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ORIGINAL ARTICLE

The Role of Mastoid Pneumatization in the Pathogenesis of Tympanosclerosis

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Objective: To evaluate the importance of the degree of mastoid pneumatization in the pathogenesis of tympanosclerosis.

Study Design: Prospective study.

Materials and Methods: Mastoid pneumatization of 20 patients with tympanosclerosis were compared to 33 patients with chronic otitis media without tympanosclerosis and 100 ears of 50 normal subjects.

Results: The mean volume of mastoid pneumatization was 7,9 cm^3 (4,0-14,0 cm^3) in normal subjects, 2,3 cm^3 (0,3-6,4 cm^3) in tympanosclerotic patients and 0,2 cm^3 (0,0-0,8 cm^3) in patients with chronic otitis media without tympanosclerosis. The differences were statistically significant.

Conclusion: Tympanosclerotic patients had larger mastoid air cell system than the patients with chronic otitis media without tympanosclerosis. The difference of the volume of the mastoid pneumatizations may be the cause of the tympanosclerotic degeneration. Production of free oxygen radicals may be the cause of the predisposition to tympanosclerosis. In the situation of well-pneumatized mastoid air cell system, there may be an increase of the production of free oxygen radicals because of hyperoxidation if there is an infection / inflammation in middle ear. The findings of this study point out the importance of free oxygen radicals in the pathogenesis of tympanosclerosis.

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Introduction

Tympanosclerosis is an abnormal connective tissue reaction with hyaline degeneration and calcification in the tympanic membrane and submucosa of the middle ear. It is an irreversible, non-spesific end-result chronic inflammation or infection of the middle ear. The process occurs in the lamina propria layer of submucosa. A homogenous mass takes place by thickening and fusion of the collagenous fibrils in lamina propria layer. An accumulation of calcium and phosphorus gradually takes place, leading to crystallization and tympanosclerosis [1]. Tympanosclerotic degeneration may damage the middle ear both anatomically and functionally. Tympanosclerotic masses may assume clinical importance by interfering with the transmission of sound vibrations across the middle ear structures and may also affect the hearing results of middle ear surgical operations.

In temporal bone, mastoid air cells constitute the biggest air cell group. Controversy still exists concerning the relation between the mastoid pneumatization and the middle ear diseases. There are two basic theories on this fact. According to "environmental theory", the pneumatization process is reduced by inflammation of the middle ear or tubal dysfunction [2]. Because of this, middle ear diseases in the later periods of life are the cause of the reduced pneumatization in infancy and childhood. According to "genetic theory", the extent of pneumatization is

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genetically determined. Reduced pneumatization predisposes to acute or chronic otitis [3]. It is well documented that the relation between the middle ear infections and the mastoid pneumatization. The extent of the mastoid air cell system is smaller in patients with chronic suppurative otitis media (CSOM) and chronic otitis media with effusion (COME) than the normal population. Mastoid pneumatization was discussed as a valuable indicator in middle ear infections [4-5].

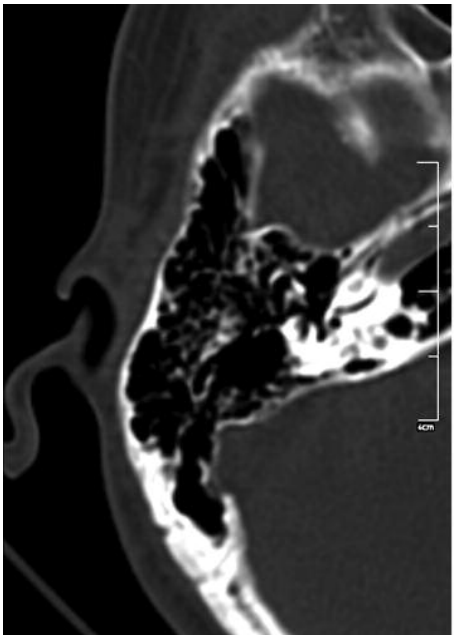
Mastoid air cell system is now believed an important contributor to the physiology of the middle ear but it has never been studied in tympanosclerotic patients. The cause leading to sclerotic degeneration in tympanosclerosis is still unknown. The purpose of this study is to find out the effect of mastoid pneumatization in the pathogenesis of tympanosclerosis by comparing the extent of mastoid air cells in tympanosclerotic patients and normal population. The results may help in understanding in the pathogenesis of tympanosclerosis.

