could not find significant difference in level of parathyroid hormone between patients with nodules and those without nodules.

In conclusion, the nodule incidence in uremic patients are higher than the normal population. However, the details of the underlying pathophysiologic mechanism have not been clearly defined yet.

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IN VITRO SUSCEPTIBILITY OF MYCOBACTERIUM TUBERCULOSIS TO AZITHROMYCIN

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SUMMARY

There are a number of new drugs that have been evaluated in children and adults for activity against tuberculosis. These include amikacin, quinolones, rifamycin derivatives, clofazimine, beta-lactams and macrolides. We investigated the efficiency of azithromycin, a new macrolide antibiotic, against *Mycobacterium tuberculosis* in vitro. Forty-three isolates of *Mycobacterium tuberculosis* were tested by standard proportion method on Löwenstein-Jensen medium containing 0.25, 0.5, 1.0, 2.0 and 4.0 mg/l of azithromycin. Cultures were evaluated after three or four weeks of incubation at 37° C. Azithromycin at concentration of 0.25 mg/l inhibited 38 of 43 strains, similarly 0.5, 1.0 and 2.0 mg/l inhibited 39 of 43 strains and 4.0 mg/l inhibited 40 of 43 strains. Three of 43 strains were resistant to rifampin. Two of these three were also resistant to azithromycin in all drug concentrations. One strain was also resistant to azithromycin in 0.25 mg/l concentration. The other one strain was only resistant to streptomycin. Our results showed that azithromycin was effective against *Mycobacterium tuberculosis* in vitro.

Key words: *Mycobacterium tuberculosis*, azithromycin

Azithromycin is the prototype of a new class of antibiotics known as azalides(1,2). The antibacterial spectrum and chemical properties of azalide group antibiotics are very similar to the macrolides such as erythromycin, clarithromycin, josamycin and roxithromycin(3).

Azalides are distinguished from other antibiotics by their unusual pharmacokinetics notably high and sustained half life(1,2). Azithromycin achieves high concentrations in phagocytic cells and in fibroblasts(4). Azithromycin has a broad spectrum of activity against gram-positive and gram-negative bacteria (1,3,5). Azithromycin is also active against legionella species, chlamydia species, mycoplasma pneumoniae and mycobacteria, especially *Mycobacterium avium intracellulare*(3,5,6).

The aims of the present study were to determine the efficiency of the azithromycin against *Mycobacterium tuberculosis* and to compare the drug susceptibility, resistance patterns of azithromycin with the first line antituberculosis agents.

MATERIALS AND METHODS

Sputum specimens were obtained from 43 patients with pulmonary tuberculosis admitted to the Department of Chest Disease and Tuberculosis Faculty of Medicine, University of Ankara. None of the patients had antituberculosis therapy previously nor had a positive family history.

Azithromycin was obtained from Pfizer Inc. To make a stock solution, we dissolved 50 mg of the drug in 5 ml of methanol and then diluted the solution to a volume of 25 ml with phosphate buffer(pH 6.5). This stock solution, 2 mg/ml, was diluted further with phosphate buffer to make appropriate working solutions, which were kept refrigerated for not more than 2 weeks(7).

Löwenstein-Jensen(L-J) media were prepared containing 0.25, 0.5, 1.0, 2.0 and 4.0 mg/l concentration of azithromycin. The susceptibilities of all strains against antituberculosis drugs (streptomycin 4.0 mg/l, isoniazid 0.2 mg/l, ethambutol 2.0 mg/l, thiacetazone 2.0 mg/l, and rifampin 40.0 mg/l) were studied at the same time. Standard proportion method was used for antibiotic suscep-

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tibility testing. *Mycobacterium tuberculosis* strains were grown on L-J media. Colonies were collected and the turbidity of the resulting suspensions were adjusted with distilled water to match that of a standard suspension of *Mycobacterium bovis* BCG(1.0mg/ml). For inoculation of L-J medium the suspensions were further diluted 10^{-3} and 10^{-5} and were inoculated with and without drugs L-J media(8). After incubation for three weeks at 37°C, the colonies were counted and the number of them compared to the number of viable bacteria in inoculum. Forty-three clinical isolates of *Mycobacterium tuberculosis* were inoculated into these media with and without drugs by standard proportion method. After incubation for 3 weeks at 37°C the colonies were counted, and the number of them compared to the number of viable bacteria in the inoculum.

RESULTS

The in vitro inhibition rates of *Mycobacterium tuberculosis* for the tested concentrations of azithromycin are shown in Table 1.

Azithromycin in a concentration 0.25 mg/l inhibited 38 of 43 strains(88.4%), and 0.5, 1.0 and 2.0 mg/l inhibited 39 of 43 strains(90.7%), 4.0 mg/l inhibited 40 of 43 strains(93%). These results showed that MIC 90 value of azithromycin for *Mycobacterium tuberculosis* is about 0.5 mg/l.(Table 1)

Thirty-eight of 43 strains were found to be susceptible to five conventional antituberculosis agents (isoniazid, streptomycin, rifampin, ethambutol and thiacetazone). Three of 43 strains were resistant to rifampin. Two of them were also resistant to azithromycin in all drug concentrations. One strain was resistant to isoniazid. The same strain was also resistant to azithromycin in 0.25 mg/l concentration. One strain was only resistant to streptomycin. In vitro susceptibility and resistance rates to antituberculosis drugs of *Mycobacterium tuberculosis* shown in Table 2.

TABLE 1: Susceptibility of 43 *Mycobacterium tuberculosis* isolates to azithromycin.

Azithromycin concentrations (mg/l)	Susceptibility No	Susceptibility Rate (%)
0.25	38/43	88.4
0.5	39/43	90.7
1.0	39/43	90.7
2.0	39/43	90.7
4.0	40/43	93.0

TABLE 1: Susceptibility test results with conventional antituberculosis agents and different azithromycin concentrations.

Drug	S	R	RA 0.25	RA 0.50	RA 1.0	RA 2.0	RA 4.0
Rifampin	40	3	2	2	2	2	2
Isoniazid	42	1	1	-	-	-	-
Streptomycin	42	1	-	-	-	-	-
Ethambutol	43	-	-	-	-	-	-
Thiacetazone	43	-	-	-	-	-	-

S: number of sensitive strains, R: number of resistant strains, RA: number of azithromycin resistant strains in different concentrations

DISCUSSION

The increase in the prevalence of drug resistance prompted a continued research for suitable alternative antituberculosis chemotherapeutics. A number of new drugs that have been evaluated in children and adults for activity against tuberculosis. These include amikacin, quinolones, rifamycin derivatives, clofazimine and beta-lactams(9). Recently, a large number of in vitro studies have been performed in mycobacterial infections, especially in *Mycobacterium avium* intracellulare infections using macrolides(10,11,12,13). The purpose of this study was to determine the in vitro activity of azithromycin, a new macrolide antibiotic, against 43 clinical isolates of *Mycobacterium tuberculosis*.

Infections caused by intracellular pathogens are often difficult to treat, because the concentrations of drug achieved within the cell are insufficient to maintain a bactericidal effect. The effectiveness of azithromycin against a number of intracellular pathogens has been found in specifically developed animal models(14). Baldwin et al. have recently shown that patients undergoing fiberoptic bronchoscopy had alveolar macrophages with peak levels of azithromycin in the order of 20 µg/ml 48 hours after administration of 500 mg of azithromycin. These peak concentrations were six fold greater than those in bronchial mucosa and were well above the minimum inhibitory concentration (MIC) for commonly encountered respiratory pathogens and mycobacterium species(15).

Azithromycin has been proposed for single daily dose treatment of infections caused by organisms with MICs at or even above 1 mg/l (3).

Evaluation of azithromycin against *Mycobacterium avium* complex(MAC) has been performed by Inderlied et al. They showed azithromycin to have a MIC 90 of 64

mg/ml in vitro for 15 strains of MAC obtained from acquired immune deficiency syndrome (AIDS) patients. Bactericidal activity of azithromycin was reported to be more than or equal to 64 mg/l (16). The same study group evaluated the efficiency of azithromycin in male homosexuals with AIDS and MAC disease. It has been shown that a single dose of 500 mg azithromycin per day for 10 to 30 days causes a consistent reduction of mycobacteremia and a clinical improvement in three quarters of patients (17).

To our knowledge there has been no study evaluating the effectiveness of azithromycin against *Mycobacterium tuberculosis*. In our study the inhibitory activity of azithromycin in vitro against *Mycobacterium tuberculosis* was found to be comparable to the activity of this drug reported against *Mycobacterium avium*.

These results indicate a need for further studies, including evaluation of the bactericidal activity of this drug against *Mycobacterium tuberculosis*, and experiments in mice to determine the potential efficacy of this new agent for treatment of tuberculosis.

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EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY (ESWL) OF BILIARY STONES

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SUMMARY

In this study 13 patients with symptomatic gallbladder stones who had surgical contraindication or refused surgery and 9 patients with common bile duct stone in whom at least one endoscopic sphincterotomy and stone extraction trial with basket or balloon catheter were performed but failed were taken into ESWL program. 10 mg/kg/day ursodeoxycholic acid was started 7 days before ESWL treatment. In 8 weeks, 5 of 13 (39%) patients with gallbladder stone had appropriate fragmentation (<5 mm) and complete clearance of fragments. In four cases (30.1%), it was impossible to obtain any fragmentation, so they were shifted to the surgical treatment while in 3 (23%) cases incomplete stone fragmentation and in 1 (7.9%) case biliary sludge were obtained in the gallbladder after ESWL. These results represent approximately 60% success rate and are a little lower than those reported in the literature. However, complete clearance was obtained in 6 of 9 (66%) patients with common bile duct stones. This result is so successful as brought up in former studies.

