Is there a relationship between myringosclerosis and atherosclerosis?

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Abstract. Is there a relationship between myringosclerosis and atherosclerosis? Objective: Myringosclerosis and atherosclerosis are two different pathologies seen in different parts of the body. Both of these occur following a similar physiopathological process. However, this has not previously been adequately discussed in the literature. Trauma to either the tympanic membrane or to the intimal layer of the arterial wall results in the formation of a sclerotic plaque. The goal of this study was to investigate the relationship between myringosclerosis and atherosclerosis.

Patients: A total of 421 patients with the diagnosis of coronary artery disease were included in the study. All of the patients were evaluated for the presence of atherosclerosis by coronary angiography and for myringosclerosis by otoscopic examination.

Main Outcome Measures: The presence of myringosclerotic plaques, plaque dimensions and bilateral involvement of tympanic membranes were compared in the groups with and without atherosclerosis.

Results: Amongst the 316 patients (75.0%) shown to have atherosclerosis, 65 (20.5%) also had myringosclerosis. Amongst the 105 patients without atherosclerosis, 24 (22.8%) had myringosclerosis. There was no statistically significant relationship between atherosclerosis and myringosclerosis (p > 0.05). Neither plaque dimensions nor bilateral involvement of the ears showed significant difference between the two groups (p >0.05 and p >0.05, respectively).

Conclusions: We conclude that there is no similar genetic tendency between atherosclerosis and myringosclerosis. The significance of the plaque dimensions and the bilateral involvement of tympanic membranes have not been satisfactorily discussed in the literature and this is the first time that they are being addressed. In contrast to the reported articles, there is no relationship between atherosclerosis and myringosclerosis other than being similar pathological processes occurring as a result of endothelial-epithelial damage.

Introduction

Tymanosclerosis (TS) is the formation of white plaques or nodules in the tympanic membrane (TM) or submucosa of the middle ear. Hyaline degeneration of connective tissue in the lamina propria of the middle ear results in TS. If only the TM is affected, it is called myringosclerosis (MS). Although TS occurs mostly as a result of repetitive middle ear infections, it can also result from any kind of trauma to the TM such as TM perforation due to chronic otitis, insertion of grommets, myringotomy or traumatic TM perforation. Formation of MS is an inflammatory response of the organism to trauma.1

Atherosclerosis (AS) is an inflammatory event, primarily affecting the intimal layer of elastic arteries. Lipid, macrophages and fibroblasts accumulate in the atheroma plaques. The current theory for the pathogenesis of atherosclerosis is endothelial damage followed by development of an inflammatory response in the arterial wall. Other theories emphasize the role of primary smooth muscle proliferation and infections. Hyperlipidemia, smoking, hypertension, family history of coronary artery disease, diabetes mellitus and obesity are the most important risk factors for AS.2,3

In both physiopathological processes, inflammatory reactions are induced secondary to trauma. AS does not develop after every intimal trauma nor does TS after every middle ear inflammation. The prevalence of coronary artery disease with at least one critical stenosis in subjects aged 40-70 years is 7.3%.4 The incidence of TS after middle ear infections or insertion of grommets in the TM varies markedly depending on the authors: Plester5; 10%, Akyildiz6; 16%, Chevretton7; 76%.

The aim of this study is to investigate whether there is a relationship between myringosclerosis and atherosclerosis, both of which occur following physiopathological processes similar to the formation of sclerotic plaques.
Materials and Methods

A total of 421 patients hospitalized in the Cardiology clinic with a diagnosis of coronary artery disease (CAD) were included in the study. For diagnosing AS, stenosis in the coronary arteries was shown by coronary angiography. Informed consent was obtained from the patients. MS was shown by otoscopic examination. For standardization of otoscopic examination, all patients were examined by a single observer. Patients having an active middle ear infection or history of past middle ear surgery were excluded from the study.

The median age of the patients was 61.7 years (35-93). Of all, 284 (67.5%) patients were male and 137 (32.5%) female. The patients were questioned about the major risk factors for AS, such as smoking history, hypertension, diabetes, hyperlipidemia and family history of coronary artery disease.

In the group with MS, the dimension and localization of the sclerotic plaques were defined for each ear. Plaque dimensions were categorized into four groups according to the area it covered on the tympanic membrane: 1-25%, 26-50%, 51-75% and 76-100%.

Results

AS was confirmed in 316 patients (75.0%) whilst MS was present in 20.5% and 22.8% of the patients with and without AS respectively. The median age of patients with AS was 62.8 years (range, 37 to 93). The ages of the 105 patients without AS were between 35 and 82 (median 60.4). The age of the two groups was not statistically different.

