



Original Article

A Post-Tympanoplasty Evaluation of the Factors Affecting Development of Myringosclerosis in the Graft: A Clinical Study

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OBJECTIVE: Myringosclerosis (MS) is a pathological condition characterized by hyaline degeneration and calcification of the collagenous structure of the fibrotic layer of the tympanic membrane, which may develop after trauma, infection, or inflammation as myringotomy, insertion of a ventilation tube, or myringoplasty. The aim of our study was to both reveal and evaluate the impact of the factors that might be effective on the post-tympanoplasty development of myringosclerosis in the graft.

MATERIALS and METHODS: In line with this objective, a total of 108 patients (44 males and 64 females) aged between 11 and 66 years (mean age, 29.5 years) who had undergone type 1 tympanoplasty (TP) with an intact canal wall technique and type 2 TP, followed up for an average of 38.8 months, were evaluated. In the presence of myringosclerosis, in consideration of the tympanic membrane (TM) quadrants involved, the influential factors were analyzed in our study, together with the development of myringosclerosis, including preoperative factors, such as the presence of myringosclerosis in the residual and also contralateral tympanic membrane, extent and location of the perforation, and perioperative factors, such as tympanosclerosis in the middle ear and mastoid cavity, cholesteatoma, granulation tissue, and type of the operation performed. For statistical analysis of data, independent samples t-test was used.

RESULTS: Our study comprised 44 male and 64 female patients. Median postoperative follow-up period was estimated as 38.8 months. The rate of postoperative development of myringosclerosis in grafts was significantly higher in patients with already existing sclerotic foci in TM ($p=0.001$). The location of the perforation had no effect on the postoperative development of MS in the graft ($p=0.521$). No statistically significant difference was detected between the size of the perforation and formation of MS ($p=0.581$). Statistical analysis of both groups could not discern any significant intergroup difference as to the impact of the presence or absence of cholesteatoma on the development and extent of MS ($p=0.604$). Impact of tympanosclerosis on the postoperative development and extent of MS in the graft was significant ($p=0.001$). Presence or absence of granulation tissue on the development or extent of myringosclerosis was not detected ($p=0.697$). Myringosclerotic foci in the contralateral ears had a statistically significant effect on the postoperative development and extent of MS in the grafts ($p=0.001$). Type of surgery performed did not exert any significant effect on the development or extent of myringosclerosis ($p=0.765$).

CONCLUSION: We have determined that the presence of myringosclerosis in the residual membrane and in the contralateral tympanic membrane and tympanosclerosis in the middle ear have a significant role in the development of postoperative myringosclerosis in the tympanic membrane, contrary to the type of the surgical intervention, location and extent of perforation, presence of cholesteatoma, and granulation tissue.

KEY WORDS: Myringosclerosis, tympanoplasty, tympanic membrane

INTRODUCTION

Tympanosclerosis (TS) is defined as a pathological condition characterized by sclerotic plaques developing in the tympanic membrane, middle ear cavity, ossicular chain, and, rarely, in the mastoid cavity as a result of submucosal hyaline degeneration. It is also characterized by accumulation of calcified collagen fibrils localized in the submucosal connective tissue^[1]. Tympanosclerosis involving only the tympanic membrane is termed myringosclerosis^[2,3]. Calcareous deposits in the tympanic membrane were originally described by Cassebohm in 1734. Sclerotic changes developing during middle ear infections were first defined by von Troeltsch in 1878. However, its histological structure was originally disclosed by Walb in 1878^[4].

Even though the etiopathogenesis of tympanosclerosis is not known completely, induction of tympanosclerosis as an outcome of middle ear infections, and tympanic injuries are already acknowledged. Clinically, myringosclerosis is seen more often in patients who have undergone myringotomy and/or ventilation tube (VT) insertion for the management of otitis media with effusion (OME) and after myringoplasty^[5]. Following myringotomy or otitis media, various cells in calcified tympanic membranes, primarily macrophages and fibrocytes, express osteopontin, osteoprotegerin, and osteonectin molecules, which play a role in the pathogenesis

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of myringosclerosis (MS) [6]. TS has been also proposed as an autoimmune disease of the ear. Lower plasma fibronectin concentration has implicated the role of autoimmunity in its pathogenesis [7]. In our retrospective study, we have revealed the presence and extent of postoperative myringosclerosis that developed in the graft of cases that had undergone canal wall up type 1 tympanoplasty (TP) or type 2 TP and evaluated the impact of our predetermined pre- and intraoperative factors on this process.

