Cholesteatoma

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6.1 Introduction

Cholesteatoma is an abnormal growth of the keratinizing squamous epithelium in the middle ear. It could be congenital or acquired. Cholesteatoma is a destructive and expanding lesion that may lead to fatal complications if left untreated.

6.2 Epidemiology

Its annual incidence is 9.2/100,000 in adults and 0.3/100,000 in children with male predominance [1].

It is higher in Caucasian and rare in African. It peaks in the second and third decades [2]. The mean age for congenital cholesteatoma is 6 years.

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6.3 Types of Cholesteatoma

6.3.1 Congenital Cholesteatoma

It is more common in males (3:1). Its location is more common in the superior anterior part of the middle ear facing the Eustachian tube opening (2/3 of the cases). The second most common is the superior posterior part near the incudostapedial joint (Fig. 6.1).

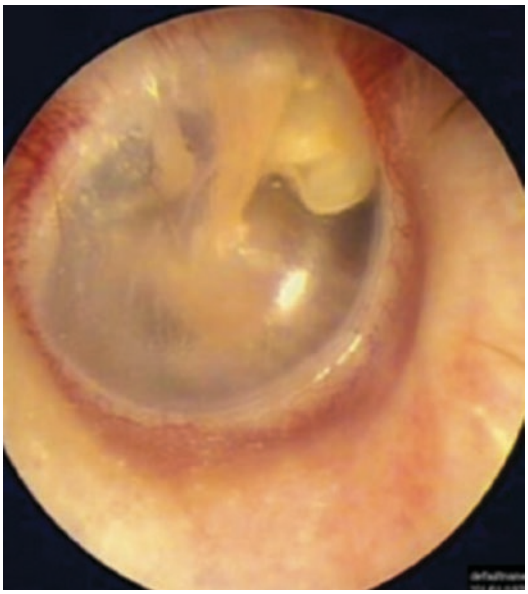

Fig. 6.1 Small congenital cholesteatoma in the anterosuperior quadrant of a right ear. (Adapted from Mansour S., Magnan J., Nicolas K., and Haider H. (2018). Middle ear disease)

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Levenson criteria for the diagnosis of congenital cholesteatoma are as follows:

(a) White mass behind an intact tympanic membrane (TM).
(b) No prior history of otorrhea.
(c) No prior history of TM perforation.
(d) No prior history of otologic procedures. Prior history of otitis media does not rule out congenital cholesteatoma.

6.3.2 Acquired Cholesteatoma

Acquired cholesteatoma has two types:

- ***Primary acquired*:** It is the most frequent type and arises from the progression of tympanic membrane retraction pocket. It can be a retraction from the pars flaccida (more common in adults), from pars tensa (more common in children), or combined (Figs. 6.2 and 6.3).
- ***Secondary acquired*:** It arises from the migration of epithelial membrane through a marginal perforation of the TM, or due to trapped skin through micro-perforation secondary to trauma or surgery.

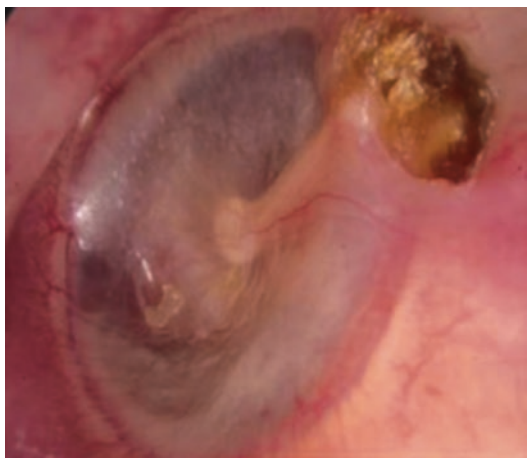

Fig. 6.2 Left attical cholesteatoma. (Adapted from Mansour S., Magnan J., Nicolas K., and Haider H. (2018). Middle ear disease)

