Delayed Hypersensitivity Skin Tests in Cholesteatoma Patients

Thesis

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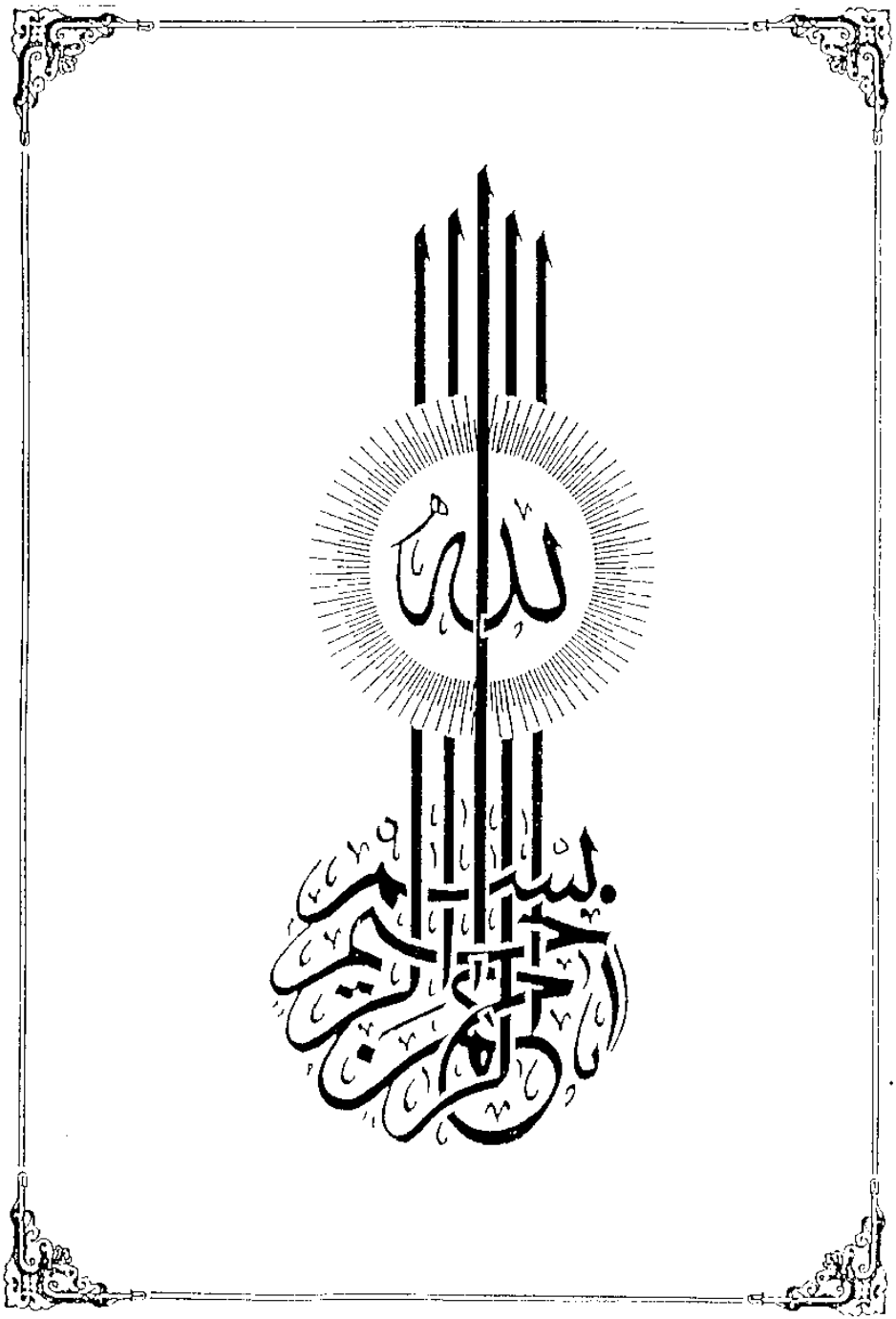
بسم الله الرحمن الرحيم