MATERIALS and METHODS

Ethics committee approval was received at 22.09.2011 from Dokuz Eylül University with 2011/31-06 assignment number. In the study, a total of 108 patients who had undergone tympanoplasties (TPs) (Type 1 TP, n=88; Type 2 TP, n=20) in İzmir Atatürk Research and Training Hospital between January 2006 and June 2011 with the indication of chronic otitis media (COM) were retrospectively analyzed. Patients with postoperatively intact grafts were included in the analysis. In all cases, temporal muscle fascia was used as graft material.

After categorization of the patients for age and gender, they were classified according to our predetermined factors, such as location, extent of the tympanic perforation, presence of a myringosclerotic focus in the residual tympanic membrane and also in the contralateral ear drum during the preoperative period, and perioperative evidence of tympanosclerosis, cholesteatoma, and granulation tissue in the middle ear, in addition to type of operation performed.

During postoperative examination of the tympanic membranes, evidence of myringosclerosis and if it affected the grafts and its extent of involvement through quadrants of the tympanic membrane were determined. The extent of TM was evaluated in all quadrants of the tympanic membrane, designated in reference to the location of the malleus.

Statistical Analysis

For the statistical analysis, Statistical Package for Social Sciences (SPSS) for Windows 15.0 was used. All study data were summarized in tables and graphics for comparative evaluations. Independent samples t-test was used for statistical analysis of the data. The results were assessed as statistically significant ($p < 0.05$) or insignificant $p > 0.05$ within 95% confidence intervals.

Surgical Technique

All of the patients were informed before the surgery, and informed consent was obtained. All of our patients were operated under general anesthesia. Through a postauricular incision, the layers were exposed, and the required graft material was prepared from the temporal muscle fascia in consideration of the extent of the perforation. If necessary, after antrotomy and/or mastoidectomy, edges of the tympanic perforation defect were debrided, and myringosclerotic foci were excised under an operating microscope. A tympanomeatal flap was elevated, and the middle ear was entered through the chordal crest to explore the middle ear and ossicles and relieve any present abnormality. The graft was placed using the over-underlay technique, and before termination of the operation, the graft was supported medially and laterally with Spongostan.™ The surgical report stated the extent of the detected pathology (cholesteatoma, granulation tissue, and tympanosclerosis), actual state of the ossicular chain, types of the reconstructive pro-

cedures performed, presence of myringosclerotic foci in the tympanic membrane, and complications (if any).

RESULTS

Our study comprised 44 male and 64 female patients whose ages ranged between 11 and 58 years (median, 29.5 years). Twenty patients (18.5%) were in the pediatric (<16 yrs) and 88 (81.5%) patients in the adult age group, while 36 (33.3%) patients had bilateral COM. Operations were performed on the left (n=50; 46.3%) and right (n=58; 53.7%) ears, respectively. Median postoperative follow-up period was estimated as 38.8 months.

The Impact of Preoperative Sclerotic Foci in the Tympanic Membrane

During our preoperative assessments, we noted the absence or presence of sclerotic foci in residual TM in 64 (59.3%) and 44 (40.7%) patients, respectively. Postoperative otomicroscopic examinations performed in the patients with preoperative sclerotic foci revealed sclerotic lesions in 4 (n=2; ++++), 3 (n=14; +++), 2 (n=20; ++), and 1 (+) quadrant of the tympanic membrane (Figure 1). In this group, MS affected an average number of 2.23 ± 0.80 quadrants (Table 1). Postoperative otomicroscopic examinations carried on in 64 patients without any evidence of preoperative sclerotic foci revealed myringosclerotic foci in 2 (n=20; ++) and 1 (n=20; +) quadrant, respectively, while MS did not develop in 24 patients. In this group, MS developed in a mean number of 0.94 ± 0.83 quadrants (Figure 2a, b). In the statistical analysis, the rate of postoperative development of myringosclerosis in grafts was significantly higher in patients with already existing sclerotic foci in TM ($p=0.001$).

