The Journal of Laryngology and Otology
July 1993, Vol. **107**, pp. 651–655

Pathology in Focus

Pathology of the eustachian tube in otitis media: an electron microscopic study

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Abstract
The ultrastructure of the mucosa of the eustachian tube was studied in four temporal bones showing tympanosclerosis, cholesteatoma, otitic meningitis and a grafted tympanic membrane (tympanoplasty). The mucosa of tube was abnormal in the four cases confirming the relationship between the state of the eustachian tube and the inflammatory process in the middle ear. The observed abnormalities included: ciliary loss, abnormal ciliary morphology and motility, oedema of the microvilli, hyperplasia of the goblet cells and the seromucinous acini, desquamation of the non-ciliated cells and appearance of mast cells in the lamina propria of the tube. Ciliary changes were the most frequent abnormalities and the morphological changes, in general, were fewest in the case of healed tympanoplasty. The pathophysiology of the morphological changes was discussed and correlated with the disease in the middle ear.

Key words: Eustachian tube; Otitis media; Microscopy, electron

Introduction

The eustachian tube is one of the most complicated structures in the human body. Its anatomy is certainly very complicated; its physiology is still incompletely understood; and its pathological states are infrequently examined.

The epithelium of the eustachian tube consists of psuedostratified ciliated cells, non-ciliated columnar cells, goblet cells and underlying basal cells resting on a thin basement membrane. A detailed description of the fine structure of the eustachian tube has been reported previously (Lim *et al.*, 1967; Hentzer, 1970; Shimada and Lim, 1972; Lim, 1974; Harada, 1977 and 1983).

In this study the fine morphology of the mucosa of the eustachian tube in four cases of otitis media will be described and correlated with the pathological findings in the middle ear cleft.

Material and methods

Four eustachian tubes were removed from the temporal bones of four patients with different forms of otitis media. The ages, diagnoses, as well as the pertinent histopathological findings of the cases are shown in Table I. The disease was active in cases i.e. nos. 2 and 3, and was inactive in the other two cases. The distinction between active and inactive cases was based on the histopathological picture of the middle ear mucosa.

Within two hours postmortem, four per cent paraformaldehyde solution in buffer was instilled through the tympanic membrane into the middle ear cavity and the temporal bones, including the whole lengths of the eustachian tubes, were removed and transferred to a four per cent paraformaldehyde solution in buffer. The temporal bones were stored at room temperature for one to three weeks. This technique minimizes, to a great extent, the effect of postmortem autolysis which may result in changes such as loss of cilia and desquamation of the epithelial cells (Smith and Vernon, 1976).

The entire eustachian tubes were dissected from the temporal bones under the operating microscope. The eustachian tubes

TABLE I

BRIEF DESCRIPTION OF THE FOUR CASES

Case no.	Diagnosis	Histopathological findings
1 (38 years)	Tympanosclerosis	Fusiform thickening of the posterior part of the tympanic membrane due to the presence of a large eosinophilic tympanosclerotic plaque.
		Deposition of hyalinized collagen fibres over the promontory.
2 (45 years)	Cholesteatoma	Desquamated keratin debris involving the posterior mesotympanum, mastoid antrum and air cells.
		Fistula over the lateral semicircular canal.
3 (16 years)	Otitic meningitis	Purulent exudate surrounding and infiltrating the nerves in the internal auditory canal.
		Purulent exudate within the middle ear and scala tympani
4 (27 years)	Tympanoplasty	A thin healed tympanic membrane which is retracted medially in its posterior half.
		Fibrous tissue adhesions filling the oval window niche and extending around the crura of the stapes.

Accepted for publication: 16 April 1993.