Keywords: ESWL, gallbladder stone, common bile duct stone

So far, cholecystectomy has been the golden standard for the treatment of gallbladder stones. The patient's requirements to recover with less invasive techniques motivated the studies for the development of alternative methods in the treatment of gallbladder stones. Extracorporeal shock wave lithotripsy (ESWL) was first performed in the treatment of human gallbladder stones in 1985 by Sauerbruch et al. (1). Today, ESWL combined with oral bile acid treatment is effective in the short term and giving hope in the long term treatment of gallstones (2).

In the treatment of common bile duct stones, ESWL is mainly an adjuvant modality. When the endoscopic treatment is unsuccessful, it can be effective in stone fragmentation (3). However, after ESWL most patients require additional endoscopic interventions.

In this study a second generation high energy electrohydraulic Dornier lithotripter was used for the treatment of gallbladder stones in patients who had surgical contraindications or refused surgery. We also included a limited number of patients with

common bile duct stone in whom endoscopic methods failed to clear the stones.

MATERIALS AND METHODS

Patients with symptomatic gallbladder stones who had surgical contraindications or refused surgery were taken into the lithotripsy program. Patients with chronic liver disease, coagulopathy, abdominal vascular anomaly, acute cholecystitis, acute gastroduodenal ulcer, acute pancreatitis and biliary obstruction were excluded. Thirteen patients, 8 female 5 male, age between 41-83 (mean 64) years were eligible for the study. The diagnosis and the number of the stones were established by ultrasonography. Seven patients had solitary stones, 5 patients had 2 and one had 3 stones in the gallbladder. The diameter of the stones were between 1.4-3.2 cm (average 2.1 cm). In all patients, possibility of calcified stone was excluded by plain abdominal X-ray. The patency of cystic duct and a functioning gallbladder (50% decrease in size after a standard

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meal) were demonstrated by oral cholecystography. Ursodeoxycholic acid (UDCA), 10 mg/kg/day, was started 7 days before ESWL and continued until the stones disappeared completely. Following ESWL, ultrasonographic controls were made on 3 consecutive days and then every 2 months.

Nine patients with common bile duct stones in whom at least one endoscopic sphincterotomy and stone extraction trial with basket or balloon catheter were performed but failed were also taken into the lithotripsy program. They consisted of 5 female and 4 male, age between 45-79 (mean 59) years. The diagnosis of common bile duct stone was made by endoscopic retrograde cholangiopancreatography (ERCP). Six patients had 1 stone, one had 2 and the other 2 patients had multiple stones. ESWL was applied to a total number of 15 stones. Average diameter of stones was 2.8 cm.. Nasobiliary drainage catheter was applied to every patient in order to focus the shock waves on to the stone during ESWL, to prevent cholangitis and to obtain control cholangiogram after ESWL.

Hemoglobin, white blood cell, platelets, prothrombin time, ALT, AST, GGT, alkaline phosphatase, bilirubin, amylase, BUN, creatinin levels and urine analysis were done before and after ESWL.

In fragmentation of the stones, high energy Dornier lithotripter was used. Premedication was done by diazepam and meperidin. In each session a maximum of 1600 shock waves were applied. Stone fragment size under 5 mm was considered to be a successful end point of fragmentation. When successful fragmentation was not obtained in one session, further treatment schedules were applied for the second or third times. Follow-up of patients after ESWL continued for 2-21 (mean 13) months.

RESULTS

Gallbladder stones: An average of 1400 shock waves were applied to gallbladder stones. Appropriate fragmentation (<5 mm) was achieved in 5 of 13 (39%) patients in 8 weeks. All of these patients had solitary stones. Only one session of ESWL was needed in 4 of 5 patients and only 1 patient had stone recurrence 9 months after the treatment. Remaining 8 cases needed 2 or 3 ESWL sessions but appropriate fragmentation could not be gained in 4 (50%) of them, therefore they shifted to surgical therapy. While 3 patients had incomplete fragmentation, the other one had biliary sludge after ESWL sessions.

UDCA treatment resulted in complete fragmentation and stone clearance in 2 of 3 patients with incomplete fragmentation during the follow-up. Unfortunately, after incomplete fragmentation one patient was not able to clear the fragments under 6 months UDCA therapy and treated by surgery. One patient who had sludge in the gallbladder was successfully treated with UDCA and was sludge-free 1 year after ESWL.

Common bile duct stones: The number of shock waves applied to common bile duct stones were between 1200-1600. Complete clearance was obtained in 6 out of 9 (66%) patients. Spontaneous clearance was observed in 2 patients after ESWL while remaining 4 patients needed endoscopic stone extraction following ESWL. Fragmentation and stone clearance could not be obtained in 2 patients with solitary stone and in 1 patient with multiple stones following 3 unsatisfactory ESWL sessions. These patients underwent surgical therapy.

Complications of ESWL: There was no abnormality in blood and urine analysis in patients with gallbladder or common bile duct stone after ESWL. Biliary pain occurred in 4 cases and 2 of them needed additional analgesics. Among patients with common bile duct stones, additional analgesics were given to 6 cases. One patient had macroscopic hematuria while another one had echimotic lesions over the skin. Hemobilia was observed in one patients with common bile duct stone, but it spontaneously resolved.

DISCUSSION

Surgical treatment of biliary stones is the classical and most efficient way of therapy but it is invasive. As there is a need for a non-invasive technique, different types of medical treatment methods are under investigation for the treatment of biliary stones. Oral dissolution therapy can be effective on very small stones and only 40-50% complete clearance of gallbladder stones can be obtained in 1-2 years (4,5). In spite of a high success rate of direct dissolution therapy, reaching to 80%, it is relatively an invasive treatment option. Today ESWL which has taken a part in the treatment of biliary stones has the following advantages: 1. It is non-invasive 2. Patients can be treated without hospitalization 3. Biliary tract injury is not seen 4. It has low mortality and acceptable morbidity 5. It is effective. However, to reach acceptable success rate, patients must be care-

fully selected. Because of the limitations in the selection of patients, only 10-20% of the patients who have symptomatic calculus are appropriate for the treatment with ESWL (1,2).

Today, ESWL is combined with oral bile acid therapy in the treatment of biliary stones. Combined treatment has a remarkable superiority when compared with ESWL alone (1,2,6,7). The success rate of ESWL with solitary stones smaller than 2 cm. is around 80% (60-90%) (6,7). Success rate decreases to 60% if the size of the solitary stone is 2-3 cm. and even to 50% if there are 2 or 3 stones (7,8). Successful fragmentation with fragment size <5 mm can be achieved in 83% of cases and is necessary for complete clearance (8). In our study complete clearance was obtained in 5 out of 13 patients with gallbladder stones. This result represents a 40% success rate and is lower than those reported in the literature. Nevertheless, if 2 patients with incomplete fragmentation and 1 with biliary sludge after ESWL who had complete clearance during the UDCA therapy are added to these 5 patients, success rate rises to 61.5%. Although we have limited number of patients to make a clear-cut statement, the main reason of our low success rate seems to be related to our lack of experience with ESWL, especially in focusing the shock waves on to the gallbladder stones. In our study, factors affecting the fragmentation rate such as stone volume, number of stones and stone's being or not being radioluscent were the same as in other studies. After the treatment of gallbladder stones with ESWL, recurrence rate in the first year has been reported to be around 9% (9,10). After the successful clearance of stones, there was only one recurrence but because the number of our cases is very few it is hard to derive any conclusion.

The main treatment modality for common bile duct stones is endoscopic techniques. However en-

doscopic mechanical lithotripsy and stone extraction can not be achieved in 10% of these patients (11,12). 8-25% of the patients who are under endoscopic treatment are taken into ESWL program (13,14). The success rate in the clearance of common bile duct stones can be high as 80% (12,13). In our study successful stone disintegration occurred in 6 out of 9 (66%) patients. In common bile duct stones although stone fragmentation is obtained in many cases, adjuvant endoscopic stone extraction is needed as seen in our study. More recent approach in the treatment of common bile duct stones is intracorporeal lithotripsy (15). However, recent studies showed that there is no superiority of this modality to ESWL (16)

No mortality was observed in our study. However, 0.5-1% mortality rate has been reported previously (17,18). With respect to complications seen after ESWL, we have not observed any serious complication such as pancreatitis and cholecystitis. However pain was common and easily controlled by additional analgesics. Hemobilia was the most serious complication that was seen in one patient with common bile duct stone. This patient did not require any blood transfusion. It was transient and thought to be related with catheterization of common bile duct.

In conclusion, ESWL can be used in the treatment of gallbladder stones in patients who have a surgical contraindication or who refuse surgery. In this study it is not found so successful with respect to clearance of the gallbladder stones as brought up in some of the former studies. On the other hand ESWL is a useful adjuvant method especially in the treatment of patients with common bile duct stones in whom the stones can not be cleared by sphincterotomy and mechanical stone extraction.

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ASSOCIATED ANOMALIES IN CONGENITAL GASTROINTESTINAL OBSTRUCTIONS AND ABDOMINAL WALL DEFECTS. THE CHALLENGE OF PEDIATRIC SURGEON

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SUMMARY

Between the years of 1987 and 1995, 147 patients with congenital gastrointestinal obstructions and abdominal wall defects included to the study. The cases were evaluated retrospectively according to gestational age, birth weight, primary and associated anomalies.

The 59 (40.1%) of the patients had associated anomalies. Twenty-six (44.1%) of them were major anomaly and included a life threatening condition. Associated anomalies were multiple in 18 (30.5%) patients.

As a conclusion, the pediatric surgeon must be more careful in completing of physical examination for the patient's health and always keep in mind a chromosomal analysis of the patient and genetic counseling to the family.