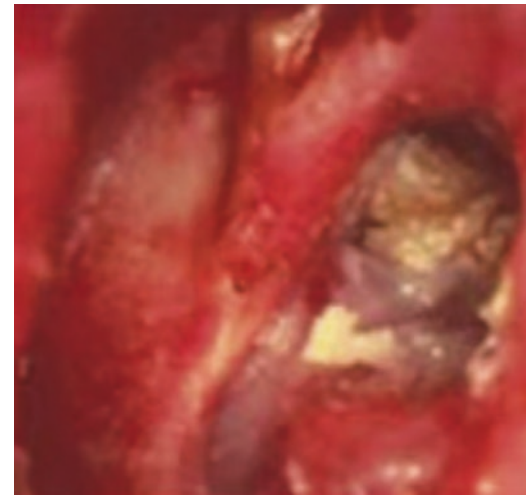

Fig. 6.3 Left ear mesotympanic and retrotympanic cholesteatoma. (Adapted from Mansour S., Magnan J., Nicolas K., and Haider H. (2018). Middle ear disease)

6.4 Histopathology of Cholesteatoma

Light microscopy shows a cyst with three components:

1. Amorphous center composed of squamous keratin debris.
2. Matrix, a stimulated proliferative skin (Keratinizing squamous epithelium).
3. Perimatrix which is granulation tissues and inflammatory cells. It is the site of the inflammatory process.

6.5 Pathogenesis of Cholesteatoma

6.5.1 Theories for Congenital Cholesteatoma

1. Epidermal rest theory: cell rests of non-keratinizing squamous epithelium localized near Eustachian tube ostium, having the potential to become a cholesteatoma.

2. Inclusion theory: migration of cells originatimg from the external auditory canal skin to the middle ear secondary to non-evident injury to the TM [3].

6.5.2 Theories for Acquired Cholesteatoma

1. Invagination theory: the precursors of cholesteatoma are retraction pockets secondary to dysventilation syndrome of the middle ear compartments. Two histological features present in cholesteatoma but not found in retraction pockets: **epithelial hyperplasia and skin migration**.
2. Migration theory: squamous epithelium of the TM or the ear canal skin migrates through the perforated eardrum into the middle ear.
3. Squamous metaplasia theory: this theory stipulated that under chronic inflammation, middle ear mucosa changes into a squamous epithelium. But this theory lacks histological or experimental proof, so such a hypothesis is not accepted anymore.
4. Basal cell hyperplasia (Papillary) theory: a keratin-filled microcysts or buds arise from the basal layer of flaccida epithelium that invade the subepithelial tissue and fuse together to form a cholesteatoma [4].

Recent advances in the pathogenesis of cholesteatoma postulate that the cholesteatoma is a result of the defective healing process, in which the normal maturation end-stage of the wound-healing process will not be achieved (non-stop wound healing process). Moreover, the pathogenesis of this condition does not rely only on the middle ear pathological conditions but also on the immunological status of the bottom of the skin ear canal [5].

6.6 Molecular Biology of Cholesteatoma

1. Histochemical studies found quantitative and qualitative modifications of ***Langerhans' cells***; these cells emit long dendritic expansions, which create a true network between the neighboring cells: keratinocytes and lymphocytes. This close contact between these cells is essential for the immune reaction production [6].
2. There are *paracrine and autocrine interactions* between keratinocytes of the matrix and fibroblasts of the perimatrix that regulate homeostasis and tissue regeneration within a cholesteatoma [4].
3. The fundamental difference between the healing process in a normal skin and in cholesteatoma is that in cholesteatoma, there is a loss of the growth inhibition by "cell to cell contact". Two factors are involved in that:

   (a) The cholesteatoma develops beyond its normal anatomical site for a "skin".
   (b) The inflammatory process produces a self-maintained immunological cycle, which enhances the epithelial growth.

4. The loss of balance between apoptotic and antiapoptotic markers, the increased antiapoptotic activity in cholesteatoma favors its continuing expansion [6, 7].
5. The presence of antibiotic-resistant bacterial Biofilms in cholesteatomas may also explain their aggressiveness [8].

6.7 Cholesteatoma Origin and Growth Pathways [6]

Posterior epitympanic cholesteatoma: It is the most common pattern of spread for cholesteatoma originating from Prussak's space. The cholesteatoma spreads into the superior incudal space lateral to the body of the incus, and from there, it can potentially enter the mastoid through the aditus ad antrum (Fig. 6.4).

