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Research Article

CHOLESTEATOMA- THE SILENT KILLER

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ABSTRACT

Objective-Cholesteatoma has been discussed in all International and National conferences periodically because it is an enigma. The treatment options keep on changing due to sustained recurrence even after perfect surgery. It is a silent killer and therefore is of utmost importance to diagnose and treat this condition early to reduce the mortality and morbidity.

Method-In this study we discuss in detail about the etiopathogenesis and various modalities of treatment of Cholesteatoma with reference to modern surgical management. This study has been done in our hospital for a cross section of patients attending the outpatient department during the period January 2012 to Sep 2013 with evidence of cholesteatoma. Various aspects of the disease including age, socio economic status, clinical presentation, Per Op findings and complications were also analysed.

Results-In this study of 30 patients with cholesteatoma all of them underwent surgery –Modified Radical Mastoidectomy with exenteration of all accessible diseased air cells. The disease was common in middle aged females of lower socio economic class. The incidence of complication due to disease was 30% [n=9]. The Post op follow up showed recurrence in only 20% [n=6].

Conclusion-Cholesteatoma is one of the entities in ear which requires immediate attention to prevent devastating complications. In the present era with the advent of higher antibiotics and advanced surgical methods the incidence of complications has drastically come down and the disease is also managed more effectively with least morbidity. This study aims to be a comprehensive one to throw light on the dimension of this disease and its management.

Keywords: Cholesteatoma, Mastoidectomy, Intracranial complications, Squamous epithelium, Endoscope.

INTRODUCTION

The term cholestatoma is a misnomer as it does not contain cholesterol crystals and is not a tumor. Until 1838, as Müller coined the term cholesteatoma, nothing new appeared in medical publications[1].Toynbee first mentioned the similarity between the squamae of what he called "Molluscoum Contagiosum" and the stratum corneum in 1850, not yet knowing how to explain the presence of epidermis in the middle ear [2].Normally middle ear cleft is lined by ciliated columnar epithelium in the anterior and inferior part ,cuboidal epithelium in middle and pavement in attic. Middle ear cleft is nowhere lined by stratified squamous epithelium and the presence of this epithelium is coined as the term cholesteatoma-"SKIN IN THE WRONG PLACE". The genesis of cholesteatoma is a matter of debate. Any theory regarding this should explain the reason for the presence of squamous epithelium in the middle ear . Cholesteatomas are classified as congenital or acquired; acquired cholesteatomas are subdivided into primary (attic retraction) or secondary [3].Cholesteatoma has a keratinized stratified squamous epithelium named cholesteatoma matrix. It also presents as a connective tissue, containing collagen fibers, fibrocytes and inflammatory cells, named perimatrix which in most of the cases is in contact with squamous or ciliated cylindrical cells, and remains from the original middle ear mucosa. Some authors [4] describe the perimatrix as the most peripheral portion of the cholesteatoma, comprising granulation tissue or inflammatory subepithelial connective tissue, with lymphocytes, histiocytes and neutrophils. The perimatrix appears as an inflammatory network that involves the cholesteatoma. Sprekelsen BM et al. [5] stated that the matrix and perimatrix, in normal or pathological tissues, are formed by type IV collagen, tenascin, fibronectin, and metalloproteinase (MMP).