Key Words: Associated anomalies, neonatal surgery

To all intents and purposes neonatal surgery is the surgery of congenital malformations(1). It is therefore important for the pediatric surgeon to know something about the frequency of malformations, associated anomalies, their etiology. During this century congenital malformations have gradually increased in importance as a cause of perinatal and neonatal mortality. This is not because malformations have increased in frequency but because other causes of infant death such as infection, poor nutrition and birth asphyxia have been controlled. Most of the congenital anomalies are not unique but also have associated anomalies with them. Some of these associated anomalies are not so important but some have vital importance. When receiving the patient to the newborn service one must always complete a full physical examination to exclude other associated anomalies. We here present our experience with associated anomalies in congenital intestinal obstructions and abdominal wall defects.

MATERIAL AND METHOD

Between the years of 1987 and 1995, 147 patients with congenital intestinal obstruction and ab-

dominal wall defects included to the study in the Ankara University Faculty of Medicine Pediatric Surgery Department. The cases were evaluated retrospectively according to the gestational age, sex, birth weight, primary anomaly and associated anomaly.(Fig.1)

RESULTS

From the congenital intestinal obstructions, primary malrotation, jejunoileal atresia, apple peel syndrome, esophageal atresia and tracheoesophage-

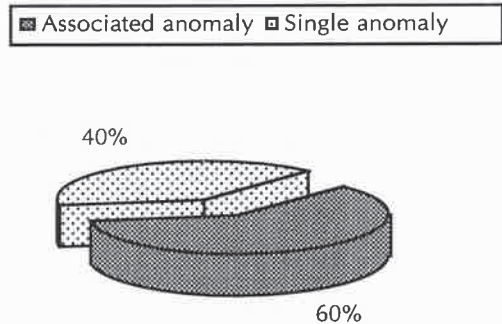


Figure 1: The overall incidence of associated anomalies

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al fistula, annular pancreas and anorectal malformations included to the study while gastrochisis, omphalocele and extrophia vesicalis were accepted as abdominal wall defects. (Fig.2)

There were 7 primary malrotation patients, the associated anomalies with the disease were; internal herniation (1), gastroesophageal reflux (1), Down syndrome (1).

From the 15 intestinal atresia patients 10 were simple jejunal atresia and 5 were apple peel syndrome. The 2 cases with jejunal atresias had associated anomalies; one had a Meckel diverticulum and the other one had right femur distal agenesis, left pes equinovarus and bilateral metacarpophalangeal multiple deviations. Four of the 5 apple peel syndrome also had associated anomalies such as; malrotation (1), total aganglionosis (1), VSD,PDA,syndactily (1) and PDA (1).

There were five duodenal atresia and all of them had associated anomalies such as; malrotation (1), Down syndrome(1), Down syndrome + Meckel diverticulum (1),esophageal atresia and trachaesophageal fistula (1) (Fig.3) and polidactily (1).

Four of twenty-nine esophageal atresia and trachaesophageal fistula had associated anomalies ; renal anomaly (1), GER (1), Meckel diverticulum + bifid uvula (1), tracheal diverticulum (1).

There were four patients with annular pancreas and 2 had associated anomalies; malrotation (1) and Meckel diverticulum (1).

The last group in congenital intestinal obstructions were anorectal malformations (40 patients) which showed the maximum incidence of associated anomalies in our series. 2 anal atresia+ duodenal atresia, 2 anal atresia+EA+TEF, 1 persistent cloaca+prune-belly+bilateral renal dysplasia, 1 persistent cloaca+bilateral hydronephrose, 3 anal atresia+hipospadias, 1 anal stenosis + ASD + VSD + Hirschprung, 1 anal atresia + Bilateral undescended testis + polydactly, 1 rectal atresia+meckel diverticulum+sigmoid duplication, 1 anal atresia+cleft palate and lip, 1 anal atresia+syndactily, 1 anal atresia+hydrocephalus, 1 anal atresia+Down syndrome, 1 anal atresia and penoscrotal transposition (Fig.4), 1 persistent cloaca+left renal aplasia.

There were 46 patients with abdominal wall defects.(Fig.5) Twenty-four of them were omphalocele which shows the maximum incidence of associated anomalies; 4 malrotations, 2 malrotation+meckel diverticulum, 1 bilateral undescended testis, 1 cloacal extrophia, 1 ulnar and radial hipogenesis+bilateral undescended testis+hipospadias, 1 syndactily, 1 polydactily+syndactily, 1 down syndrome+meckel diverticulum, 1 Meckel diverticulum, 1 multiple intestinal atresia, 1 E.vesicalis+cloacal extrophia+bila-

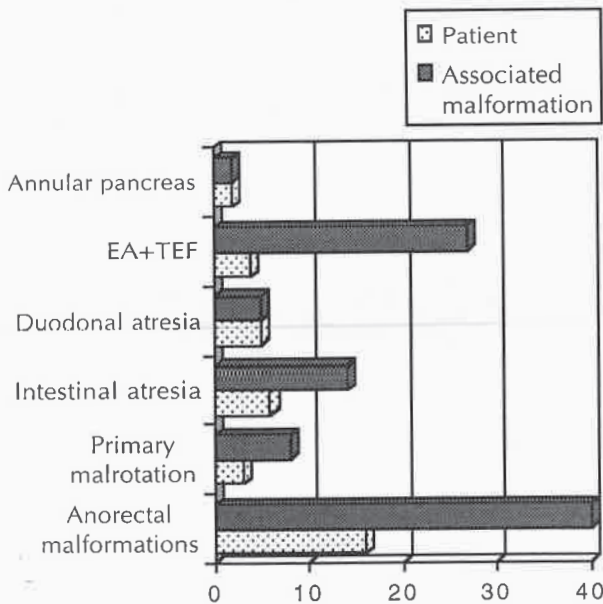


Figure 2: The ratios of associated anomalies in gastrointestinal system obstructions

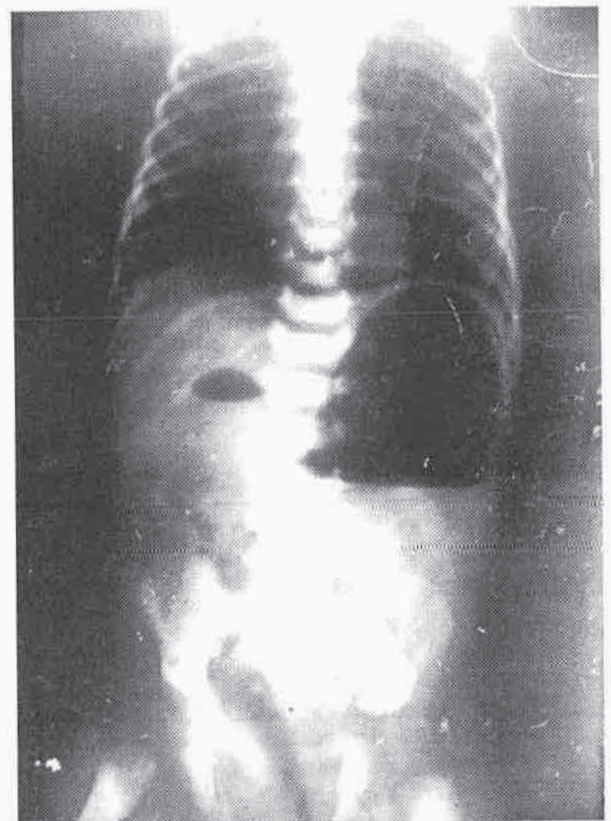


Figure 3: Gastrointestinal system.



Figure 4: Anal atresia and penoscrotal transposition.

teral coanal atresia, 1 meckel+hipospiadias, and 1 patent ductus omphalomesentericus. From the 13 gastrochisis patient only 2 had associated anomalies; 1 E.Vesicalis, 1 ileocaecal atresia and all of them had nonrotation or malrotation. Only 1 of 9 E.vesicalis patients had multiple associated anomaly; anterior ectopic, stenotic anus+microphthalmia+congenital cataract. The others had inguinal hernia as an associated anomaly.

DISCUSSION

The incidence of recognizable associated congenital defects associated with EA is between 50-70% (2,3). The anomalies vary from minor skeletal deformities to uncorrectable cardiac defects. The most common associated anomalies are cardiac (30%: PDA, VSD, and ASD are the most common) and gastrointestinal (12%) especially imperforate anus (duodenal atresia, annular pancreas and pyloric stenosis are also seen with increased frequency) (2,3,4). Most importantly, every newborn with an imperforate anus should be carefully checked for the presence of EA and vice versa (6). Infants with VACTERL syndrome associated are increasing in incidence (25% to 30% of all cases) (6). There is difference in overall incidence of these associated anomalies.

Duodenal atresia and stenosis are frequently associated with an annular pancreas. Anomalies of bowel rotation and fixation are also frequently noted in association with duodenal anomalies (7). Various biliary and pancreatic anomalies have been observed in patients with duodenal atresia and stenosis. These include biliary atresia, choledochal cyst, pancreatic lipomatosis, dual pancreatic duct and bi-

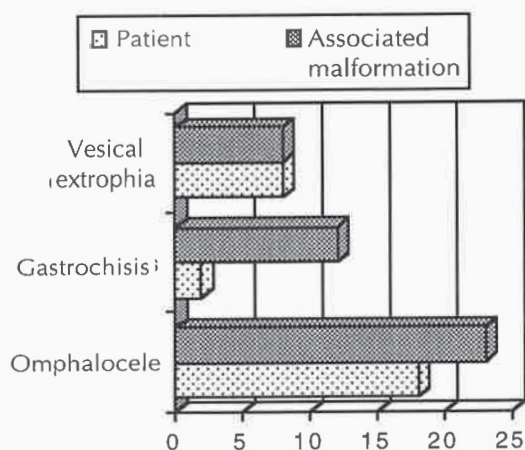


Figure 5: The ratios of associated anomalies in abdominal wall defects

le duct insertion with communication between the proximal and distal atretic segments as a result of persistence of the primitive dual duct stage of development of the bile duct (8). The association with Down's syndrome has long been recognized.