Mesotympanic cholesteatoma: the second most common type is mesotympanic cholesteatoma which spreads through the *posterior pouch of von Troeltsch*, following the embryological course of both saccus posticus and saccus superior. It grows medially along the lenticular process and stapes superstructure. Then it may grow upward through the posterior tympanic isthmus

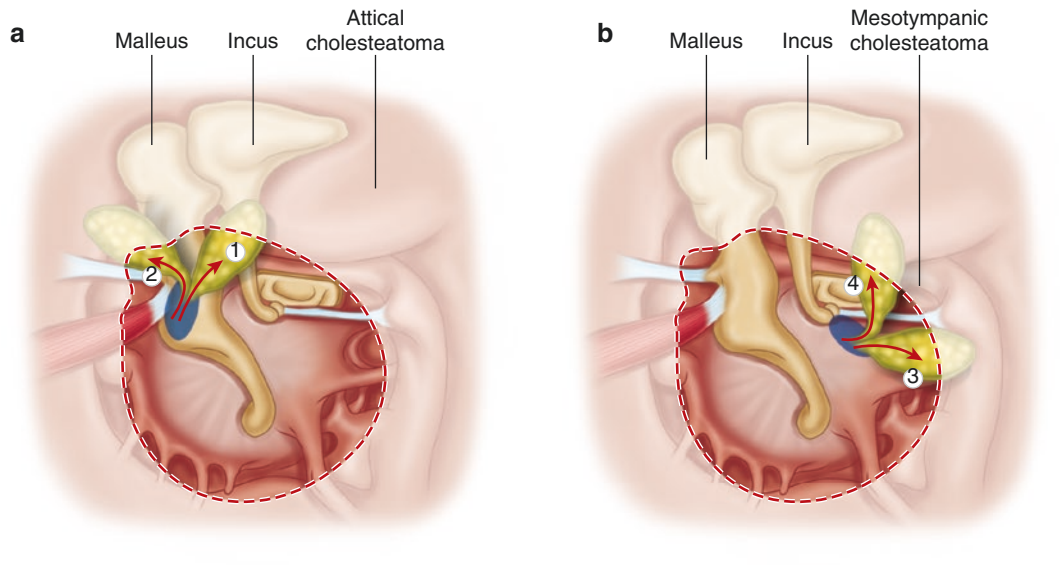

Fig. 6.4 Cholesteatoma origin and spread. (**a**) An attical cholesteatoma usually spreads posteriorly (1) as posterior attical cholesteatoma and rarely anteriorly as anterior attical cholesteatoma (2) and (**b**) mesotympanic cholesteatoma growth pattern into the facial recess and sinus tympani (retrotympanum). (Adapted from Mansour S., Magnan J., Nicolas K., and Haider H. (2018). Middle ear disease)

toward the posterior epitympanum to the mastoid antrum or backward into the sinus tympani (Fig. 6.4).

Anterior epitympanic cholesteatoma: it spreads through the superior malleal fold following the embryologic saccus anticus to enter the epitympanic recess (AER). It may remain there for a time where the geniculate ganglion will be at risk, or progress into the supratubal recess and the protympanum (Fig. 6.4).

Unclassified cholesteatoma: this pattern occurs when cholesteatomas grow beyond multiple middle ear compartments, or when arise from both pars flaccida and pars tensa retraction pockets (PFRP&PTRP).

6.8 Clinical Manifestations

6.8.1 Symptoms

1. Otorrhea: it is a chronic scanty painless foul-smelling discharge.
2. Hearing loss: ossicular erosion is the most common finding (70%), causing conductive hearing loss (CHL) [9]. However, patients may have normal hearing due to the conductive mass effect of cholesteatoma itself.
3. Vertigo: due to the bony erosion of the semicircular canal. Fistula test or Valsalva may reveal the labyrinthine insult. (Tullio phenomenon is dizziness upon exposure to sound, which can happen in conditions like superior canal dehiscence, perilymphatic fistula, and Meniere's disease.)
4. Facial palsy: it may be the first clinical manifestation especially for cholesteatoma in the anterior epitympanic recess (AER).