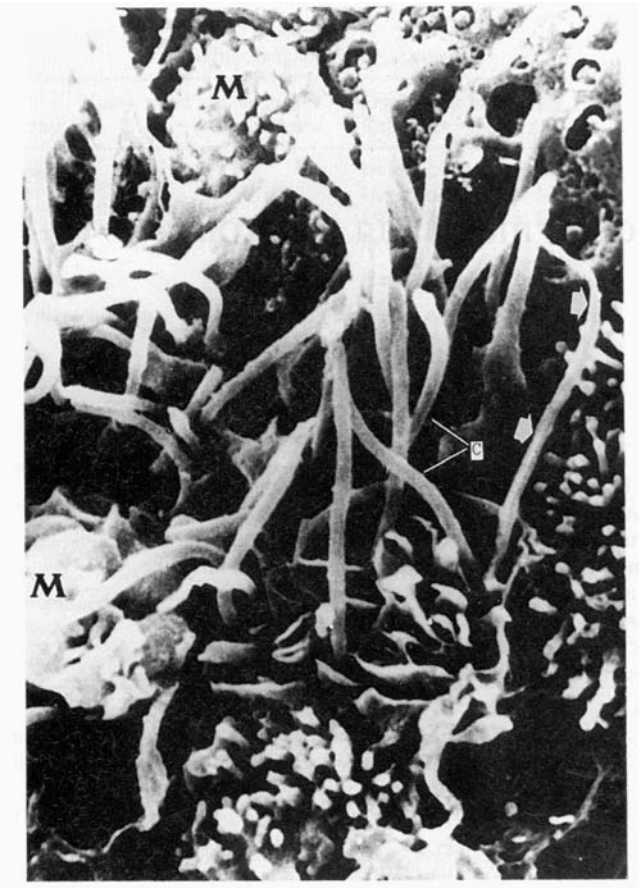

FIG. 1

Scanning electron micrograph of the surface epithelium showing marked ciliary loss. The cilia (C) are beating in different directions and some of them (wide arrows) appear abnormally thin and long. Mucous discharge (M) is seen on some cilial tips (×5800).

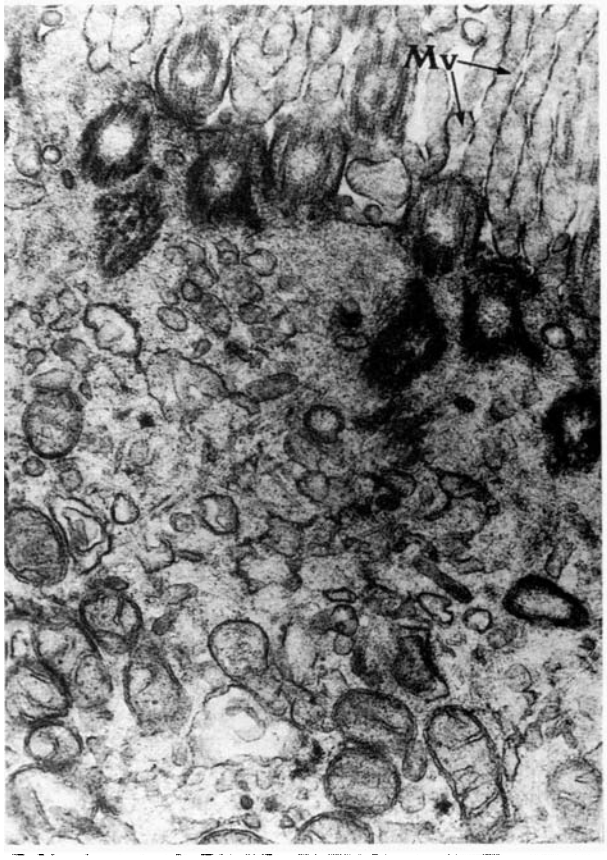

FIG. 2

Transmission electron micrograph showing oedema of the microvilli (Mv) which are swollen and have irregular outlines (× 4600).