The incidence of associated malformations with intestinal atresias excluding duodenum is somewhat similar to the other series (9). Ten of these atresias were simple jejunal atresia, the others were apple peel syndrome. With apple peel syndrome the incidence of associated anomalies rises.

Although imperforate anus usually occurs as an isolated malformation, it may coexist with duodenal atresia, EA, vertebral and cord anomalies, Down's syndrome and congenital heart diseases (11). Approximately 60% of patients with high or intermediate forms of imperforate anus have some form of associated genitourinary malformations or VUR. The incidence of genitourinary malformation with low anomalies is only 15% to 20%; however associated anomalies of the GU tract are particularly important to recognize early if deterioration of renal function is to be avoided (10). In our series the incidence of genitourinary associated anomalies is not as high as other series, this may result from not routinely detecting them.

Gastrochisis: Nonrotation always accompanies this condition, and the bowel is not fixed to the abdominal wall. In contrast to infants with omphalocele, the incidence of associated anomalies in patients with gastrochisis is relatively infrequent. The exception to this general observation is the occurrence of intestinal atresia which may complicate gastrochisis in 10% to 15% of these patients. Atresia

of the bowel is often related to intrauterine volvulus or an interruption of the blood supply to a segment of exposed intestine by compression in a tight defect in the abdominal wall (11). We have seen this phenomenon only in one patient. The lower incidence of associated anomalies in this group may result from the number of our cases.

Omphalocele: More than 50% of the cases have other serious defects involving the alimentary tract, and the cardiovascular, genitourinary, musculoskeletal, and central nervous systems (13,14). Many infants born with an omphalocele are premature. Others may be affected by a number of chromosomal syndromes including Beckwith-Wiedemann syndrome characterized by gigantism, macroglossia, and an umbilical defect in the form of either an umbilical hernia or an omphalocele (14). Infants with Beckwith-Wiedemann syndrome have visceromegaly and pancreatic islet cell hyperplasia that may result in significant hypoglycemia complicated by seizures in the newly born. These infants also have an increased incidence of malignant tumors including Wilms' tumor, NB and adrenocortical tumors. Omphalocele may occur in infants with other serious chromosomal abnormalities such as trisomy 13-15, trisomy 16-18 and trisomy 21. The maximum incidence of associated anomalies have

seen in this group and correlated with large series in literature.

Among extrophic anomalies, vesical extrophia is somewhat different than the others. It is almost entirely associated with inguinal hernias. In our series the high incidence of inguinal hernias do exist. One of our patients had a multiple congenital defect. The physician has to keep in mind the coexistence of inguinal hernias and vesical extrophia.

CONCLUSION

Associated anomalies are major problems. These retrospective study have shown us its incidence is not low. When you examine this article you will find that nearly all of these datas were related to physical examination. If you increase the diagnostic capabilities of the hospital be sure that you will find more. And you will see that some of these associated malformations have vital importance. An associated anomaly protocol must be prepared as soon as possible for not to omit them.

Congenital malformations and associated anomalies are major problems that a physician (neonatalog or pediatric surgeon) must solve. The pediatric surgeon must see the problems as a whole.

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APPLICATION OF SILICONE SHEETING IN THE TREATMENT OF BURNS (HISTOPATHOLOGIC STUDY)

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Sarper Yılmaz** • Erdem Yormuk***

SUMMARY

Silicone dressings have been widely used in the treatment of burns, split thickness graft donor sites, hypertrophic scars and keloids. However, controversy still exists among the authors making research about the biologic effects of silicone. In this experimental study, we created second degree deep burns on the backs of pigs and treated them with silicone sheeting and compared the results with conventional dressings. According to clinical and histopathologic results, silicone sheeting seems to have better results.

Keywords: Silicone, Silicone sheeting, Burn wound, Burn dressing.

Although silicone is a subject of various arguments, in practicable aspects of Plastic and Reconstructive Surgery it has been widely used for a long time and still maintains its validity.

History of silicone applications in burn treatment dates back to 1960s (1). In 1963 Gerow et al (2), in 1965 Miller et al (3) and in 1967 Spira et al (4) published their successful results of silicone treatment in hand burns. These studies resulted in rapid and complete healing in second degree burns. Rapid growth of granulation tissue with better vascularization provided better recipient areas for grafting and immediate return of hand functions. In 1967, Weeder et al (5) treated seven patients who had second degree burns in other parts of the body by silicone immersion and they reported similar successful results.

Nowadays, combinations of different forms of silicone with various materials became one of the main concerns of many burn centers in order to make them more effective in the management of burns.

In our department, silicone sheeting dressings have been used in the treatment of hypertrophic scars and keloids since 1989. Successful results obtained with silicone applications encouraged us to use this method in the management of donor and recipient sites of split thickness skin grafts. Compared to conventional dressing methods we obtained

rapid and regular epithelialization with relatively lower degrees of wound contraction. These results gave rise to the idea of applying the same method in the treatment of second degree burn wounds on an experimental basis.

MATERIALS and METHODS

In this study five 7 months old pigs (two females and three males) were used. The similarity of the pig skin characteristics to man led us to prefer pig in our study (6).

We planned to create 10 second degree deep burns sized 6 x 6 cm on the back of each pig. Wounds were parallel and symmetrical to each other on the back of each pig. In order to accomplish this, a custom made iron providing an aluminum plate with a surface area of 36 cm² and thickness of 7 mm was used. This iron also had a thermostatic control which enabled us to regulate the intensity of heat.

Pigs were anaesthetised with Ketamin Hydrochloride (10 mg/kg IM). Previously planned areas were burned for 15 seconds with 900 C° after being shaved and cleaned properly.

Burns created on the left side of the back served as control and right side for experimental purposes. Control sides were dressed with chlorhexidine + vaseline impregnated gauze and the experimental si-

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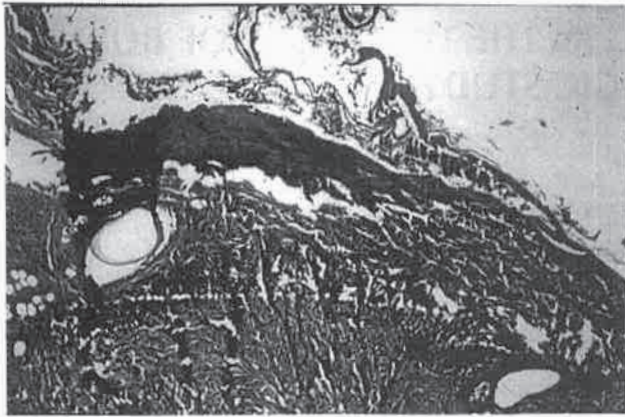


Figure 1: At the 7th day, there were edema and polymorphonuclear cell infiltration in the dermis and no epithelialization was observed at the specimens harvested from either sides (hematoxylin-eosin; original magnification, x40).

des were covered with 0.5 mm thick silicone sheeting. Dressings were changed in every other day under ketamine anesthesia. Incisional biopsies were performed on 7, 14 and 21st days after burn.

RESULTS

On day 7, histopathological examinations of the biopsy specimens revealed no epithelialization on either sides. There were also intense inflammatory cell infiltration and edema in dermis (fig 1).

On day 14, epithelialization began to creep as a thin layer on the right side dressed with silicone sheeting. Also inflammatory cell infiltration and fibroblastic proliferation were limited to superficial dermis (fig 2). In the conventionally dressed group, there was no sign of significant epithelialization and there



Figure 2: At the 14th postburn day a thin layer of epithelialization was appeared at the specimens of silicone side (hematoxylin-eosin; original magnification, x20).

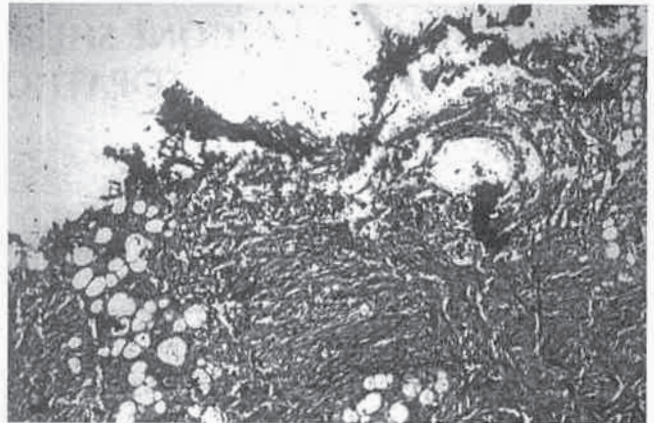


Figure 3: At the 14th postburn day, there was significant inflammatory cell infiltration and no epithelialization at the specimens of the conventional therapy side (hematoxylin-eosin; original magnification, x40).

was an intense inflammatory cell infiltration down to the deeper layers of dermis (fig 3).

The results obtained on day 21 demonstrated complete epithelialization, connective tissue proliferation together with scarce existence of inflammatory cells in the silicone sheeting dressed group (fig 4). On the other hand, irregular and inadequate epithelialization along with the intense inflammatory cell proliferation and excessive amounts of connective tissue were observed in the conservatively treated group (fig 5).