DISCUSSION

A basic knowledge of the anatomy of the middle ear provides the basis for understanding the disease progression and concepts of surgical management. Attic is the portion that lies above the level of short process of malleus containing head of malleus, body of incus with ligaments and mucosal folds. It is situated in the notch of Rivinus and lacks middle fibrous layer. The mucosal folds compartmentalise the attic with isthmus tympanic anticus and isthmus tympanic posticus. Anterior isthmus is longer, lies medial to body of incus and passes between medial incudal fold and posterior tympanic wall. These are the only two channels that communicate with mesotympanum. They will resist the spread of epitympanic cholesteatoma to mesotympanum and also these are important to aeration of mastoid. Aditus like a corridor connects attic to mastoid antrum, which forms passage for cholesteatoma. Handle of malleus and long process of incus are two passages through which cholesteatoma descend. Prussac's space or upper tympanic space is bounded laterally by Shrapnell's membrane, medially by neck of malleus, inferiorly by lateral malleolar fold attached to notch of Rivinus, anteriorly and posteriorly by anterior and posterior malleolar fold. Prussac's space and anterior epitympanic recess are two sites where cholesteatoma hides. Epitympanic cholesteatomas start in Prussack's space. Cholesteatomas from Prussack's space spread via the posterior epitympanum, posterior mesotympanum and anterior epitympanum, in that order. The most common is the posterior epitympanic route where the cholesteatoma spreads to the superior incudal space lateral to the body of the incus potentially gaining access to the mastoid through the aditus ad antrum. The second most common is the inferior route, through the posterior pouch of von Troeltsch . This route allows cholesteatoma to gain access to the regions of the stapes, round window, sinus tympani and facial recess. Anterior epitympanic cholesteatomas form anterior to the malleus head. Facial nerve dysfunction may occur with these lesions, which can also gain access to the supratubal recess of the middle ear via the anterior pouch of von Troeltsch. Sinus tympani is a cleft like space connecting lower part of oval window and upper part of round window behind promontory medial to the facial recess, bounded medially by bony labyrinth and facial nerve, laterally by pyramidal eminence, superiorly by lateral semicircular canal. Facial recess is a triangular space, lateral to sinus tympani bounded above by lateral semicircular canal and fossa incudi with short process of incus, medially by vertical part of facial nerve, laterally by chorda tympani nerve. Both are hidden areas of cholesteatoma.

Cholesteatoma is considered dangerous as it spreads or invades adjacent structures by several ways. Cholesteatoma also has late presentation due to its scanty discharge. The patient does not appreciate it at an early stage until it becomes foul smelling or blood stained. It is also one of the reasons for complications as the patient is unaware of the disease. The growth of cholesteatoma may depend on the angiogenesis in the perimatrix connective tissue. Angiogenesis enables and supports the sustained migration of keratinocytes into the middle ear cavity [6].The most important mode of spread is by bony erosion. The enzymatic activity at the margin of the cholesteatoma enhances osteoclastic activity, which greatly increases the speed of bone erosion. These osteolytic enzymes appear to increase when a cholesteatoma becomes infected[7] . The presence of bacteria may provide a critical link between the cholesteatoma and the host, which prevents the cholesteatoma epithelium from continuing specific differentiation programs and returning to a quiescent state in which it becomes minimally proliferative, non-migratory, and noninvasive [8]. Cholesteatoma can also spread by progressive thrombophlebitis through Haversian venous channels near the infected site such as lateral sinus through normal anatomical pathway- oval window, round window, into the internal auditory meatus, cochlear aqueduct, vestibular aqueduct, dehiscence of tegmen tympani and dehiscent suture line of temporal bone, through fracture line caused by accidental trauma and surgical trauma, through surgical defects caused by stapedectomy and fenestration operation and through surgical defects along periarteriolar spaces of Virchow-Robin. Cholesteatoma is considered a silent killer as it can cause intra temporal and intracranial complications. These include meningitis, extradural abscess, temporal lobe abscess, cerebellar abscess, facial nerve palsy, petrositis, labyrinthitis, sensorineural loss. Bone erosion and secondary infection from cholesteatoma can lead to both intratemporal (facial paralysis, infective cochleolabyrinthitis, etc.) and intracranial complications (meningitis, brain abscess, sigmoid sinusthrombophlebitis, etc.) in both congenital and acquired forms of the disease.[9]