وما أوتيتم من العلم إلا قليلا

صدق الله العظيم



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Dedication

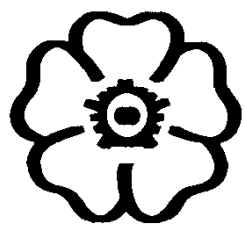
To Whom I owe so much beyond words

*To **GOD**, who has given me the mind, power, and capability.*

*To my **Father**, who has endowed me with ulterior aegis.*

*To my **Mother,** who has been my auric aura.*

*And last, but by far least, to my **Wife** and my son **Omar** who have and will always be the source of inspiration for all my endeavorous auspices.*



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Introduction

Cholesteatoma is a skin related disorder of the human temporal bone and ear. Histologically it consists of a layer of stratified squamous epithelium of the keratinizing type covering a stroma of fibrous granulation tissue infiltrating the middle ear and mastoid space. Electron microscopic findings of human cholesteatoma matrix have shown that the cellular composition of this matrix and its mucosal lining is not static, but there is a "Langerhans" cell and T-cell traffic" through cholesteatomas, which actually originates from a mobile cell population of monocytes then migrates into and out of the body's lining, thus playing a key role in cholesteatomas as well as other skin disorders *(Veldman et al., 1984 and Palva et al., 1987)*.

Since such "traffic" does not occur normally in the middle ear mucosa, it is presumed that a key role in pathogenesis of cholesteatoma is played by cell mediated immune mechanism.

Aim of the study:

Evaluation of cell mediated immune response in cholesteatoma patients by means of intradermal skin test using a group of common antigens.

Part 1.: Cholesteatoma

I. 1. A. Definition of cholesteatoma

Cholesteatoma was first described by Cruveilheir in 1829 as "Pearly tumour" of the temporal bone. In 1839 it was misnomered by Muller as "Cholesteatoma" since it is not a tumour nor contains cholesterol as a constant finding. In 1959 Friedman defined it as "a cystic structure in the middle ear lined by keratinizing stratified squamous epithelium resting on fibrous stroma of variable thickness which may contain some elements of the original mucosal lining". In the same year 1959, Shambaugh described it as epidermal mass consisting of matrix or germinal layer attached to the bony wall of the attic or antrum from which masses of squamous epithelium are casted off.

McGuckin in 1961 used the term "keratosis" or destructive ear disease, referring to the arousal of cholesteatoma by keratotic invasion from outside the middle ear, i.e., skin of the deep part of the bony external meatus and epithelial layer of tympanic membrane.

The most accurate term was stated by Tumarkin in 1961 as "epidermosis". Gray in 1964 gave the simplest definition, :skin in

the wrong place: and the most descriptive definition was given by Abramson in 1978 as "epidermal inclusion cyst of the middle ear or mastoid, containing non-malignant accumulation of its keratinizing squamous epithelial lining characterized by progressive growth and ability to induce resorption of underlying bone."

I. 1. B. Classification of cholesteatoma

Etiopathologically, cholesteatoma is classified into:

1. Congenital cholesteatoma.
2. Primary and secondary acquired cholesteatoma.
3. Tertiary cholesteatoma.
4. Intrinsic and extrinsic cholesteatoma.

1. Congenital cholesteatoma:

Various theories were proposed for explanation of the origin of congenital cholesteatoma:

* Aimi in 1983 stated that congenital cholesteatoma is a pearly epidermal cyst behind normal tympanic membrane which occurs in the middle ear because of migration of the external auditory canal ectoderm during middle ear development. The main function of the tympanic ring is to define the annular plane for the external ectoderm. The tympanic ring acts as an inhibitory factor against growth of the ectoderm behind the annular plane. Congenital cholesteatoma appears to be the result of error of this function.
* Samna et al. in 1984 stated that congenital cholesteatoma results from embryonic inclusion of the squamous epithelium during development of the temporal bone.

2. Primary and secondary acquired cholesteatoma:

This develops as a result of various factors including inflammation, trauma, tubal insufficiency...etc.. Various theories of the pathogenesis of cholesteatoma can explain this type *(Palva, 1988)*. Primary acquired cholesteatoma is due to invagination of the tympanic membrane with superadded infection on top of the accumulated desquamated keratin *(Cole et al., 1985)*. Secondary acquired cholesteatoma is due to epithelial immigration through a tympanic membrane defect *(Palva et al., 1982 and Habermann, 1989)*.