Materials and Methods

The subjects were subdivided into three groups and written informed consents were obtained from all subjects before taking CT images. During all stages of the study, the current ethics standarts were taken into account. All individuals have axial temporal high resolution computed tomography (HRCT) scans reconstructed with three-dimensional multiplanar volume rendering technique (3D-MPVR) described earlier [6]. In Group 1, fifty patients (100 ears) with "normal" mastoid pneumatization were studied (figure 1 and 2). These are the patients referred to Haseki Education and Research Hospital otology policlinic with the complaints of tinnitus, otalgia, sensorineural hearing loss and investigated with HRCT in Marmara University Hospital Radiology Department. These patients do not have any otitis media or perforation of tympanic membrane. In group 2, 20 patients with chronic otitis media (COM) with tympanosclerosis (20 ears) have axial HRCT scans (figure 3 and 4). These patients have sclerosis over 25 % of the tympanic membrane or obvious middle ear tympanosclerosis seen from the perforation. In Group 3, 33 patients (33 ears) with COM without tympanosclerosis in tympanic membrane or middle ear have axial HRCT scans (figure 5 and 6).

Results

Of 50 patients in Group 1, 32 were female and 18 were male, while the mean age was 39 (15-72). In this group, the mean volume of mastoid pneumatization was 7,9 cm^3 (4,0-14,0). Of 20 patients in Group 2, 13 were female and 7 were male, and the mean age was 28



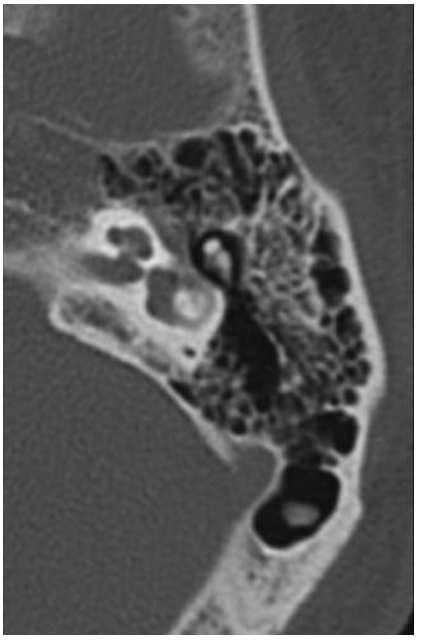


Figure 1 and 2) axial high resolution computerized tomographic images of mastoid air cell system of a subject with normal mastoid pneumatization.