There are other forms of cholesteatoma like congenital, iatrogenic, petrous apex, external auditory canal and antral cholesteatomas. Congenital cholesteatoma is an inclusion epidermoid. The lesion is at a histological transition zone in anterosuperior quadrant of tympanic membrane (T.M) due to non absorption of embryogenic cell nest in dorsolateral epitympanum of human foetus (Teed 1936). Criteria for diagnosis includes: White mass medial to intact TM, normal pars tensa and pars flaccid, no prior history of otorrhoea or perforation or otological procedure. Bilateral congenital cholesteatoma is a rare condition but has been reported [10] Iatrogenic cholesteatomas are surgically made cholesteatoma that occurs following myringotomy done with dull knife or bent knife causing imposition and shedding of drum, pushing grommet through a ragged opening forcing the edges to turn inwards, tympanoplasty graft used to repair TM placed adversely over unrecognised area of squamous epithelium that have remained on the surface of tympanic membrane. Petrous apex cholesteatoma also called as virgin cholesteatoma involves petrous associated with chronic suppurative otitis media (C.S.O.M) or chronic apex petrositis. It may arise and expand within petrous apex of temporal bone itself or having started in middle ear or mastoid or external auditory canal later invading apex. External auditory canal cholesteatoma - it arises external to TM and is associated with atresia of external canal or incomplete canalisation of the ear. Antral cholesteatoma- arises as a complication of chronic mastoiditis that breaks through the tip cells into soft tissues. Recidivism encompasses all residual and recurrent cholesteatoma. Residual cholesteatoma is a disease that grows back from viable squamous epithelium over vital structures like dehiscent facial canal and foot plate that was not removed at the initial surgical procedure due to fear of damage to the same. Recurrent cholesteatoma is a disease that grows back because of inadequate surgical removal. Inability of eustachian tube to adequately aerate the middle ear cleft results in retraction of eardrum with keratin accumulation and bone absorption.

Conservative management is only indicated when small cholesteatoma sac is confined to the attic with normal hearing. It is removed by suction clearance under microscope. Life long periodical inspection is essential. SURGERY IS THE LINE OF MANAGEMENT FOR CHOLESTEATOMA. The objective of the surgical procedure is for complete removal of the disease process while preserving any useful and healthy tissue to obtain a long standing and safe ear, to retain or improve hearing with reconstruction of tympanic membrane and ossicles and ventilation of middle ear cavity. Attico-antrostomy is a procedure where without disturbing the intact TM (except for attic perforation) and ossicles, the superior osseous meatal wall and part of posterior osseous meatal wall are taken down thus exteriorizing attic and antral cholesteatoma into open. This generally denotes removal of the bone from within outwards. When restricted to the epitympanum, good results in hearing following surgery (atticoantrostomy) are often possible especially if the cholesteatoma is diagnosed and treated early [11,12].Failure and recurrence of cholesteatoma is due to inadequate surgery and incomplete exenteration, failure in lowering down of canal wall to vertical part of facial nerve and mastoid cavity, postoperative meatal stenosis and air cell posterior to epitympanum which are blocked off and unventilated becoming source of infection and failure. ENDOSCOPIC APPROACH is a recent approach to visualise the hidden areas of middle ear like sinus tympani. Previously these areas were viewed with angled mirrors. Now it is possible to visualise clearly and clean these areas completely using angled endoscope thereby avoiding a post tympanotomy and canal wall procedures. Endoscopes not only reduces the width of exposure but also helps in good documentation and proper post operative follow up.