3. Tertiary cholesteatoma:

Meyerhoff et al. (1986) stated that there is tertiary cholesteatoma which is acquired and exists behind a normally appearing tympanic membrane, this may result from a single chronic inflammatory event of the middle ear, or it may occur as a result of a penetrating or implosive injury to the tympanic membrane implanting squamous epithelium into the middle ear.

4. Intrinsic and extrinsic cholesteatoma:

Alaminos et al.(1988) classified cholesteatoma into intrinsic and extrinsic forms.Intrinsic when the cholesteatoma grows inside the middle ear space and afterwards grows into the external auditory meatus, or produces a tympanic membrane perforation, and extrinsic when the squamous epithelium grows from the external auditory meatus into the tympanic cavity through a perforation in the tympanic membrane.

I. 1. C. Peculiar forms of cholesteatoma presentation

A. External canal cholesteatoma:

It is an uncommon otologic entity, the most prominent findings are erosion of the inferior bony external ear canal and accumulation of keratin debris. Previously the condition was confused with keratosis obturans. The origin is not clear, but the most acceptable theories are:

i. Faulty migration of squamous epithelium.

ii. Circumscribed periostitis.

The condition should be differentiated from keratosis obturans, iatrogenic cholesteatoma, malignant otitis externa and benign and malignant neoplasms ***(Sismanis et al., 1985)***.

B. Cholesteatoma confined to the hypotympanum:

Oats et al. (1988) stated that cholesteatoma confined to the hypotympanum were recorded in 3 cases, and this finding was difficult to explain by current theories of the aetiology of cholesteatoma as there was satisfactory aeration of the posterior and attic regions in 2 of the reported cases contradicting the theory of negative middle ear pressure.

C. Tympanic membrane cholesteatoma (Keratoma):

Cholesteatoma involving the middle ear usually originates from either inward sacculation of the pars flacida, a retraction pocket in the posterosuperior part of the pars tensa or from the ingrowth of squamous epithelium via a marginal perforation. Occasionally there may be minimal ingrowth of the tympanic membrane. In central perforations of the tympanic membrane, the squamous and mucosal layers appose at the edge of the defect in the fibrous layer and the atrophic squamous epithelium becomes in contact with the inner mucosal layer at the mucocutaneous junction and within hours (approximately 48 hours) the squamous epithelium reaches several layers thick at the margin of the perforation, and this layer exhibits hyperkeratinization and migrates actively while the fibrous and mucosal layers heal more slowly ***(Graham et al., 1984)***.

Tympanic membrane cholesteatoma is characterized by the following:

i. The cholesteatoma originates from a central perforation in the pars tensa of the tympanic membrane.
ii. It appears to be confined to the undersurface of the pars tensa.
iii. There is neither encapsulation nor sacculation of the squamous epithelium.
iv. There is active desquamation of epithelial debris into the normal middle ear ***(Graham et al., 1984)***.

D. Temporal bone cholesteatoma:

This may arise from a middle ear cholesteatoma growing along petrous cell tracts around the bony labyrinth or from embryonic epithelial remnants, this latter type is what is named :primary cholesteatoma. This latter may develop from inclusion of misplaced epithelial cells, ectodermal cells of the neural groove between the 3rd and 5th weeks of embryonic life, or epithelial remnants trapped in the foramen lacerum during cephalic flexion of the head *(Characom, 1985)*.

I. 1. D. Pathogenesis of cholesteatoma

This subject has been debated for over a century, several theories have been proposed for explanation of the development of aural cholesteatoma. Generally speaking, theories have been divided to those explaining acquired cholesteatoma, and others explaining congenital cholesteatoma.

A. Theories of acquired cholesteatoma:

There are five basic theories of pathogenesis of acquired cholesteatoma;

i. Invagination of the tympanic membrane.
ii. Basal cell hyperplasia.
iii. Epithelial ingrowth through a perforated tympanic membrane.
iv. Metaplasia of middle ear epithelium.
v. Implantation theory.

I. Invagination theory: (Mechanical retraction pocket).

(Bezold 1891, Buckingham 1969, Austin 1977, Cody 1977 and Chole 1986).

Retraction of the tympanic membrane -whether the pars flaccida or pars tensa- is assumed to be towards middle ear cavity. According to this theory, middle ear cholesteatoma occurs due to