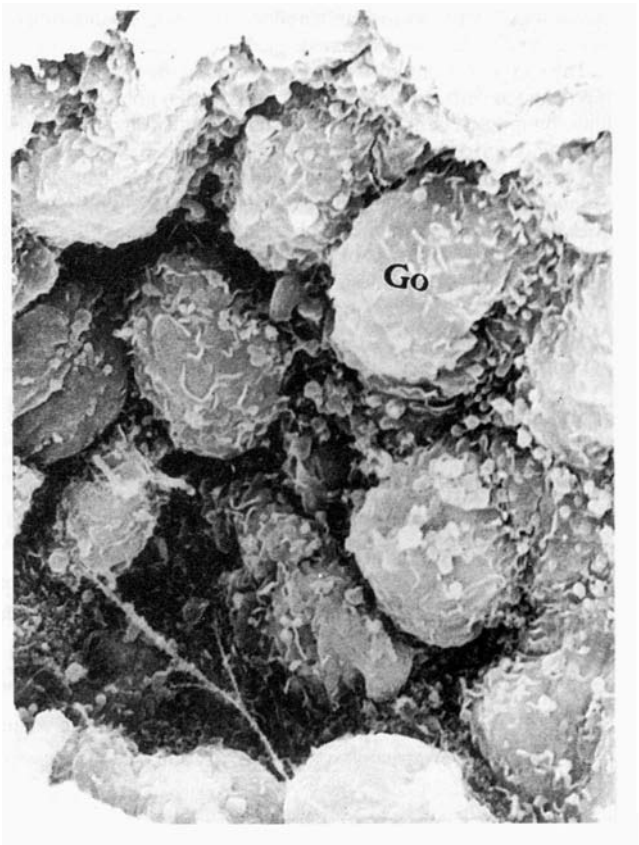

FIG. 3

Scanning electron micrograph showing numerous crowded goblet cells (Go). No ciliated cells are seen in this field (× 4320).

were divided into several pieces and postfixed in one per cent osmic acid for 24 hours and dehydrated in a series of a graded ethyl alcohol solutions.

Specimens prepared for scanning electron microscopy were placed in isoamyl acetate for 30 minutes and critical point-dried with liquid carbon dioxide. The specimens were then coated with palladium gold and examined under a JOEL-35C scanning electron microscope.

Specimens prepared for transmission electron microscopy were impregnated with CY212 TAAB araldite, using propylene oxide as an intermediate solvent and then polymerized at 60°C in TAAB embedding capsules. Ultra-thin sections were cut with an LKB ultramicrotome, stained with four per cent uranyl acetate and Reynold's lead acetate and examined with an Hitachi H-600 transmission electron microscope.

Results

The mucous membrane of the eustachian tubes revealed several morphological changes including:

(1) Moderate to marked ciliary loss. Some of the remaining cilia appeared abnormally long and thin and many of them showed irregularity in their orientation and appeared beating in different directions (Fig. 1).

(2) Swelling and oedema of the microvilli of the ciliated cells (Fig. 2). The microvilli occasionally exhibited a beaded appearance.

(3) Hyperplasia of the goblet cells (Fig. 3). Numerous goblet cells were observed particularly in the ciliated part of the eustachian tube. A few cells were also seen extending into the normally non-ciliated medial third of the

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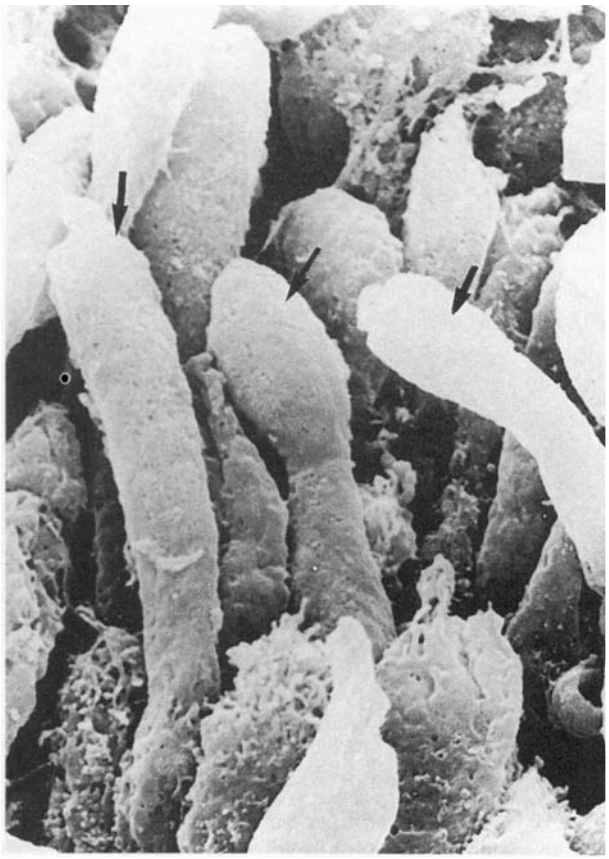