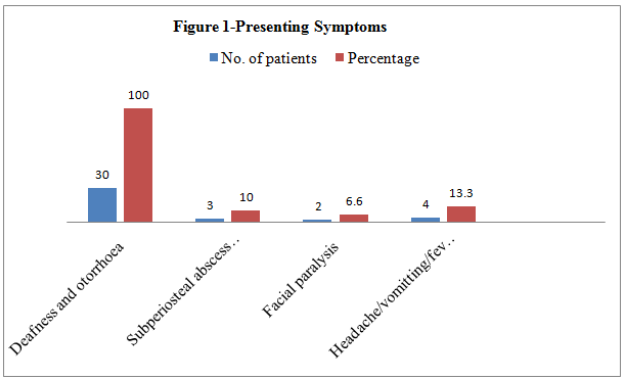
MATERIALS AND METHODS

The present study consists of a series of 30 patients who presented with complaints of ear discharge with evidence of cholesteatoma at Sree Balaji Medical College and Hospital, Chennai during the period of Jan 2012- September 2013.A detailed history of each patient was recorded. Clinical examination in detail was also noted in proforma. Accurate otological examination after proper aural toiletting was done. A detailed examination under magnification with a microscope or Siegel's speculum was done in certain selected cases. Tuning fork tests were carried out using tuning fork of 512Hz and 1024 Hz. In every case a complete haemogram, urine examination and Xray of mastoids were done. All these cases were subjected to audiometry preoperatively. An ear swab was taken in each case and sent for culture and sensitivity. In some cases, CT scan was done to study the extent of disease and to plan the surgery. All the patients underwent surgery under General Anaesthesia. An informed and written consent in patient's vernacular language was taken explaining the further implications of cholesteatoma and its sequelae and also the outcomes of different surgical procedures used in each case depending on its clinical presentation. 26 (n=26, 86.7%) patients underwent Modified Radical Mastoidectomy and 2 (n=2, 6.7%) patients Atticoantrostomy. The mode of surgery was decided depending on the extent of the disease, which was assessed pre operatively, and the complications. The hidden areas were visualized with angled endoscopes and the disease was cleared. Post operatively, patients were put on broad spectrum antibiotics, anti inflammatory and anti histamines. External canal packs and sutures were removed on the 7th post op day. Patients were regularly followed every week for 6 weeks.

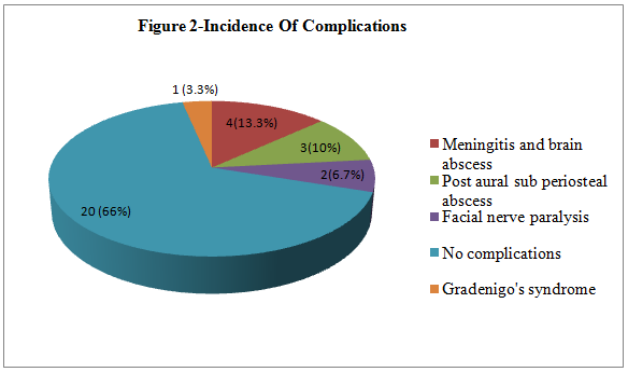
RESULTS AND OBSERVATION

Almost all the patients had purulent, scanty malodorous foul smelling and persistent ear discharge with hard of hearing of varying duration. 4 patients (n=4,13.3%) presented with fever, headache, mastoid tenderness and swelling behind the ear. 14 patients (n=14,46%) presented with attic perforation surrounded by white debris which is nothing but cholesteatoma. 4 patients (n=4,13.3%) presented with posterosuperior marginal and attic granulation,(n=8,26.8%) 8 patients presented with granulation at attic region with cholesteatoma. Such type of granulation is an important sign suggesting deep seated disease with mucosal changes and necrosis of bone and possibly the presence of cholesteatoma.4 patients (n=4, 13.3%) presented with polyp in the external auditory canal. 23 patients (n=23, 76.7%) had conductive deafness, 4 patients (n=4,13.3%) had mixed deafness and 3 patients

(n=3,10%) had dead ear. The commonest age group was between 11-30 years. The youngest was 5 years and the oldest was 40 years. Intra cranial complications are common in younger age group. Males were commonly affected (n=7, 66%) than females (n=3, 33%). The left ear was more commonly affected (n=13, 43%) than the right ear (n=12, 40%). Both ears were involved in 17% (n=5) of cases and single ear was involved in 83% (n=25) of cases.



Otorrhoea and deafness were the main presentation in all the cases followed by subperiosteal abscess (n=3, 10%), facial nerve palsy (n=2, 6.6%) and headache, vomiting, fever and ear pain (n=4, 13.3%) (Figure 1).Of the 30 patients, 9 (n=9, 30%) were having complications. 4 (n=4,13.3%) patients were having intracranial complications. Sub periosteal abscess was the commonest extracranial complication (n=3, 10%) followed by facial nerve palsy in 2 cases (n=2,6.7%) (Figure 2) .One of the patient presented with Gradenigo's Syndrome (Retro orbital pain, ear discharge, diplopia) (Figure 3) with evidence of petrositis in CT scan. (Figure 4)