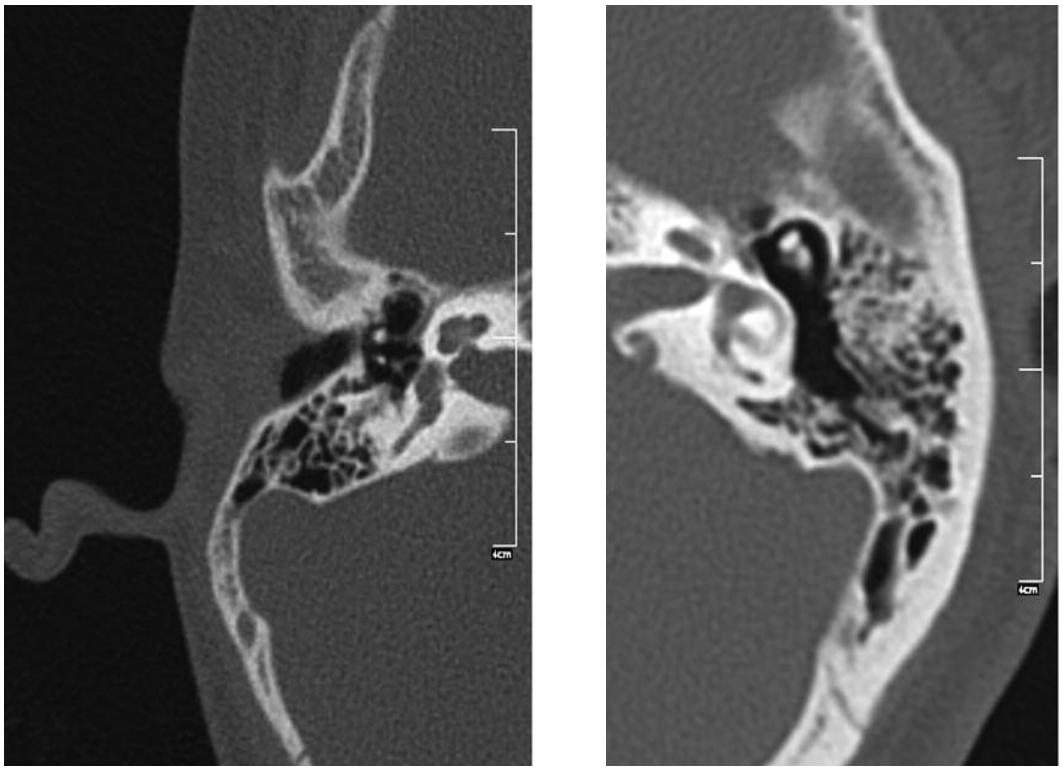


Figure 3 and 4) axial high resolution computerized tomographic images of mastoid air cell system of a subject with chronic otitis media with tympanosclerosis.