FIG. 4

Abnormally large goblet cells (arrows) distended with mucous secretion (× 3000).

tube. Some of the goblet cells appeared three to five times larger than ordinary cells (Fig. 4).

(4) Desquamation of the superficial epithelial cells in the non-ciliated portion of the tube. Some of the remaining cells showed a significant reduction of their cytoplasmic mass (Fig. 5). This was especially observed in case no. 2 (cholesteatoma) and no. 3 (otitic meningitis).

(5) Hyperplasia and hyperactivity of the seromucinous acini which were scattered along the whole length of the tube. The glandular cells appeared packed with secretory granules (Fig. 6).

(6) Appearance of fully granulated mast cells in the submucosa of the tube (Fig. 7). This was observed in the case of tympanosclerosis.

The frequency of the observed morphological changes in the four cases was semiquantitatively assessed and is shown in Table II. In general, the changes were fewest in case no. 4 (tympanoplasty) being limited to abnormal ciliary morphology and moderate ciliary loss. This was, apparently, in harmony with the inactivity of the inflammatory process in the middle ear. Ciliary changes were present in the four cases and were the most constant feature. Hyperplasia of the goblet cells and the seromucinous acini was most marked in the case of tympanosclerosis where there was evidence of an active allergic reaction (mast cells). On the other hand, desquamation of the non-ciliated cells was most severe in the case of otitic meningitis and it appeared to be directly related to the severity of the inflammatory reaction.

Discussion

There have been several reports on the morphological changes of the ciliated epithelial cells of animal and human respiratory mucosa under various experimental and non-experimental conditions. Similar reports on the mucosa of the pathological eustachian tube are, on the other hand, very scarce due to its inaccessible nature.

Duncan and Ramsey (1965) reported that under the influence of bacterial inflammation, the ciliated epithelial cells of the pig nasal respiratory mucosa often become polyhedral in shape. The principal changes were in the cilia which were reduced in number. Von Mecklenburg *et al.* (1974) described the presence of abnormal cilia in the ciliated cells of the rabbit tracheal mucosa after heat exposure. Similar ciliary abnormalities have been also described in association with allergy (Elwany and Bumsted, 1987), inflammatory conditions (Friedmann and Biud, 1971), and radiotherapy (Elwany, 1985).

The present investigation revealed several morphological changes in the mucosa of the eustachian tube in association with inflammation of the middle ear cleft. It is of interest that in the four cases the mucosa of the eustachian tube was pathological. This confirms the relationship between the state of the eustachian tube and inflammatory conditions of the middle ear and mastoid and highlights the possible role of the tube in the pathogenesis of these conditions.

Ciliary loss and abnormal ciliary morphology were the most noteworthy morphological alterations. There is a general opinion that the morphological changes of the cilia usually occur prior to those of the cytoplasm. However, the ciliary changes are not inevitably followed by death of the ciliated cells.