The Impact of the Location of Perforation

In our assessments, we observed central (n=84; 74.2%) and subtotal/total (n=24; 25.6%) perforations. Among 84 patients with central perforation, postoperative sclerotic foci were detected in 4 (n=1; ++++), 3 (n=11; +++), 2 (n=30; ++), and 1 (n=19; +) quadrant, respectively, while sclerotic focus did not develop in 19 patients. The mean number of affected quadrants (1.43 ± 1.02) was also estimated in this group. In Group 2, 24 patients with subtotal/total perforations, postoperative sclerotic foci were observed in 4 (n=1; ++++), 3 (n=3; +++), 2 (n=10; ++), and 1 (n=5; +) quadrant, respectively. In 5 patients, sclerotic foci were not seen. The mean number of the affected quadrants in this group (1.58 ± 1.10) was also calculated (Table 1). Our statistical analysis detected that the location of the perforation had no effect on the postoperative development of MS in the graft ($p=0.521$).



Figure 1. Diffuse postoperative myringosclerosis at the anterior and posterior quadrants of the graft

Table 1. Postoperative mean number of myringosclerotic quadrants of the cases distributed among groups

	n	mean±SD	p value
Cholesteatoma (+)	10	1.30±1.16	0.604
Cholesteatoma (-)	98	1.48±1.03	
Myringosclerosis in the residual membrane (+)	44	2.23±0.80	0.001
Myringosclerosis in the residual membrane (-)	64	0.94±0.83	
Type of the perforation			
Central	84	1.43±1.02	0.521
Total	24	1.85±1.10	
Size of the perforation <3 mm	35	1.54±1.04	0.581
Size of the perforation >3 mm	73	1.42±1.04	
Granulation (+)	30	1.40±1.00	0.697
Granulation (-)	78	1.49±1.05	
Tympanosclerosis in the middle ear (+)	24	2.29±0.86	0.001
Tympanosclerosis in the middle ear (-)	84	1.23±0.96	
Myringosclerosis in the contralateral ear (+)	31	2.10±0.83	0.001
Myringosclerosis in the contralateral ear (-)	77	1.21±1.00	
Tympanoplasty	20	1.40±0.94	0.765
Tympanoplasty+Antrotomy/mastoidectomy	88	1.48±1.06	

**Figure 2. a, b.** Postoperative development of myringosclerosis at the anterior quadrants of the graft implanted in two separate patients

The Impact of the Size of the Perforation

The size of the perforation was smaller than 3 mm in 35 (32.4%) and greater than 3 mm in 73 (67.6%) patients. Postoperative otomicroscopic analyses conducted in the patients with perforations smaller than 3 mm revealed sclerotic foci in 4 (n=1; +++++), 3 (n=4; +++), 2 (n=15; ++), and 1 (n=8; +) quadrant, respectively. However, in seven patients, sclerotic foci did not develop. The mean number of affected quadrants in this group (1.54±1.04) was also calculated. In the group of patients with perforations larger than 3 mm, the postoperative otomicroscopic examination disclosed development of sclerosis in 4 (n=1; +++++), 3 (n=10; +++), 2 (n=25; ++), and 1 (n=20; +) quadrant, respectively, while sclerotic development was not observed in 17 patients (Figure 3). The mean number of sclerotic quadrants in this group was estimated as 1.42±1.04. No statistically significant difference was detected between the size of the perforation and formation of MS (p=0.581).

Impact of the Presence of Cholesteatoma

Intraoperatively, patients (n=10; 9.3%) with or without (n=98, 90.7%) cholesteatomas in the middle ear and mastoid cavity were detected. Postoperative microscopic examinations performed in the patients with intraoperatively detected cholesteatomas revealed development of myringosclerosis in 3 (n=2; +++), 2 (n=2; ++), and 1 (n=3; +) quadrant, respectively. However, myringosclerosis was not observed in 3 patients. Myringosclerotic foci were observed in an average of 1.30±1.16 quadrants. Postoperative microscopic examinations conducted in the non-cholesteatoma group, revealed development of myringosclerosis in 4 (n=2; +++++), 3 (n=12; +++), 2 (n=38; ++), and 1 quadrant (n=25; +), respectively. However, development of myringosclerotic foci was not observed in 21 patients. In this group, myringosclerotic foci were observed in an average of 1.48±1.03 quadrants. Statistical analysis of both groups could not discern any significant intergroup difference as to the impact of the presence or absence of



Figure 3. Lack of evidence of postoperative development of myringosclerosis cholesteatoma on the development and extent of myringosclerosis ($p=0.604$).