DISCUSSION

Throughout the history, burn wounds have been treated with dressings of various materials to obtain the benefits of accelerated healing (7,8). Altho-



Figure 4: At the 21st postburn day epithelialization was completed on the silicone side (hematoxylin-eosin; original magnification, x10).

ugh, none of the dressings satisfy all the requirements of a perfect wound dressing, recently Quinn et al (9) described that a silicone gel sheet fulfils some of the requirements of the ideal burn dressing; it forms an effective bacterial barrier, is permeable to water vapor and allows gas exchange. The silicone sheet also offers good, moist environment for optimal wound healing. After introduction of silicone immersion management of burns first by Gerow et al in 1963 and followed by others (2,3,4,5,10), silicone gel sheet was first used in 1982 by Perkins et al successfully for the treatment of hypertrophic scars (11). Effectiveness of this mode of therapy was confirmed by others (9,12,13,14). The effect of silicone sheet dressings on the healing of split skin graft donor sites were investigated and controversial results were reported (15,16). The exact mechanism of the positive influences of silicone in wound healing is not clear.

Since most of the previous studies mentioned above, were uncontrolled clinical reports, they have always been a matter of criticism. Therefore the results of this study, including histopathological observations on experimentally controlled burn wounds of pigs, confirmed that topical use silicone sheet has a beneficial effect on epithelialization of

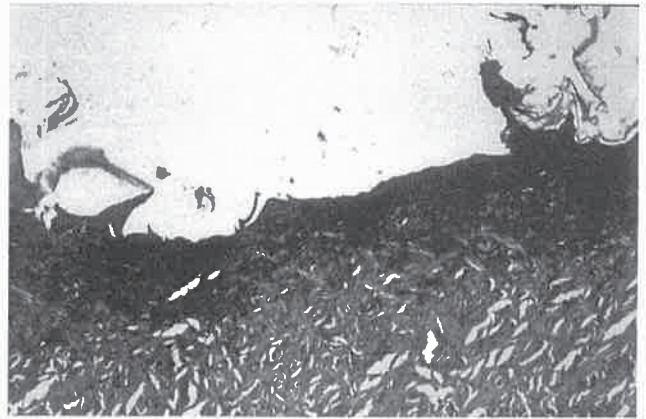


Figure 5: At the 21st postburn day epithelialization was still irregular on the conventional therapy site (hematoxylin-eosin; original magnification, x40).

burn wounds over the vaseline and chlorhexidine impregnated tulle gras dressing in burn care.

CONCLUSION

In view of the simplicity of this treatment and absence of major side effects, this mode of therapy should not only reserved for the management of hypertrophic burn scars but also be used in acute burn wound care.

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VENTRICULAR TACHYCARDIA IN PATIENTS WITH STRUCTURALLY NORMAL HEARTS

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SUMMARY

Ventricular tachycardia may occur in various clinical settings. But, approximately in 10% of patients with ventricular tachycardia, no definite structural heart disease could be disclosed. Characteristic features of that kind of tachyarrhythmias include absence of obvious structural heart disease, presence of single sustained monomorphic ventricular tachycardia, less well defined underlying electrophysiologic mechanism, and a good arrhythmic prognosis. Ventricular tachycardia in structurally normal hearts mainly originates from right ventricular outflow tract or left ventricle inferoapical septum. The distinction can be made easily with use of surface ECG findings. In this article, characteristic features of idiopathic ventricular tachycardia have been reviewed..

Key words: Tachycardia, ventricular arrhythmia

Ventricular tachycardia may occur in individuals of all age groups, and most patients have a structural cardiac abnormality or a recognized predisposing condition underlies the arrhythmia. Paroxysmal sustained ventricular tachycardia in patients without clinically demonstrable organic heart disease and without any identifiable predisposing factors for arrhythmia is termed idiopathic, benign, primary or functional ventricular tachycardia (1). The prevalence rate of sustained ventricular tachycardia in subjects without organic heart disease is rather rare (2-4). In early reports, idiopathic ventricular tachycardia was estimated to constitute approximately 5 % to 18 % of patients who manifested recurrent paroxysmal ventricular tachycardia (1). But, it is important to notice that in many of the published cases the presence of myocardial pathology has not been excluded with detailed investigation. Abnormalities may be present in apparently normal patients without evident cardiac abnormalities, the question is, when can a given heart be called normal? As with any diagnosis that is reached through a process of exclusion, the 'absence of proof' is not the same as 'proof of absence'. Inapparent coronary ar-

tery disease, unrecognised cardiomyopathy, subclinical myocarditis, localized myocardial disease are the potential causes of undetermined heart disease in patients with apparently normal hearts. Nonetheless, when no evidence is forthcoming from investigation to invoke structural heart disease as the basis for the arrhythmia, the ventricular tachycardia is designated 'idiopathic'.

There are some common features of ventricular tachycardia in this population, which include

- 1) no obvious structural heart disease
- 2) usually a single monomorphic configuration of QRS complex
- 3) less well-defined underlying electrophysiologic mechanisms
- 4) generally a good prognosis in terms of arrhythmic mortality (5).

We can organise the discussion of idiopathic ventricular tachycardias, that follow, according to QRS morphology or underlying electrophysiologic mechanisms. We preferred to divide this kind of tachycardias according to QRS morphology, because we get some evidence about the tachycardia from ECG at first.

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Idiopathic ventricular tachycardias according to QRS morphology:

1-Sustained ventricular tachycardia with QRS configuration of right bundle branch block.

2-Sustained ventricular tachycardia with QRS configuration of left bundle branch block.

Sustained ventricular tachycardia with QRS configuration of right bundle branch block:

This form of ventricular tachycardia is primarily seen in a young population (6,7). The clinical presentation of ventricular tachycardia has been relatively benign. Majority of patients have only palpitations, a minority presents with near syncope or syncope (6,7). ECG pattern is suggestive of an arrhythmia focus in the left ventricle. Catheter ablation data confirmed the origin of ventricular tachycardia in those cases. The results revealed that ventricular tachycardia originated in mid-apical region of the left inferior septal site in patients whose QRS morphology during ventricular tachycardia showed left axis deviation, and from mid-apical anterosuperior site in patients whose QRS morphology during ventricular tachycardia showed right axis deviation (8). Ventricular tachycardia can be easily induced by programmed electrical stimulation. On the other hand, after attaining a critical range of cycle lengths, the sinus, atrial and ventricular paced rhythm can initiate onset of ventricular tachycardia without extrastimulation (1,5). Unique features of this ventricular tachycardia has been its uniform responsiveness to intravenous and oral verapamil administration (VERAPAMIL-RESPONSIVE VENTRICULAR TACHYCARDIA). This has led the suggestion that the electrophysiologic mechanism of this form of ventricular tachycardia may be due to triggered rhythmic activity related to delayed afterdepolarizations. Reentry involving calcium channel-dependent slow responses within the reentrant circuit is an alternative mechanism (9,10). This form of ventricular tachycardia can be terminated by ventricular overdrive pacing. Intravenous propranolol and intravenous procainamide may slow the rate of ventricular tachycardia without suppressing its inducibility (9,10). It seems that aggressive antiarrhythmic therapy is often not required and that oral verapamil continuous to control ventricular tachycardia in cases requiring treatment (7).

As mentioned above, idiopathic verapamil-sensitive left ventricular tachycardia has characteristic QRS aspects during tachycardia. These are right bundle branch block with either left axis or right

axis (less common) deviation and relatively narrow (0.13-0.16 s) QRS duration. And a His bundle potential is consistently recorded after the onset of each QRS complex (with short V-H interval) during tachycardia. So some cardiologists prefer to call this kind of tachycardia as 'fascicular tachycardia' (11-13). The occurrence of a His bundle deflection with an H-V (before the QRS) or V-H (after the QRS) interval less than that recorded during sinus rhythm, in the absence of preexcitation, implies that retrograde activation of His bundle. In that case, some investigators suggest that the site of origin of such a tachycardia is within the His-Purkinje system. Therefore, these rhythms have generally been referred to as fascicular tachycardia, although proof that they originate in the fascicles of the conducting system and differ from other forms of ventricular tachycardia is lacking (14).

Sustained ventricular tachycardia with QRS configuration of left bundle branch block:

Idiopathic ventricular tachycardia with left bundle branch morphology represents heterogenous group. First, there is a distinct group of patients exists with a tachycardia with QRS configuration of left bundle branch block, that can be called as VERAPAMIL-IRRESPONSIVE VENTRICULAR TACHYCARDIA (5). The QRS morphology of this type of tachycardia is primarily of a complete left bundle branch block with a rightward frontal axis suggestive of a right ventricular outflow tract origin (1). Sung et al discussed this kind of tachycardia in their article as a subgroup of verapamil-unresponsive exercise-induced ventricular tachycardia (15). During electrophysiologic study it cannot be induced by programmed stimulation. Exercise, isoproterenol infusion or both are more effective in initiation of tachycardia. Furthermore, ventricular tachycardia cannot be converted to sustained sinus rhythm with ventricular overdrive pacing, but resolves with discontinuing isoproterenol infusion (1,5,9,15,16). The effectiveness of isoproterenol infusion has led to the suggestion that catecholamine-related automaticity may operative. Whereas intravenous verapamil exerts no effects, beta adrenergic blockade with intravenous propranolol can completely suppress the inducibility of this form of ventricular tachycardia during isoproterenol infusion. This form of ventricular tachycardia is believed to be caused catecholamine-sensitive enhanced automaticity. Intravenous procainamid with its ability to suppress phase 4 diastolic depolarization, is also effective this kind of

ventricular tachycardia (9,10,15). In patients with verapamil-responsive ventricular tachycardia, an intravenous bolus infusion of adenosine or vagal maneuvers may terminate the arrhythmia in some of patients—mostly in those exhibiting ventricular tachycardia with a left bundle branch block morphology but also in a few patients displaying ventricular tachycardia and with a right bundle branch block morphology. It has been suggested that triggered ventricular tachycardia in this subgroup of patients may be due to increased intracellular cAMP.