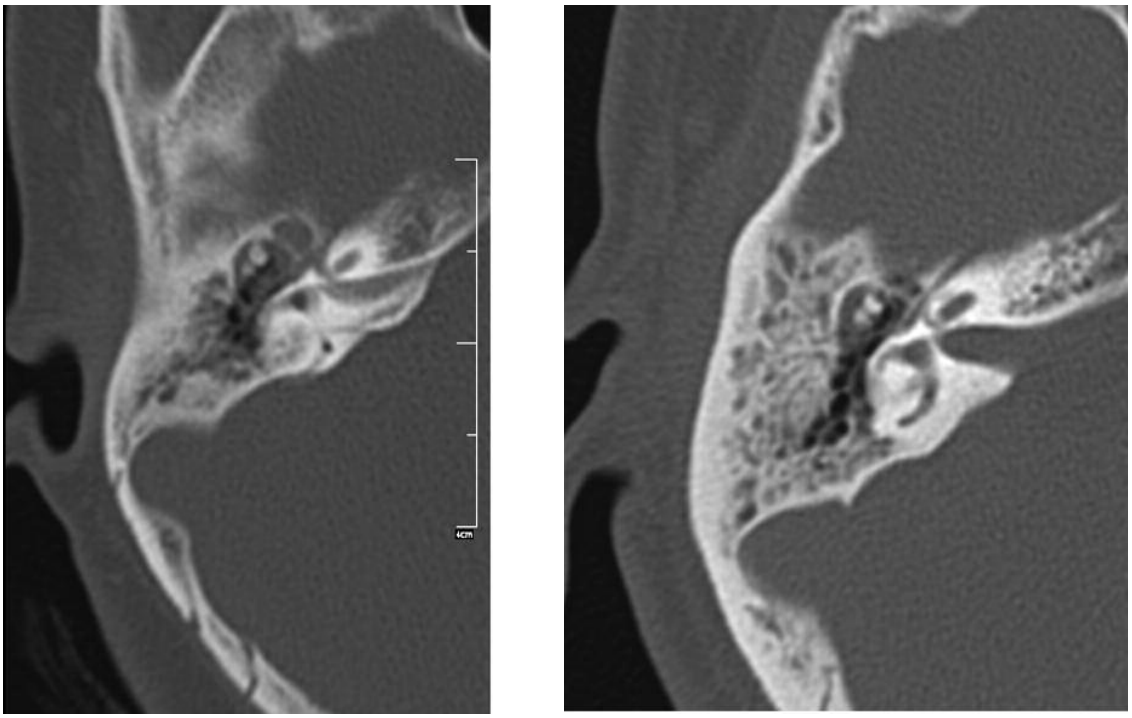


Figure 5 and 6) axial high resolution computerized tomographic images of mastoid air cell system of a subject with chronic otitis media without tympanosclerosis.

(19-54). The mean volume of mastoid pneumatization was 2,3 cm³ (0,3-6,4). Of 33 patients in Group 3, 19 were female and 14 were male, the mean age was 33 (22-59). The mean volume of mastoid pneumatization was 0,2 cm³ (0,0-0,8) (Table 1).

Discussion

There is a general agreement that tympanosclerosis is an end-result of chronic inflammation, but the pathogenesis is still unknown. Controversy focused on whether tympanosclerosis is a spesific inflammation or a non-spesific terminal stage of different inflammatuar conditions. Tympanosclerosis is an irreversible end-result process, leading to anatomical and functional damage in middle ear. It's usually because of inflammation, but rarely may appear after trauma or surgery. There is not any spesific inflammation leading to tympanosclerosis, nevertheless any non-treated inflammatory process may cause it [7]. Hypothesis on the development of tympanosclerosis are: 1) infection followed with necrosis and granulation, 2) ischemic alterations, 3) stasis of infected materials. One hypothesis suggets that tympanosclerosis is caused by immunologic reaction. According to this hypothesis, connective tissue components are stimulated with infection, inflammation or trauma and damaged to connective tissue initiates the local immunological reaction. Immune reaction is initiated in the submucosa by the materials which located in middle ear effusion coming through the mucosa [8]. It's believed that otitis media episodes which take place in the history of tympanosclerotic patients, induce the local tissue respond leading to tympanosclerosis. Infection is accused of stimulating the fibroblastic activity and tympanosclerotic degeneration [9]. In rats, tympanosclerosis was evoked during the course of a sterile otitis media, induced by Eustachian tube obstruction [10]. Other causes are allergic reaction, hemorrhage in middle ear mucosa and effusion in the middle ear space. The causes leading to tympanosclerosis are well-known, but the underlying mechanism is stil unknown.

It is believed that mastoid pneumatization have a very important part in middle ear physiology. It is an argument that mastoid air cell system is an air-reservoir for middle ear and plays a role in middle ear pressure regulation [11]. Holmquist stated that the success of the middle ear surgery depends on the degree of mastoid pneumatization [12]. It was reported that poor pneumatization have a part in development of atelectasis [2]. The greater part of the ears with cholesteatoma is the ears with poor mastoid pneumatization. Sade reported that in his patients with cholesteatoma, 82,2 % have poor or non-pneumatized mastoid [13]. Postoperative atelectasis is seen very often in ears with cholesteatoma. The ears with atelectasis and cholesteatoma are poor-pneumatized ears in the majority. This situation points out the direct relationship between functions of the middle ear and mastoid pneumatization.

The predisposition for otitis media with effusion (OME) in the ears with low mastoid pneumatization and the advance of OME episodes to COME or atelectasis point out that mastoid air cell system is a structure which regulates and buffers the irregularities in the middle ear pressure. In different forms of otitis media, there is negative pressure in middle ear and the regulation of this pressure can not be done in case of low-pneumatized ears. Sade reported the rate of COME as 52,2 % in low-pneumatized ears and 20 % in well-pneumatized ears in 72 adult patients who were

Table 1. Characteristics and mean mastoid pneumatization volume of patients.