Abnormal ciliary motility was another important observation confirming the findings of Birch and Elbrand (1986) who reported disordered mucociliary transport in patients with cholesteatoma. Normal cilia should beat in the same direction (metachronal beating). Abnormal ciliary mobility (Dudley *et al.*, 1982) is usually indicative of early ciliary damage. Ciliary loss

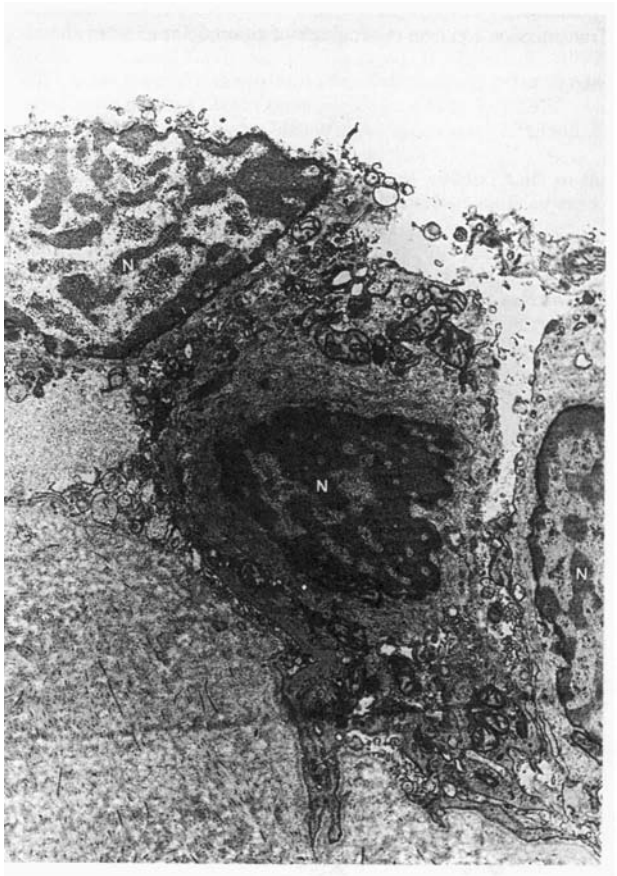

FIG. 5

Desquamation of the non-ciliated cells. Only one row of epithelial cells is still in existence. There is a marked reduction of the cytoplasmic mass of the remaining cells and the nuclei (N) appear occupying most of the cells (× 8000).

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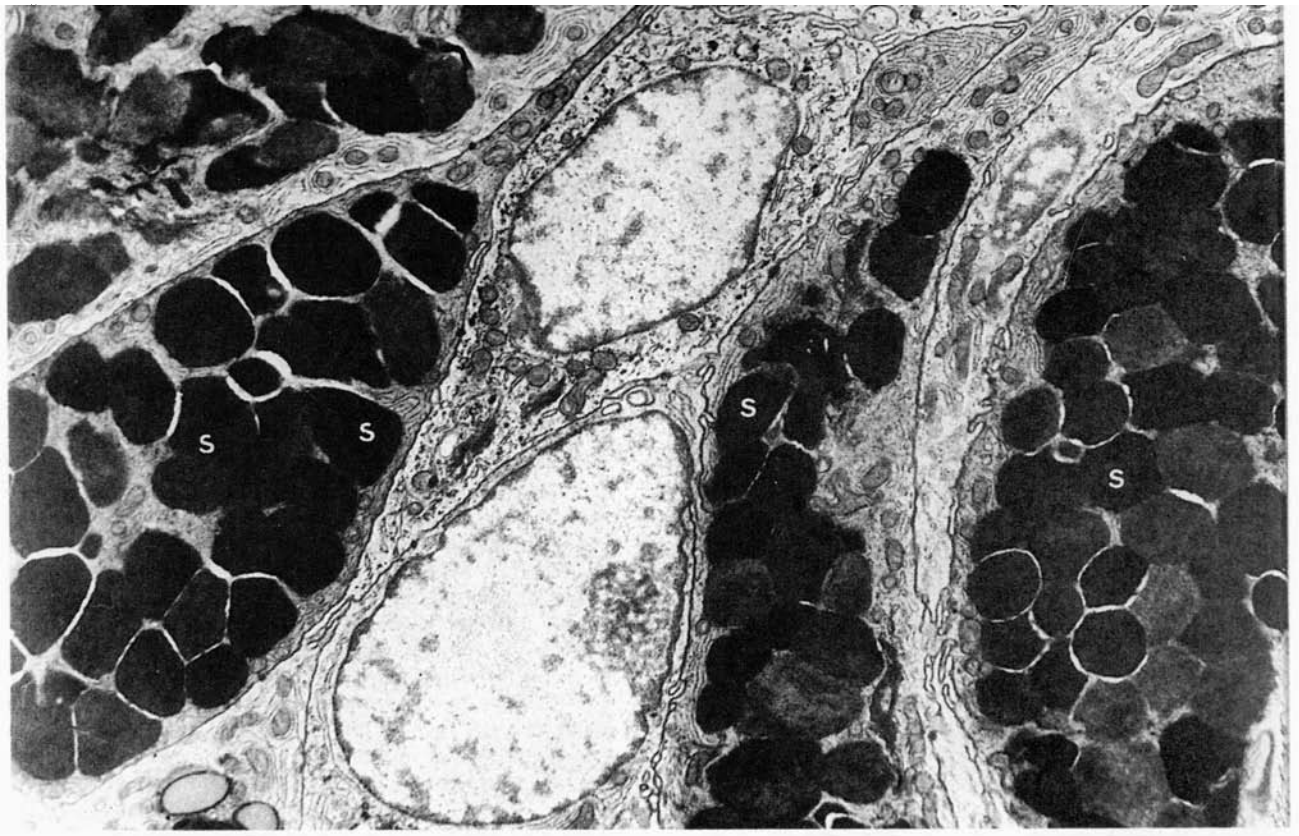