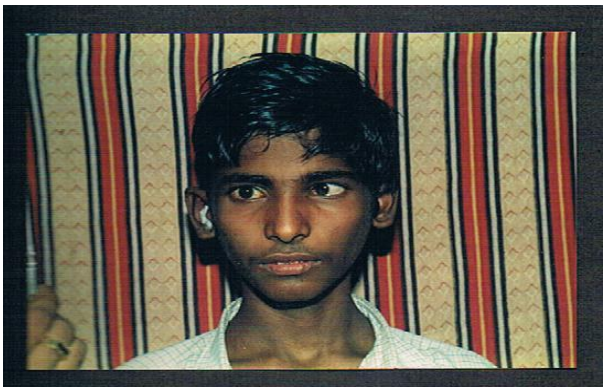


Figure 3: Gradenigo's Syndrome with Right Lateral Rectus Palsy.

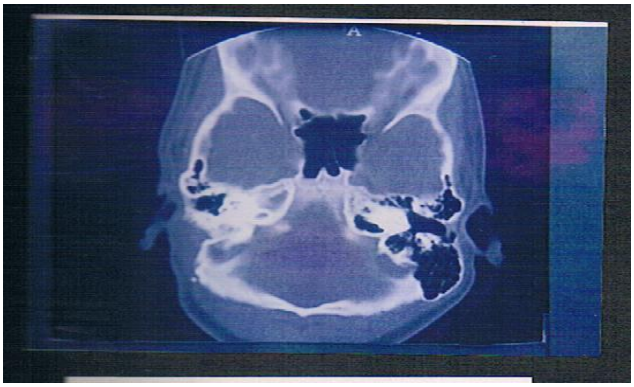


Figure 4: CT Scan showing Right Petrositis.

The common type of hearing loss is conductive hearing loss (n=23, 76.7%), 4 patients had mixed loss (n=4, 13.3%) and 3 had dead ear (n=3, 10%). Attic perforation with cholesteatoma was the commonest ear finding in 14 cases (n=14, 46.8%), followed by attic granulations in 8 cases (n=8, 26.6%). All patients were given aural toileting and the discharge was sent for culture and sensitivity as antibiotic resistance is a major problem post operatively. In a study 87% of the K. pneumoniae isolates showed resistance to all the three third generation cephalosporin antibiotics and this resistance to all the three was found to coexist with resistance to other antibiotics[13]. Another study done in Doha Qatar, showed that all gram negative bacilli were sensitive to Amikacin and resistance of Gram Negative Bacilli to Gentamicin was 20%.[14].In our study the commonest organisms frequently found in cultures was Proteus, Pseudomonas and Staphylococci and all were susceptible to Cephalosporins ,Aminoglycosides . The commonest

X- Ray mastoids finding were sclerosed in 24 patients (n= 24, 80%) followed by cavity in the antrum was seen in 6 patients (n= 6, 20%). 1 case showed cavity in the sinodural angle. (Figure5)

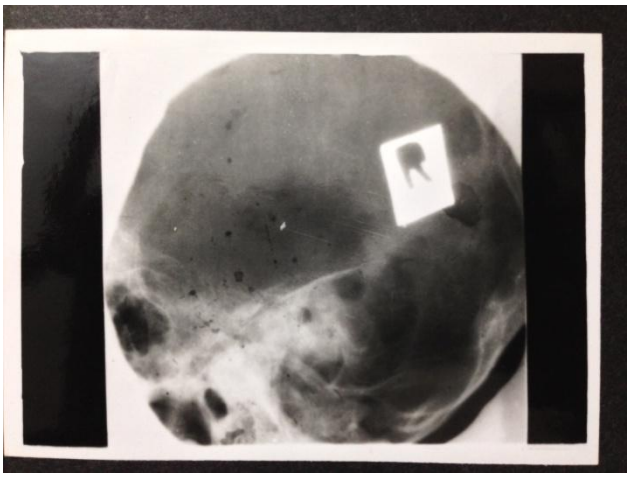


Figure5: X Ray Mastoid Showing Cavity in Sinodural Angle.