Group 1: 50 patients (100 ears) (COM (-), Ts (-))	32 female, 18 male (mean age 39 (15-72))	7,9 cm³ (4,0 – 14,0)
Group 2: 20 patients (20 ears) (COM (+), Ts (+))	13 female, 7 male (mean age 28 (19-54))	2,3 cm³ (0,3 – 6,4)
Group 3: 33 patients (33 ears) (COM (+), Ts (-))	19 female, 14 male (mean age 33 (22-59))	0,2 cm³ (0,0-0,8)

COM: Chronic otitis media, Ts : Tympanosclerosis

followed up to 33 months [5]. Clinical studies emphasized that the response of OME to treatment is better in well-pneumatized ears [14]. Nakano stated that if volume of mastoid air cell system of children with OME is large or it shows an increase with treatment, then the prognosis becomes more favourable [15]. It was reported by Lindeman and Shea that the volume of air cell system was smaller in children with long-lasting OME that healthy children [16]. All of these studies emphasize that the level of mastoid pneumatization is an important prognostic factor in the prognosis of OME.

Normal mastoid air cell system is an air reservoir and also an active cavity which has gas exchange capability independent from Eustachian tube [17]. Air cell system is capable of gas exchange by submucosal capillary network. Because gas exchange occurs in cellular mucosa, total area of mucosal surface affects gas exchange rate. Mastoid cavity buffers the effects of pressure changes in the middle ear by supplying air to the middle ear. The capacity of this system is its volume. Increased mastoid pneumatization enhances the ability of regulating middle ear pressure. It was reported that in case of large mastoid pneumatization, there is a decreasing risk of middle ear barotrauma in SCUBA (self contained underwater breathing apparatus) divers [18].

Numerous different methods have been described for the measurement of mastoid pneumatization: water-weight method, pressure transducer method, planimetric method and computerized tomography (CT) [19-20]. Andreasson and Flisberg measured the volume of the mastoid air cells as between 5,8 and 12,2 ml [21-22]. Turgut measured the air cell system volume as 7,32 cm^2 in 60 fresh frozen adult temporal bones with x-ray, CT and surgical dissection in his planimetric studies [23]. Park reported the mean volume of mastoid pneumatization as 10,43 cm^3 (6,25-20,52) in normal population with CT [19]. Isono measured the volume as 5,97 ml with CT [24]. Akdas et al. measured the mean mastoid volume in healthy persons as 9,04 cm^3 (right ears) and 8,95 cm^3 (left ears) by CT [25]. It is a well-known process that mastoid pneumatization is smaller in ears with CSOM, COME and ears with cholesteatoma. Sade reported the rate of poor-pneumatized mastoids (sclerotic and diploic) as 96,3 % in adult patients with cholesteatoma (183/190) and 57,8 % in pediatric patients with cholesteatoma (63/109) [4]. Turgut and Tos found out that in temporal bones with obvious middle ear pathology, the mastoid and temporal pneumatizations are smaller [23]. In this study, it was measured the mastoid pneumatization as 0,2 cm^3 (0,0-0,8) in non-tympanosclerotic patients with CSOM with or without cholesteatoma. This result emphasized that mastoid pneumatization in patients with COM is smaller than mastoid pneumatization of normal subjects (p=0,001, One Way Anova test). It was measured the mastoid pneumatization as 2,3 cm^3 (0,3-6,4) in tympanosclerotic patients. This measurement is smaller than the mean volume of normal subjects (p=0,007, One Way Anova test), but greater than the patients with COM without tympanosclerosis (p=0,047, t test). The differences between the groups are statistically significant.