FIG. 6
Transmission electron micrograph of seromucinous acini showing the acinar cells packed with secretory granules (S) (× 5000).

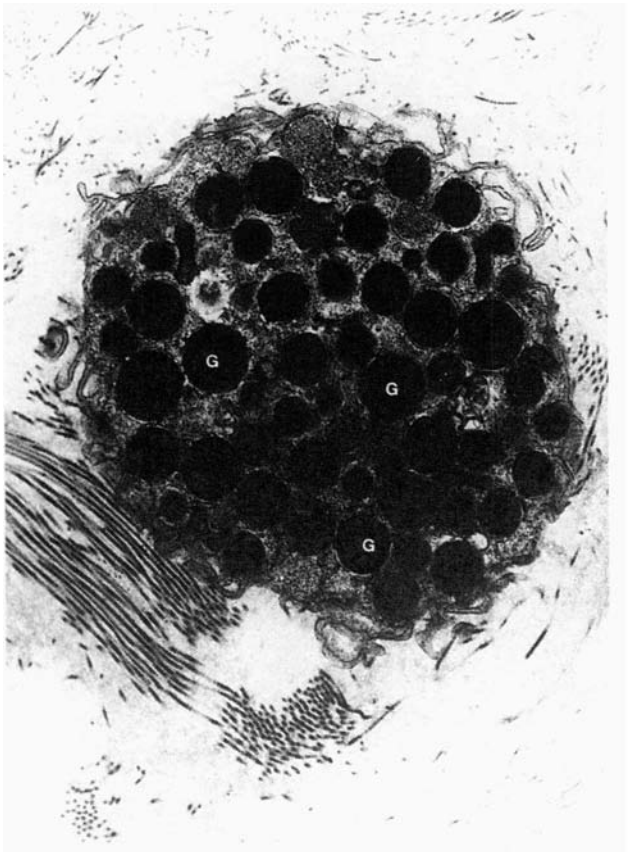

FIG. 7
A mast cell containing many electron dense granules (G) (× 5000).

on the other hand, obviously, represents the end stage of the ciliary disease.