All the 30 patients had cholesteatoma as a Per operative finding. 14 patients had granulation (n=14, 46.8%), 3 had cortical erosion (n=3, 10%), 1 had posterior canal wall erosion (n=1,3.3%), 1 had perisinus abscess (n=1, 3.3%). Tegmen erosion was seen in all 4 cases who presented with intra cranial complications (n=4, 13.3%)(Figure 6). Out of 4 patients with intracranial complication 1 had cerebellar abscess (Figure-7).

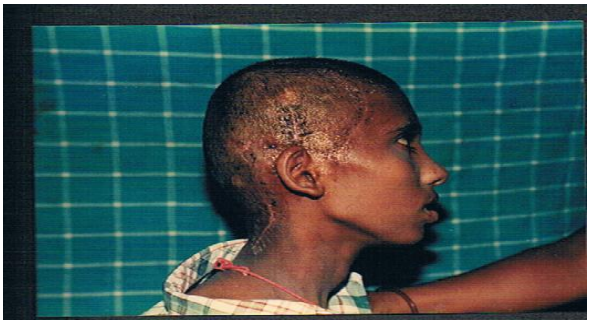
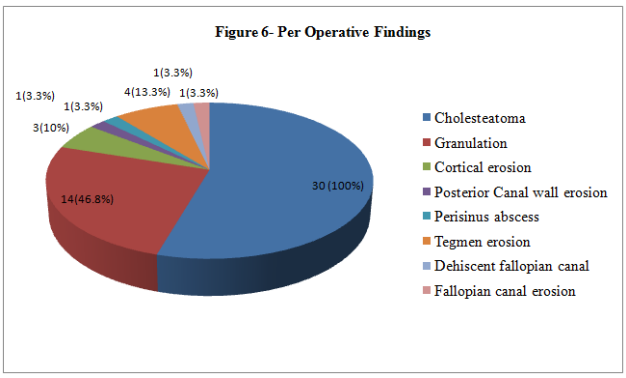


Figure 7:Post Op Picture of Patient with Cerebellar Abscess Drained

Out of the 2 patients who presented with facial palsy 1 had dehiscent Fallopian Canal with cholesteatoma causing pressure on the horizontal part of the facial nerve and another had erosion of the Fallopian canal at the level of second genu.

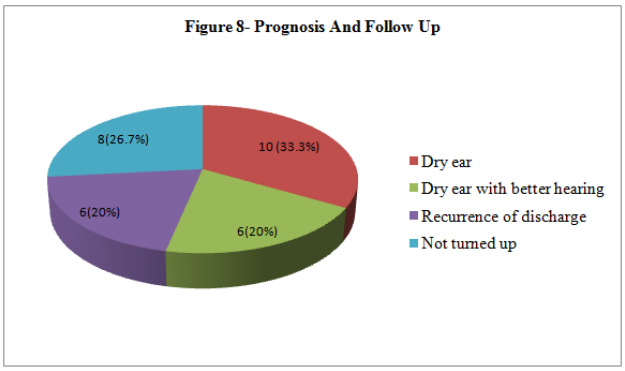


Most of the patients had undergone a Modified Radical Mastoidectomy (n=26, 86.7%) out of which 3 underwent the inside out type (n=3,11.5%). 2 patients had undergone Atticoantrostomy (n=2,6.7%) followed by 1 patient undergoing Marginectomy (n=1,3.3%) and 1 patient undergoing Radical Mastoidectomy with obliteration of cavity (n=1, 3.3%) (Table 1). Complications were dealt with simultaneously depending on the extent of the disease.