The patients with MS were evaluated according to the dimensions of the myringosclerotic plaques. The most commonly seen plaques were those covering less than 25% of the TM, these being detected in 52.3% and 66.7% of the right and 30.7% and 41.7% of the left ears of patients with and without AS respectively. Myringosclerotic plaque dimensions were not statistically different between the two groups (p > 0.05).

Discussion

MS is a sequela that occurs during the healing process of any trauma to the TM. During this process, hyaline degeneration and calcified accumulations occur in the lamina propria of the middle ear secondary to inflammation. With the development of metaplasia in the lamina propria, fibrosis and then granulation occurs. Development of TS is completed following mineralization, collagen accumulation and development of lacunae in these regions.1,7,8

A series of inflammatory events following intimal trauma results in the formation of atheromatous plaques. The earliest lesion is a subendothelial accumulation of lipid-laden macrophage foam cells and associated T lymphocytes, known as a fatty streak. Following this, the lesion progresses and the core of the early plaque becomes necrotic, containing cellular debris, cholesterol, and inflammatory cells, particularly macrophage foam cells. There is an endothelialized fibrous cap in the necrotic core at the luminal surface, consisting of smooth muscle cells embedded in an extensive collagenous extracellular matrix. Advanced lesions may show evidence of calcification, ulceration, new vessel formation, and finally rupture or erosion.2,9

In the present study, 20.5% of the patients with an atherosclerotic plaque and 22.8% without AS were shown to have a myringosclerotic lesion. There was no significant difference between the two groups. However, Koc and Uneri10 found MS in 66.6% of 1024 patients with AS in their study. In that study, 12% of the 300 patients without AS were shown to have MS and it was concluded that there was a similar genetic tendency between AS and MS. Ferri et al.11 evaluated 84 patients with and 84 without AS and found MS in 38% and 13% of the patients, respectively. They concluded that both events were the end result of an inflammatory response resulting from endothelial damage and infection.

During the formation of an atherosclerotic plaque following damage to the vessel intima, macrophages, T4, T8 and B lymphocytes accumulate at the site of the lesion. The proteolytic enzymes like collagenase and
elastase released from the macrophages lead to the formation of the lesion while dead macrophages also accumulate and are incorporated into the lesion. The matrix formed by the dead macrophages form a background for calcification. B lymphocytes produce autoantibodies against LDL (low density lipoprotein). Lipoproteins and fibrinogen pass from the plasma to the intima. Intimal smooth muscle cells produce type 1 and type 3 collagen and elastin. Elastin fibres become calcified and produce lipid-collagen and calcium-rich atherosclerotic tissue.9,11

Studies which experimentally produce otitis media and investigate the development of TS show that the inflammatory response and inflammatory mediators that are involved in TS are very similar to those involved in the process of AS. Following otitis media, firstly macrophages and later B and T lymphocytes and IL-6 accumulate beneath the damaged mucosa. Macrophages release enzymes and mediators such as nitric oxide. With the effect of the cytokines, macrophages are converted to osteoclasts. The osteoclasts, which are induced by IL-6, cause new bone formation. After calcification and mineralization tympanosclerotic tissues form.12,11

As in our study, the incidence of MS was similar in both groups, we concluded that there was no similar genetic tendency nor relation between atherosclerotic and myringosclerotic plaque formation. As mentioned above, the similar inflammatory responses in both physiopathological processes results in the formation of similar sclerotic plaques.

When myringosclerotic plaques in the patients with atherosclerosis were evaluated for dimension and bilaterality, no significant difference was found. The myringosclerotic plaques that formed in the patients with atherosclerotic plaques in the coronary arteries were shown to be similar to the patients without CAD when evaluated according to the dimension, side involved and localization of the plaque. As far as we know, comparison of plaque dimensions and involvement side are reported for the first time. Among the patients with AS, the area of the TM involved was not greater than for the patients without AS. The ratio of bilateral involvement was not greater than in the patients without AS either. These findings indicate that these processes are limited to the local inflammatory response.

Conclusions

AS and MS are two different diseases with similar pathologies. The similarity of the physiopathological processes could occur in a similar group of patients as a result of genetic susceptibility. But in our study, we showed that the incidence of MS, dimensions of the plaques and bilateral involvement rates were similar in patients with and without AS. Contrary to the literature, we conclude that there is no relationship between these two diseases.

AS and MS are similar pathologic processes that result from the inflammatory processes developing in response to endothelial-epithelial damage. But, with the results of this study, it is improbable that there is a similar genetic tendency between these two diseases. Novel molecular studies could give new insights and basic evidence to this question in a near future rather than further small cohort studies.

References