The pathogenesis of the ciliary changes and ciliary loss is still uncertain. However, until the true nature of these changes is elucidated, the possibility remains that they may be a degenerative phenomenon. Bacterial colonization and increased carbon dioxide partial pressure were suggested as the cause of the degenerative process (Ohashi *et al.*, 1987). Similar changes, however, were reported in cases of vasomotor rhinitis in the absence of evident bacterial infection (Elwany and Bumsted, 1987). Regardless of the pathogenesis of the ciliary disorder, it will definitely impede the rhythmic action of the mucociliary apparatus and hinder the drainage of the middle ear cleft. The problem of postmortem autolysis should also be taken into consideration and the proper fixation technique should be adopted.

The microvilli normally participate in the formation of the sol layer of the mucous blanket (pericilliary fluid) by facilitating the transudation of fluid from the subepithelial fenestrated capillaries. Oedema of the microvilli apparently denotes increased fluid transudation across the cells. This may be a compensatory mechanism to compensate for the increased production of viscous mucous by the hyperplastic goblet cells.

Hyperplasia of the goblet cells was observed in three cases and was associated with hyperplasia of the mucous glands. A similar hyperplasia has been described in allergic rhinitis (Elwany *et al.*, 1983) and during pregnancy (Toppozada *et al.*, 1982). A study of the distribution of the goblet cells in the developing human nose found no supporting evidence for the view that the ciliated cells were capable of transformation to goblet cells. The modern view is that the goblet cells are derived from the nasal cells of the epithelium (Friedmann and Bennett, 1986).

Glandular hyperactivity has been a constant feature in secretory otitis media (Sadé, 1979; Elwany, 1990). In the present work it is of note that hyperplasia of the goblet cells and the seromucinous acini was greatest in the case of tympanosclerosis which

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TABLE II

THE FREQUENCY OF THE MORPHOLOGICAL CHANGES IN THE EUSTACHIAN TUBE MUCOSA IN THE FOUR CASES

Morphological changes	Case no. 1	Case no. 2	Case no. 3	Case no. 4
Ciliary changes	++	++	++	+
Oedema of microvilli	+	+	+	–
Hyperplasia of goblet cells	++	+	+	–
Desquamation of non-ciliated cells	–	+	++	–
Hyperplasia of seromucinous acini	++	+	+	–
Mast cells	++	–	–	–

Case no. 1 = tympanosclerosis; case no. 2 = cholesteatoma; case no. 3 = otitic meningitis; case no. 4 = tympanoplasty. – = absent; + = present; ++ = marked.

showed mast cells in the lamina propria of the eustachian tube indicating an active allergic process. This agrees with the findings of Tos (1979) who reported increased density of the goblet cells in the middle ear in chronic tubal occlusion, secretory otitis media and active chronic suppurative otitis media. The viscid mucus will further slow down the already crippled ciliary movements. Moreover, the formation of mucous plugs will mechanically obstruct the lumen of the tube and diminish the aeration of the middle ear cleft.

The pathological changes were not limited to the ciliated and goblet cells. Desquamation of the non-ciliated epithelium was observed in two cases and was marked in the case of fulminating meningitis indicating that it is more likely to occur in association with acute severe inflammatory reactions of the middle ear cleft. Shedding of the epithelial cells is usually preceded by reduction of the cytoplasmic mass of the cell and separation of the junctional complexes between the epithelial cells (Elwany, 1985).

Two further observations are worth mentioning. Firstly, the morphological changes in the eustachian tube mucosa were more or less paralleling the inflammatory process in the middle ear cleft, being least frequent in the case with grafted healed tympanic membrane. Secondly, healing of the graft did occur in spite of the pathological findings in the eustachian tube. The results of the operation, however, were suboptimal as shown by the medial displacement of the tympanic membrane and the presence of excessive fibrosis around the stapes.

The relationship between the eustachian tube and otitis media has been previously established basically on clinical and tympanometric grounds. The present work documents this relationship on an ultrastructural basis and reconfirms the importance of paying the proper attention to the condition of the eustachian tube during the treatment of otitis media.

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