Table 1- Surgical Procedure

Procedure	No.of patients	Percentage
Radical mastoidectomy with obliteration	1	3.3
Marginectomy	1	3.3
C.A.T	2	6.7
M.R.M	26	86.7
Inside out	3	11.5
Total	30	100

25 patients had no post operative complications (n=25, 83.5%), 2 presented with gaping of the postaural wound (n=2, 6.6%) followed by another 2 presenting with meatal stenosis (n=2,6.6%) and 1 patient developed facial nerve paresis (n=1,3.3%). Secondary suturing was done in both the cases of wound gaping. Facial nerve weakness recovered over a period of 1 month with physiotherapy, electrical stimulation and steroids. On following up the post operative patients it was observed that 10 patients developed dry ear (n=10, 33.3%) followed by 6 patients having dry ear with better hearing (n=6, 20%). 6 patients however presented with recurrence of discharge (n=6, 20%). 8 patients (n=8, 26.7%) did not turn up for follow up. (Figure 8)



CONCLUSION

Chronic suppurative otitis media with cholesteatoma is an alarming finding for many ENT surgeons in view of the late presentation, higher incidence of complications and more recurrence inspite of good surgical clearance. But nowadays with newer surgical modalities and advanced technologies we are able to give a better outcome for the patient with less morbidity. The angled endoscopes help in visualizing hidden areas very precisely and clear all diseased air cells upto petrous apex. Further newer methods are being tried out everyday like lining the cavity with graft and reconstructing the posterior canal wall preventing cavity problems.

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REFERENCES

1. Soldati D., Mudry A., Knowledge about cholesteatoma, from the first description to the modern histopathology,OtolNeurotol, 2001, 22(6):723–730.
2. Toynbee J., Sebaceous tumors in the external auditory meatus. In: Pathological researches into the diseases of the ear, Churchill Livingstone, London, 1855
3. Jackler R. K., The surgical anatomy of cholesteatoma, OtolaryngolClin North Am, 1989, 22(5):883–896
4. Ferlito O., Devaney K. O., Rinaldo A. et al., Clinicopathological consultation ear cholesteatoma versus cholesterol granuloma, Ann OtolRhinolLaryngol, 1997, 106:79–85.
5. Sprekelsen B. M., Ebmeyer J., Anonopoulos A., Sudhoff H., Alteracionesdelamembrana basal en el colesteatoma de oídomedio, ActaOtorEsp, 2001, 52:330–335
6. Sudhoff H., Dazert S., Gonzales A. M. et al., Angiogenesis and angiogenic growth factors in middle ear cholesteatoma, Am J Otol, 2000, 21:793–798.
7. Stenfors L. E., Does occurrence of keratinizing stratified squamous epithelium in the middle-ear cavity always indicate a cholesteatoma?, J LaryngolOtol, 2004, 118:757–763
8. Albino A. P., Kimmelman C. P., Parisier S. C., Cholesteatoma: a molecular and cellular puzzle, Am J Otol, 1998, 19(1):7–19.
9. M. M. Zarandy and J. Rutka, *Diseases of the Inner Ear* 9DOI: 10.1007/978-3-642-05058-9_2, Springer-Verlag Berlin Heidelberg 2010.
10. Kuczkowski J, Babinski D, Stodulski D (2004) Congenital and acquired cholesteatoma middle ear in children [Polish]. Otolaryngol Pol 58(5):957–964
11. Okano T, Iwanaga M, Yonamine Y, Minoyama M, Kakinoki Y, Tahara C, Tanabe M (2004) Clinical study of congenital

cholesteatoma of the middle ear [Japanese]. Nippon JibiinkokGakkaiKaiho 107(11):998–1003.

12. Faramarzi A, Motasaddi-Zarandy M, Khorsandi MT (2008) Intraoperative finding in revision chronic otitis media surgery. Arch Iran Med 11(2):196–199
13. Panta K, Ghimire P, Rai SK, Mukhiya RK, Singh RN, Rai G. Antibiogram typing of gram negative isolates in different clinical samples of a tertiary hospital. Asian J Pharm Clin Res. [2013] 6 [1]:153-156
14. Ahmed A, Lutfi S, Hail M, Sadia M. Antibiotic susceptibility patterns of microbial isolates from blood culture in the neonatal intensive care unit of hamad medical corporation (hmc), Doha, Qatar. Asian J Pharm Clin Res. [2013] 6 [2]: 191-195