The Impact of Tympanosclerosis in the Middle Ear

During the operation, 24 (22.2%) patients with and 84 (77.8%) cases without tympanosclerotic plaques in the middle ear or mastoid region were determined. Postoperative microscopic examinations performed in 24 patients with tympanosclerotic plaques displayed formation of myringosclerosis in 4 ($n=2$; ++++), 3 ($n=7$; +++), 2 ($n=11$; ++), and 1 ($n=4$; +) quadrant, respectively. The mean number of affected quadrants was estimated to be 2.29 ± 0.86 . Postoperative microscopic examinations performed in 84 patients without any evidence of tympanosclerosis detected the formation of myringosclerosis in 3 ($n=7$), 2 ($n=29$; ++), and 1 ($n=24$; +) quadrant, respectively. However, myringosclerosis did not develop in 24 patients. A mean of 1.23 ± 0.96 quadrants was affected. When correlations between groups regarding development of MS were analyzed, a statistically significant impact of tympanosclerosis on the postoperative development and extent of MS in the graft was detected ($p=0.001$).

Impact of Granulation Tissue in the Middle Ear

Intraoperatively, granulation tissue was observed in 30 (27.8%) patients, while in 78 (72.2%) patients, no evidence of granulation tissue was revealed. Postoperative otomicroscopic examinations performed in patients with granulation tissue ($n=30$) detected formation of myringosclerosis in 3 ($n=4$; ++++), 2 ($n=11$; ++), and 1 ($n=8$; +) quadrant, respectively. However, no myringosclerotic foci were observed in 7 patients. In this group, a mean number of 1.40 ± 1.00 quadrants was affected. Postoperative otomicroscopic examinations conducted in 78 patients without any evidence of granulation tissue revealed formation of myringosclerosis in 4 ($n=4$; ++++), 3 ($n=10$; +++), 2 ($n=29$; ++), and 1 ($n=20$; +) quadrant, respectively. However, in 17 patients, no myringosclerotic foci were observed. In this group, a mean of 1.40 ± 1.00 quadrants was affected. In the statistical evaluations, no significant effect of the presence or absence of granulation tissue on the development or extent of myringosclerosis was detected ($p=0.697$).

The Impact of the State of the Contralateral Ear

In our study, sclerotic foci in TM or residual TM with or without COM were found in the contralateral ears of 31 (28.7%) patients, while they were not observed in 77 patients (71.3%). In postoperative microscopic examinations performed in 31 patients with contralateral myringosclerosis, sclerotic foci were detected in 4 ($n=1$; ++++), 3 ($n=9$; +++), 2

($n=13$; ++), and 1 ($n=8$; +) quadrant, respectively. In this group, myringosclerosis affected an average of 2.10 ± 0.83 quadrants. In the postoperative otomicroscopic analyses conducted in the other group of 77 patients, myringosclerosis was detected in 4 ($n=1$; ++++), 3 ($n=5$; +++), 2 ($n=27$; ++), and 1 quadrant ($n=20$; +), respectively. However, development of myringosclerosis was not observed in 24 patients. In this group, myringosclerosis affected an average of 2.10 ± 0.83 quadrants. Statistical analysis of both groups revealed that myringosclerotic foci in the contralateral ears had a statistically significant effect on the postoperative development and extent of MS in the grafts ($p=0.001$).

The Impact of the Type of the Surgery

Cases of our series underwent only TP ($n=20$; 18.5%), antrotomy, and/or simple mastoidectomy plus TP procedure. In the postoperative otomicroscopic examination performed in 20 patients in whom we applied only TP, development of MS was observed in 3 ($n=2$; +++), 2 ($n=8$; ++), and 1 ($n=6$; +) quadrant, respectively, while in 4 patients, formation of MS was not detected. In this group, an average of 1.40 ± 0.94 quadrants was affected. In the second group of 88 patients, postoperative otomicroscopic examinations revealed formation of MS in 4 ($n=2$; ++++), 3 ($n=12$; +++), 2 ($n=32$; ++), and 1 ($n=28$; +) quadrant, respectively. MS was not observed in 20 patients. In this group, an average of 1.48 ± 1.06 quadrants was affected. Statistical analysis of both groups as to the development of myringosclerosis revealed that type of surgery performed did not exert any significant effect on the development or extent of myringosclerosis ($p=0.765$).