In this study, tympanosclerotic patients have perforated tympanic membrane, obvious sclerotic degeneration in tympanic membrane and/or middle ear mucosa and a history with at least one episode of middle ear infection. In these subjects, the factor leading to tympanosclerosis is previous middle ear infection. These patients have smaller mastoid pneumatization than normal subjects and this may explain the predisposition to middle ear infections. In patients with COM without tympanosclerosis, pneumatization is smaller and this separate these two patient groups. The degree of pneumatization explains the difference of having tympanosclerosis in these two groups. Mastoid pneumatization is larger in tympanosclerotic patients (Group 2) than the patients with COM without tympanosclerosis (Group 3). In these patients, there must be a reason for the tympanosclerotic end-result of infection. It may be genetically determined, or the anatomical differences in temporal bones, the abnormal reaction in middle ear/mastoid air cell mucosa, differences in vascularization or different immune reaction [26]. The differences of the volume of mastoid pneumatization as it was found out in this study, may be the cause of the tympanosclerotic degeneration. Why the ears with greater pneumatization have a tendency to sclerotic degeneration ?. The cause of this predisposition may be production of “free oxygen radicals” (FOR).

Middle ear gases have an equilibrium with blood gases[27-28]. The oxygen concentration in middle ear is smaller than atmosphere. The oxygenization of the tissues increases when the oxygen concentration of the middle ear rises. Following this, the production of FOR increases and this starts the fibrosis and hyaline degeneration. Fibrosis and hyaline degeneration are the histopathological findings of tympanosclerosis. The increased production of FOR may be the first step of the accumulation of calcium and phosphate. FOR may irreversibly damage the cells [29-30]. The degeneration may lead to cell necrosis. FOR are unstable molecules, their volume may be determined by measuring the protective antioxidative enzymes [31-35]. Superoxide dismutase is the most analyzed between these enzymes[36]. It has been shown that ventilating tube insertion cause relative hyperoxidation in middle ear cavity [37]. With these findings, we can say that, the patients with insertion of a ventilating tube are subjected to two factors producing FOR: inflammation and hyperoxidation. It is well known process that the most frequent complication from the use of a ventilating tube is tympanosclerosis[38-41]. FOR produced by hyperoxidation may be the cause of the development of tympanosclerosis in these children.

To elucidate possible role of the FOR in the development of tympanosclerosis, Mattsson developed sclerotic lesions in rats with perforated tympanic membranes exposed to oxygen concentrations of 40%. Mattsson stated that FOR play a significant role in development of tympanosclerosis[42]. Because of fenspiride (an anti-inflammatory agent) has capacity to block FOR, Mattsson tested the capability of fenspiride to block the development of myringosclerosis. Using topical or intraperitoneal fenspiride to rats by 12 days, he observed that topical fenspiride prevented the development of sclerotic lesions [43]. Similarly, it was shown that some free radical scavengers like ascorbic acid, selenium, vitamin E (α–tokoferol), N-acetylcysteine prevent the development of myringosclerosis in rats because of their anti-oxidative properties [44-48].

These studies show us the role of FOR in the development of tympanosclerosis. Hyperoxidation, production of FOR and sclerotic degeneration are observed after the insertion of ventilation tubes. If there is an infection / inflammation in middle ear / mastoid cells, in the situation of well-pneumatized mastoid cell system, there may be an increase of FOR beacuse of hyperoxidation. This may cause tympanosclerosis. In ears with well-pneumatized mastoids, this may explain the relative frequency of sclerotic degeneration. In this study, it was observed that the mastoid air cell volume is larger in tympanosclerotic patients that the patients without tympanosclerosis as supporting these findings. Submucosal vascularization is excess in ears with well-pneumatized mastoid because of the excess of submucosal area. In inflammatory process, excess vascularization leads to increase in blood perfusion, and the migration of inflammatory cells. The increase in inflammatory cells causes the increase in rate of the development of tympanosclerosis. It is a well known situation of the existence of inflammatory cells in tympanosclerotic tissues [1,6-8]. Increased perfusion causes the increased production of FOR. All these findings point out the importance of FOR in the pathogenesis of tympanosclerosis. As our knowledge about the pathogenesis of tympanosclerosis increase, the success of surgery for tympanosclerosis increase. Because of this, the points which we investigated must be studied with larger subject/patient groups for more definite results.

Confliet of Interest: None

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