Another group of patients with left bundle branch morphology ventricular tachycardia have presyncope or not rarely syncope. In this group, ventricular tachycardia can be induced by programmed electrical stimulation, suggesting reentry as a mechanism. There is no effect of isoproterenol infusion. Catheter mapping shows an origin near the right ventricular outflow tract (17).

PROGNOSIS

In majority of patients, the idiopathic ventricular tachycardias are well-tolerated and no cardiac disease occurs at follow-up (17-19). Hence, idiopathic ventricular tachycardia is widely believed to carry a favourable prognosis (17-19). Many patients may have long arrhythmia-free periods and in some of them the arrhythmia may disappear without treatment (7,19). In the series of Brugada et al of 20 patients with idiopathic sustained ventricular tachycardia followed for a mean 10 years after the first tachycardia episode, no cardiac deaths were reported mainly during medical therapy. But, high recurrence rate has been reported (20). It appears that in patients with a normal heart, degeneration of ventricu-

lar tachycardia into a ventricular fibrillation is an exceedingly rare event.

TREATMENT

Patients with sustained ventricular tachycardia frequently require treatment, since they are symptomatic. The mechanism of the arrhythmia, to some extent may influence the choice of treatment.

Patients with exercise-induced ventricular tachycardia often respond beta-adrenergic blockers. And most isoproterenol-sensitive ventricular tachycardias are effectively controlled by chronic oral beta-adrenergic blocking therapy.

On the other hand, ventricular tachycardia in patients without structural heart disease can be safely eliminated with radiofrequency energy delivered through a catheter with a high degree of efficacy in contrast ventricular tachycardia in patients with coronary artery disease (21). The presentation of patient and electrophysiologic mechanism of ventricular tachycardia do not affect the success rate. One of the last reports showed 94 % success rate for radiofrequency catheter ablation to eliminate ventricular tachycardia in patients without structural heart disease (21). Radiofrequency energy can be delivered to the earliest site of endocardial activation during activation mapping or to the site that showed identical QRS complexes in at least 11 of 12 surface ECG leads during pace mapping. Trying to find regions of entrainment, fractionated electrograms or middiastolic potentials is not required for successful ablation. The successful outcome of ablation of the idiopathic ventricular tachycardias would shows that accurate mapping is possible in this form of ventricular tachycardia and location of the focus is in or near the endocardium (21).

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PITFALLS OF INTERNAL MAMMARY ARTERY (IMA) DISSECTION: STEAL FROM A LARGE FIRST BRANCH AND SUCCESSFUL COIL OCCLUSION

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SUMMARY

Poor clinical results with internal mammary artery (IMA) have been attributed to inadequate flow. In this report we presented a case with angina recurred after bypass surgery including LIMA-LAD graft due to steal phenomenon caused by a large branch of LIMA. Transcatheter coil occlusion of this branch was successfully performed.

Key Words: Internal mammary artery, steal phenomenon, transcatheter coil occlusion

Internal mammary artery (IMA) graft has proved to be clearly superior to saphenous vein graft in the surgical treatment of coronary artery disease. Its excellent long-term patency determines a more complete protection against further ischemic events and a better late survival. Adequacy of IMA flow to perfuse myocardium has been experimentally and clinically demonstrated. In addition, the limited involvement of the IMA by pathological phenomena responsible for late vein graft failure determines its excellent long-term patency. (1, 2).

Poor clinical results with IMA have been attributed to inadequate flow, generally considered to be due to spasm, enlarged side branches or use of an IMA with inadequate caliber. In this report we presented a case with angina recurred after bypass surgery including LIMA-LAD graft due to steal phenomenon caused by a large branch of LIMA.

CASE REPORT

44-year old patient who had an anteroseptal myocardial infarction was admitted to the Ankara University Cardiology Department on February 14, 1993 with a postinfarction angina.

On physical examination; arterial blood pressure was 140/90 mmHg, the patient's heart rate was 92 beat/min, and in auscultation of the heart S4

was audible. A chest roentgenogram revealed normal lungs and a normal cardiothoracic ratio. The electrocardiogram exhibited normal sinus rhythm, with Q waves and T wave inversions on Lead V₁-to-V₄. Two-dimensional echocardiogram exhibited hypokinesia on the apical, and anteroseptal wall of the left ventricle. Stress test was positive.

Coronary angiography showed 85 % stenosis in the LAD, with normal circumflex and right coronary artery. Ejection fraction calculated on ventriculography was 53 %, and apical portion of the left ventricle, and interventricular septum was found hypokinetic.

He underwent coronary artery bypass grafting for LAD stenosis in May 12, 1993. The operation consisted of LIMA-LAD anastomosis. The patient tolerated the procedure well and had an uneventful postoperative course. The patient was discharged 8 days after surgery.

However effort angina recurred 4 months after surgery with ischemic electrocardiographic changes of the anterior wall. On readmission he underwent coronary cineangiography which presented no change in the native circulation. Selective LIMA Angiography was performed and flow of contrast material from IMA to LAD was not enough. The IMA had a large proximal branch (1. intercostal branch) or pectoral branch with a diameter larger than LIMA.

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(FIGURE 1) "Steal phenomenon" was evoked as a mechanism of ischemia due to preferential flow into the pectoral branch and reduced flow to by passed LAD. Therefore, coil occlusion of the large pectoral branch was planned.

Under local anesthesia 7F catheter-intraducer was inserted into the left femoral artery. Following placement of a 7F internal mammary artery guiding catheter via the left common femoral artery a rotating hemostatic Y-valve (RHV) was attached to the end of catheter and after systemic heparinization, Tracker-18 and Taper-16 assembly was inserted through RHV and guiding catheter and was placed into the first branch of internal mammary artery. After positioning the tip marker of Tracker-18, Taper-16 was retracted. Coil introducer with preloaded coil was inserted into the Tracker-18 luer fitting. Using the plunger provided in coil pouch, coil was advanced through introducer and into the Tracker-18 shaft. The plunger was retracted and pushing was continued with the coil pusher and coil was deposited into the desired vessel space. After first coil depositing flow was observed and second coil was deposited using previous steps. Second coil comparably reduced the flow. About ten minutes later, total occlusion of the first branch was observed (FIGURE 2). After the occlusion of the first branch, flow through LIMA to LAD was totally normal.

DISCUSSION

The internal mammary artery is harvested on a pedicle after two parallel diathermy tracks are made

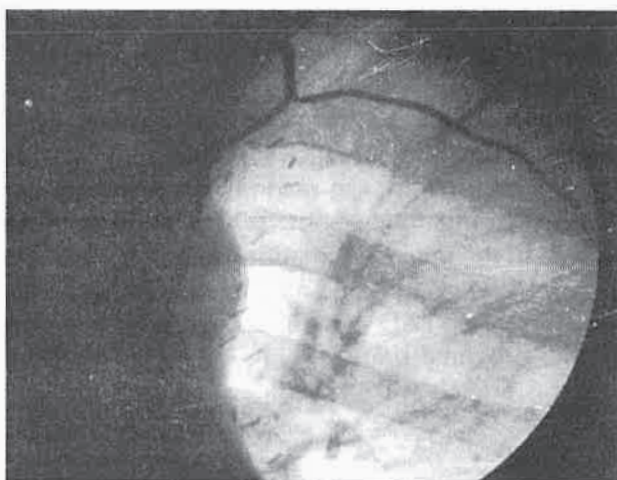


Figure 1: The LIMA had a large proximal branch (1. intercostal branch) or pectoral branch with a diameter larger than LIMA.

along the inner chest wall 1.0 cm on either side of the artery along the entire length. Using low-insensitivity electrocautery, a dissecting diathermy spatula is then used to separate the mammary pedicle from the chest wall in a medial to lateral direction. This dissection is carried on past the point of the initial entry through the endothoracic fascia. The IMA and mammary veins can then be freed from the second and third intercostal attachments.

The dissection is made downward until the IMA is freed as far as the rectus sheath. When the pedicle hangs loose but is still attached at both ends, careful inspection of its upper aspect is made and the intercostal vessels are identified and clipped with titanium clip applicator.

With the lower, mobile IMA held in the surgeon's hand, dissection upward into the neck is facilitated. The first intercostal vessels are divided in the same manner, and all lateral attachments of the mammary vessels are divided by sharp and blunt dissection and diathermy until IMA is mobilized around the back of the subclavian vein. In this case we also used our routine harvesting technique as presented above. But in this patient IMA immediately gives off the first intercostal branch which was indistinguishable because of its atypically high localization. During harvesting of the IMA this kind of branching should be considered to prevent this kind of "Steal Phenomenon"

IMA grafts enjoy better patency rates than venous autografts, but poor clinical results have been attributed to inadequate flow, generally considered to be due to use of an IMA of inadequate caliber. In a report another possible cause of poor flow, namely, steal from the enlarged side branches of IMA. Singh

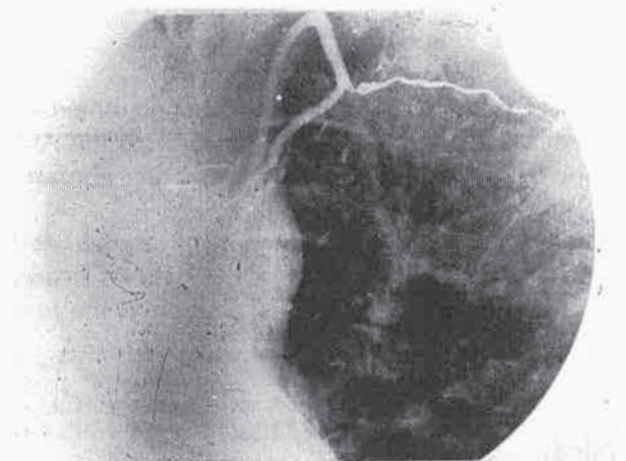


Figure 2: Total occlusion of the first branch was observed.

et al has demonstrated, 25 % symptomatic patients with IMA grafts were found to have unusually enlarged side branches on arteriographic studies (3).