DISCUSSION

Tympanosclerosis is an irreversible and nonspecific pathological condition that is characterized by hyaline degeneration of submucosal elastic fibers and calcification of the ear drum and middle ear following acute and chronic inflammation or traumas of the middle ear^[8]. Involvement of TS is termed MS.

On otoscopic examination, MS is seen as white calcified plaques with various shapes and dimensions situated on the tympanic membrane. Histological examination reveals that sclerotic lesions appear as mineralized aggregates with calcium phosphate content interspersed throughout irregular collagen fibers of the lamina propria^[9]. In a number of recent experimental studies and clinical investigations, many diverse opinions have been proposed regarding the etiopathogenesis of TS and MS. In experimental studies, an important role of free oxygen radicals (FOR) in the development of MS has been suggested. It was determined that relatively hyperoxic media or free oxygen radicals released from inflammatory cells and bacteria induce development of sclerotic plaques^[10,11].

Even though the etiopathogenesis of MS is not known completely, middle ear infections and traumas directed at ear drums (myringotomy, paracentesis) are thought to be the most important etiologic factors of TS/MS^[5]. Still, in our study, since intraoperative debridement of the edges of the perforation defect to increase blood perfusion created tissue damage, in many of our cases, postoperatively observed diffuse myringosclerotic foci in the grafts support the outcomes of the aforementioned studies.

However, TS/MS is not observed in every case of otitis media in whom a ventilation tube is inserted. This phenomenon suggests the

potential effects of many factors, such as genetic diversity or an individual's predisposition to the development of TS/MS. Koc et al.^[12] observed higher rates of MS formation on otomicroscopic examination of tympanic membranes of atherosclerotic patients when compared with the control group, and as an outcome of their findings, they proposed the impact of genetic predisposition on the development of sclerotic degeneration.

Caldas et al.^[13] investigated the prevalence of MS in 341 patients with chronic renal failure (CRF), which induces pathological calcifications in various tissues, similar to MS, and 356 normal healthy controls as a control group using otoscopic examinations. They observed myringosclerotic foci in 40 (11.7%) of 341 CRF patients and in 18 (5.1%) of 356 control subjects. Statistical analysis of both groups revealed significantly higher rates of MS in CRF patients relative to the control group ($p=0.002$). In the same study, the authors reported a lack of a statistically significant intergroup difference as to the frequency of MS regarding serum calcium, phosphate, and parathormone levels and also age, gender, and ethnicities of the study participants.

In our study, in cases where we observed MS preoperatively in residual TM and contralateral TM and also tympanosclerotic foci intraoperatively, the rates of postoperative MS development in grafts were found to be significantly higher relative to the control groups. This outcome suggested the potential effects of an individual's predisposition or genetic factors on the development of MS. Kamal et al.^[14] performed a study on 85 cases regarding the association between TS and cholesteatoma and detected cholesteatomas that were concurrent with TS, which they treated with radical surgery. Asiri et al.^[15] reported the presence of cholesteatomas in 2.2% of patients (or 90 ears with TS). Onal et al.^[16] intraoperatively determined the frequency of TS as 5.7% among 191 operated cases with chronic otitis media and reported TS-cholesteatoma concomitancy in 27% of the cases. In our study, we detected TS in 24 of (22.2%) 108 patients and cholesteatoma in 3 (12.5%) of these 24 cases. We concluded that the presence of cholesteatomas and granulation tissue in the middle ear and/or mastoid cavity has no effect on the development of myringosclerosis in the grafts during the postoperative period.

The limitation of our study was there were not enough significant differences between our parameters, and only patients having preoperative myringosclerosis, peroperative tympanosclerosis, and preoperative contralateral ear myringosclerosis were significant in postoperative myringosclerosis occurrence.

In conclusion, in our study, during postoperative controls, we determined that the preoperative presence of MS in the residual tympanic membrane and contralateral ear and perioperative TS significantly increased the incidence and prevalence of MS in the graft, while the type of operation performed, presence of cholesteatoma, and location and size of the perforation had no effect on the development of MS. These results suggest to us the potential impact of personal factors (predisposition to abnormal calcification, calcific response against inflammation, genetic differences, and immunological etiologies, etc.) on the development of MS. However, these results should be substantiated by advanced molecular and genetic investigations.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Dokuz Eylül University (2011/31-06).

Informed Consent: Written informed consent was obtained from the patients who participated in this study.

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