The side branches from the upper part of the IMA are quite variable, often escape surgical attention, and are visualized in postoperative studies. Lateral costal branch and the pericardial branches are of clinical importance. The lateral costal branch arises at or above the first rib in 12 % of individuals. It varies greatly in size and distribution. It can be either rudimentary, ending anteriorly, or quite large, traveling down the lateral chest wall and giving several intercostal branches. This latter type is capable of a large runoff. If undivided, this branch may cause tenting of the IMA which may further interfere with graft flow. The pericardial branches also arise from the upper part of the IMA and may be short or long. Normally these are very fine calibered, being distributed to the pleura and pericardium. Postoperatively, these may become slightly more prominent but usually do not exceed one fourth of the IMA diameter. They become considerably enlarged only when developing collateral connections with the pulmonary circulation due to pulmonary reaction secondary to surgical trauma (3).

Transcatheter arterial embolization using various materials, ie., steel coils with attached thrombogenic threads, detachable balloons, silastic spheres and silicone glue preparations, etc is a well-established technique for inducing arterial occlusion in the management of hemorrhage, arteriovenous fistulas and malformations, aneurysms, and neoplasm. More recently it has been applied successfully in the treatment of coronary arteriovenous anomalies, and occlusion of patent ductus arteriosus. Transcatheter embolotherapy of the IMA has been successfully applied in control of hemorrhage when this vessel has been invaded by tumor, or disrupted by trauma. Nakhajavan and his associates was represented a case in which; transcatheter coil occlusion of the pectoral branch had been successfully performed (4, 5, 6).

We conclude that the enlarged side branches cause diversion of graft flow resulting in reduced size of the distal IMA. The marked reduction of the distal IMA lumen is a useful sign of poor flow in grafted coronary artery. Awareness of this phenomenon may lead to improvement in surgical techniques aimed at its prevention.

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A CASE OF HAIR CASTS WITH SCANNING ELECTRON MICROSCOPIC FINDINGS

(Uncommon Type: Idiopathic peripilar keratin casts)

Hatice Erdi* • Esra Erdemli** • Aynur Akyol* • Hatice Uzar*

SUMMARY

Hair casts is a condition, which is relatively rarely reported but well known. Although it can be misdiagnosed as pediculosis capitis by some unexperienced physicians, it does not represent a major diagnostic problem. On the other hand microscopic and SEM findings hadn't been previously reported. In this report, we discussed our patient beyond the clinical findings with light and SEM microscopic results.

Key Words : Hair Casts, Peripilar Keratin Casts, Pseudonits, Keratin Enclosure of Hair.

Hair casts was described by Kligman in 1957. This disorder is rarely mentioned in the literature and the exact mechanism of hair casts is unknown. Hair casts are reported also in the literature with the terms "peripilar keratin casts" or "pseudonits". These patients have features of small, greyish-white tubular structure, encircling and being freely movable up and down along the individual hair shaft resembling lice eggs. In this report, we describe a patient with hair casts including the clinical findings and light and SEM observations.

CASE REPORT

A 14 year old girl with short cut-brown hair was referred by her teacher. She has been treated repeatedly with usual antiparasitic medication during the past two years for suspected pediculosis capitis. Both personal and family history were not particularities. A careful history could not elicit any triggering factor. A clinical examination of the systems was normal.

The clinical examination of the scalp hairs showed an abundance of white-greyish 2 - 3 mm cylindrical structures on the scalp hairs which could easily be move up and down the hair shaft (Figure 1). The scalp, the skin, the nails and mucose membranes appeared normal.

Investigations, including conventional microscopy and scanning electronmicroscopy of the invol-

ved individual scalp hairs were performed. Observation of the affected scalp hairs under conventional light microscopy showed hairs with a normal structure, encircled by a cylindrical structure which were all similar in size, shape and appearance, relatively uniform in density with a light partly translucent color, with smooth outlines. Their lengths were greater than their width. They were symmetrical and regular in shape (Figure 2).

Untreated hair samples placed on scanning electron microscope (SEM) stubs by means of double sided adhesive tape, using the spatter colding



Figure 1. Clinical appearance of hair casts.

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Figure 2. Light microscopic appearance of hair casts.

system were coated with 200 Å of gold. For prevention of light reflection on the background, silver painting was applied. The specimens were examined in an Jeol Model ASID 10 SEM. Photographs were taken of both normal and abnormal hairs.

Observation of the normal hairs with SEM exhibited a relatively uniform overlapping pattern of cuticular scales with their free edges directed towards the tip of hair (Figure 3). In the hair from the patient with hair casts, the surface was irregular and the scales showed polymorphism clumping and lifting. A slightly rounded irregular structure encircling the hair shaft with disintegrated ends were examined. (Figure 4)

The result of these examinations confirmed the diagnosis of hair casts.

DISCUSSION

Different classification of hair casts were performed. In Scott and Roenigk's classification of hair casts, both keratin and nonkeratin materials may coat the hair shaft. The first group, peripilar keratin casts, include internal root sheath casts, external ro-

ot sheath casts, compound root sheath casts and parafollicular and surface epidermal casts. The latter are the common casts predominant in parakeratotic dermatoses. Internal sheath casts are the rarest form of peripilar keratin casts. The second group, peripilar nonkeratin casts include mycotic, bacterial casts and artifactual hair casts. But, this group could be classified in the differential diagnosis of hair casts, because these casts could not be easily moved up and down on the hair shaft (1, 2).

Both Taieb's (1985) and Kiepert's (1986) classifications of hair casts are similar. In these classifications are two type of hair casts : The common and the uncommon types of hair casts (1, 3, 4). Features of these types of hair casts are presented in Table 1 and Table 2. According to the clinical and microscopical features our patient is of the uncommon type.

Up to 1992, only about 40 cases of hair cast have been reported by Kligman (1952, first); Brunner and Facq (1957, second); Scott (1959); Rollins (1961); Kiepert (1974); Herman (1974); Kiepert (1975); Dawber (1979), Taieb (1985); Held (1989), Staey (1991); in 1992, the incidence of peripilar keratin casts have been reported as high as 81.16 % by Shieh et al. But in this report, only two patients of all hair casts patients did not have scalp disease. From

Table 1. Classification of hair casts

Common Type (Parakeratotic Hair casts)
* frequently in both children and adults .
* associated with parakeratotic scalp disease: greatest in psoriasis, less in pityriasis capitis and seborrheic dermatitis and least in pityriasis amiantacea. In none of the disorders, trichotillomania or the role of pony-tails haven been suggested.
* composed of parakeratotic squamae and they can be termed parakeratotic hair casts
* may be present on hairs arising from the affected area of the scalp
* two, three or four hairs may perforate some casts . They surrounded the hair and can move up and down the hair shaft varying in size and shape
* usually irregular in length, width and shape
* end often with irregular outlines and angulated corners
*t heir color is often irregular and they are generally darker than uncommon type

Table 2. Classification of hair casts

Uncommon Type (peripilar keratin casts)
* only in young girls aged between 2 and 8 years
* no association with either scalp disease or skin abnormality
* probably composed of a mass of large squamae loosely adherent to each other. They are termed idiopathic peripilar keratin casts
* hairs are diffusely involved
* the hair passes centrally through the casts which is easily mobile up and down the hair
* similar in size, shape and appearance
* their shape is tubular or cylindrical encircling the hair shaft. These casts are usually symmetrical and regular in shape . Their length is greater than their width .
* end with smooth outlines and mostly rounded corners
* they are relatively uniform in density with a light partly translucent colors

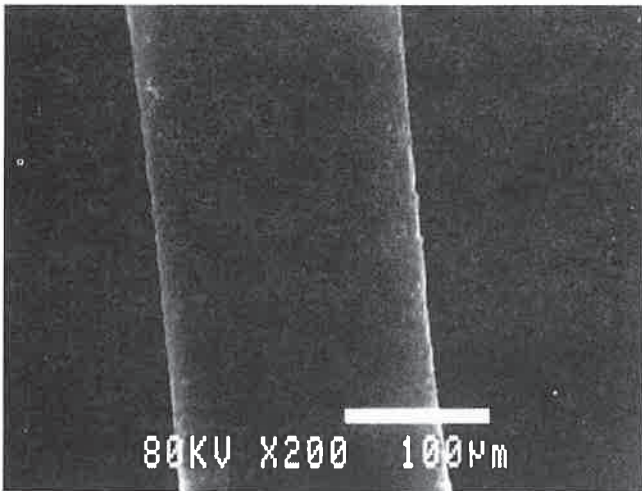


Figure 3. SEM of normal hair showing round hair shape and uniform overlapping of cuticular scales.

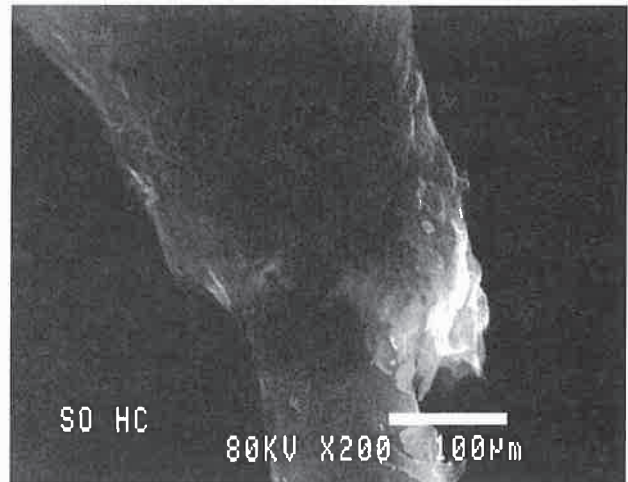


Figure 4. Scanning electron microscopic appearance of hair casts.

this point of view, the real incidence of uncommon type hair casts (peripilar keratin casts) is low. Some hypotheses have been postulated concerning common type hair casts. In a patient with lichen planus, the cause of the dense mononuclear infiltrate surrounding the hair follicle, and the normal desquamation of follicular sheath might have been prevented. Kiepert suggested hair casts to be as follicular psoriasis (1, 3).

Pathogenesis of the idiopathic peripilar keratin casts has been postulated that retention of the internal root sheath failed to desquamate, resulting in the collection of parakeratotic cell in the infundibulum by Kligman (4).

In the light microscopical and transmission electron microscopical researchs of Taieb et al they considered that the origin of these lesions are infra-infundibular, because in all the materials both keratinized inner root sheath and cornified external root sheath cells were observed but no infundibular parakeratosis were involved (4).

Held et al suggested that the hair casts occurred due to psychological trauma as both Beau's lines (transverse depressions of the nail plate) and Pohl-Pincus marks (focal narrowing of the hair shaft) were caused by slow of matrix mitotic activity after psychological trauma (6).

Shieh et al postulated that hypertraction of the hair longer than 3 to 6 months would lead to the ischemic changes of hair follicles. So, damaged external root sheath and parakeratinized internal root sheath remain, encircling the hair; passive upward transport occur when the hair grows. But traction is probably not the only mechanism responsible for causing hair casts (7).

Pediculosis capitis, scales of seborrhea, artefacts, trichonodosis, white piedra and trichorrhexis nodosa are considered in the differential diagnosis. In addition hair casts must be differentiated from nits because the use of repeated antiparasitic treatment for pediculosis capitis can lead to toxicity reaction.

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A CASE WITH TAKAYASU'S ARTERITIS AND CELIAC SPRUE (A Short Report)

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SUMMARY

We describe the initial course and follow-up of 27 year-old female patient who presented in 1994 with aortitis and celiac sprue. Segmental occlusion of the subclavian artery was demonstrated on aortography. Jejunal biopsy revealed celiac sprue. Following institution of steroid therapy and gluten free diet functional use of the upper extremity improved, constitutional symptoms resolved and biopsy findings normalized rapidly. Two months later, tapering of the corticosteroid dosage was complicated by flares in constitutional symptoms and return of upper extremity claudication.

Keywords: Takayasu's arteritis, Celiac sprue.

Takayasu's arteritis is a chronic inflammatory arteriopathy affecting large vessels, most markedly the aorta and its main branches, and to a lesser extent pulmonary arteries (1). The cause of Takayasu's arteritis is still unclear. In 1960, various reports described circulating antibodies directed against components of human artery wall, although other investigators fail to confirm these findings (2). Segar and colleagues recently found significantly high levels of lymphocyte blast transformation on exposure to partially purified human aortic extract (3). Clinical observations suggest that genetic factor may be involved in pathogenesis. Cases have been reported in twin sisters and brothers (4). Takayasu's arteritis is a systemic disease with generalized symptoms such as malaise, fever, night-sweats, arthralgias, anorexia and weight-loss. These symptoms may occur months before apparent vessel involvement. Most patients have symptoms of vascular insufficiency of the upper extremities which may vary from arm claudication to numbness.

Takayasu's arteritis has been reported in association with juvenile rheumatoid arthritis (5) and spondyloarthropathy (6). We could not cite any case with Takayasu's arteritis and non-tropical sprue in

literature. Non-tropical sprue is a disease of unknown etiology characterized by malabsorption and gluten intolerance. It has been suggested that gluten or its metabolites may initiate an immunologic reaction in intestinal mucosa. The finding of abnormal antibodies to gliadin in the serum of sprue patients, the synthesis of increased amounts of an antigliadin antibody by sprue mucosa maintained in organ culture, and the beneficial response to glucocorticoid drugs have been cited as evidence in support of this hypothesis (1). Genetic factors appear to be important in this disease. Non-tropical sprue is associated with HLA-B8 and DR-W3.

The authors present a case of Takayasu's arteritis and non-tropical sprue, which they have failed to find such a case in literature.

CASE REPORT

The patient, a 27 year-old woman, was admitted to our clinic on August 28, 1994 with symptoms such as unilateral claudication, nausea, arthralgia, and myalgia. She had had these complaints for 8 months, and a history of diarrhoea and abdominal

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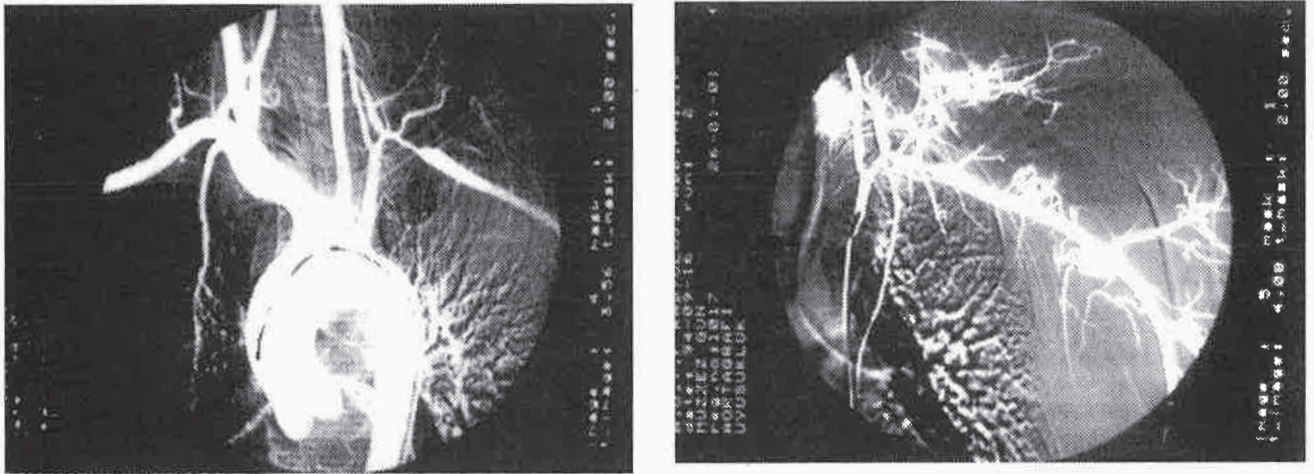


Figure 1-a,b Initial and follow-up aortograms of a young woman who was diagnosed as having Takayasu's arteritis and celiac sprue, demonstrating segmental occlusion and poststenotic dilatation of the left subclavian artery.

pain for 4 years. Her examination revealed that pulses were absent in the left arm, and bruits were noted over left carotid and subclavian vessels. Though blood pressure measured from right arm was 170/95 mmHg, it could not be obtained from left arm where brachial and radial pulses were not palpable. Her erythrocyte sedimentation rate, hematocrit, and leukocyte count were 135 mm/h, % 32 and 10,100/mm³, respectively. Rheumatoid factor, antinuclear and anti-smooth muscle antibodies were negative. Angiogram showed segmental occlusion and poststenotic dilatation at the left subclavian artery, (Fig. 1-a, b). There was not any abnormality in the abdominal and lower extremity angiograms. She had had a typical malabsorption syndrome characterized by weight loss, abdominal distention, diarrhoea, steatorrhea and abnormal tests for absorptive function. Jejunal biopsy specimen showed the typical morphologic changes: Blunting and flattening of the mucosal surface with villi either absent or broad and short, infiltration of inflammatory cells in lamina propria and elongated crypts and changes in the surface epithelium.

DISCUSSION

The authors present a patient with Takayasu's arteritis and celiac sprue. The diagnosis of Takayasu's arteritis suggested by claudication with diminis-

hed pulses was confirmed by the findings of the aortogram. The patient's weight loss, nausea, arthralgia, claudication of the affected extremities represented early manifestations of the aortitis. Jejunal biopsy specimen showed blunting and flattening of the mucosal surface, short and broad villi, elongated crypts, and dense infiltration of inflammatory cells in lamina propria. These morphologic changes are not specific for diagnosis of non-tropical sprue but: (1) evidence of malabsorption, (2) characteristic small bowel biopsy, and (3) clinical, biochemical and histologic improvement after institution of gluten free diet.

Celiac sprue has been associated with systemic lupus erythematosus, diabetes mellitus, and rheumatoid arthritis (7). This case report documents the association of celiac sprue with Takayasu's arteritis. In celiac sprue, after institution of gluten free diet, symptomatic improvement usually occurs within a few weeks, but improvement in tests of absorptive function and small bowel histologic characteristics may not occur for months. Patients with non-tropical sprue on glucocorticoid therapy who continue gluten-containing diet have shown improvements of symptoms, histological changes of intestines, and tests for intestinal absorptive function (8).

Although the optimal treatment for Takayasu's arteritis has not been established yet, corticosteroid therapy is effective in ameliorating the inflammatory aspects of this condition (fever, arthritis, myocar-

ditis) and the hemodynamic problems of vascular stenosis. Adjunctive cytotoxic agents have apparently suppressed the arteritis in patients whose disease worsens with prednisone treatment (9).

Prognosis is related with specific disease complications associated with longer duration of disease. Therefore, treatment intervention may modify the natural history of the disease.

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