6.8.2 Otomicroscopy

Otomicroscopy might show marginal TM perforation, erosion of the scutum and/or the ossicles, a retraction pocket, granulation tissue, or a polyp. Caution should be taken if removal of the

polyp is decided as it might be attached to the facial nerve or the ossicles.

6.8.3 Audiological Testing

Audiogram usually shows CHL. Speech reception thresholds are normal. Patients may have sensorineural hearing loss, which indicates a labyrinth insult.

6.9 CT Imaging in Cholesteatoma

Cholesteatoma does not have a specific density on CT, because it can demonstrate the same soft-tissue appearance as inflammatory processes, granulation or fibrous tissues, mucosal edema, or even fluid.

CT can show the following:

1. A rounded soft-tissue mass, which is a cardinal sign in the early stages.
2. Erosion of the **scutum**, which is suggestive of pars flaccida cholesteatoma (Fig. 6.5).
3. Erosion of the ossicles: The incus is the most vulnerable of the ossicles. Malleus head and stapes may be lytic in relation to the disease extension and are more suspicious of the cholesteatoma process.
4. Erosion of the **COG** is a sign of an invading cholesteatoma of the AER (Fig. 6.6). The Cog is always preserved in non-cholesteatomatous inflammatory processes. Invasion of the AER with a lysis of the Cog is important to look for, because of the silent progress of the cholesteatoma could make a facial palsy its first clinical sign.
5. Erosion of the **semicircular canals** (labyrinthine Fistula) (Fig. 6.7).
6. Erosion of the **fallopian canal**: integrity of the VII canal is not always easy to confirm by CT. CT can alert the surgeon about abnormal trajectory of the VII (Fig. 6.8).
7. Erosion of the **tegmen** (Fig. 6.8).
8. Extension of cholesteatoma into the mastoid: CT can be strongly indicate an extension of cholesteatoma to the mastoid when filled with condensations with irregular borders, or when the antrum is entirely filled with condensations that have smooth rounded borders (Fig. 6.7).
9. Posterior wall of the external auditory canal lysis: it has an impact on surgical option selection.

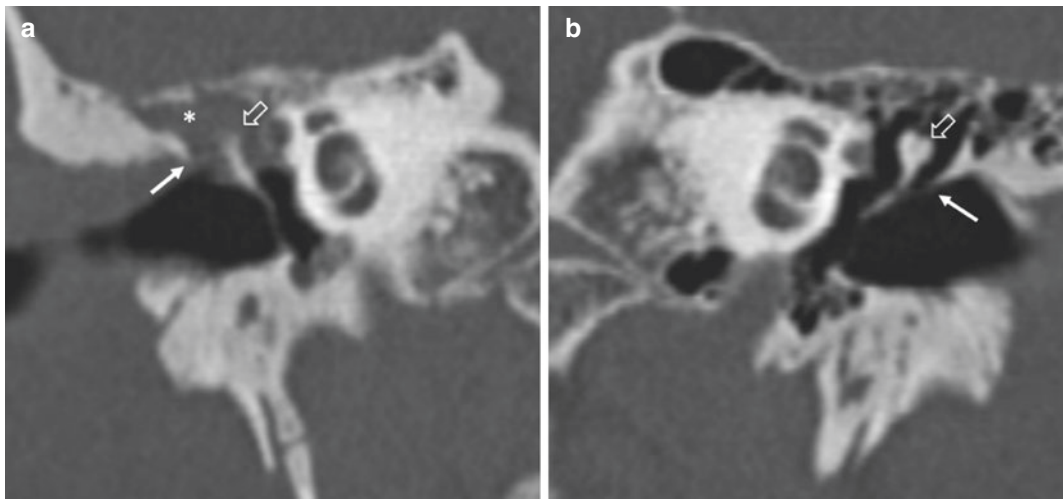

Fig. 6.5 Coronal reformatted CT images: (**a**) Right ear with amputation of the scutum (arrow), Prussak's space cholesteatoma extended to the attic (asterisk), lyses of the malleus head (empty arrow). (**b**) Left normal ear with triangular-shaped scutum (arrow), normal aspect of the malleus head (empty arrow)

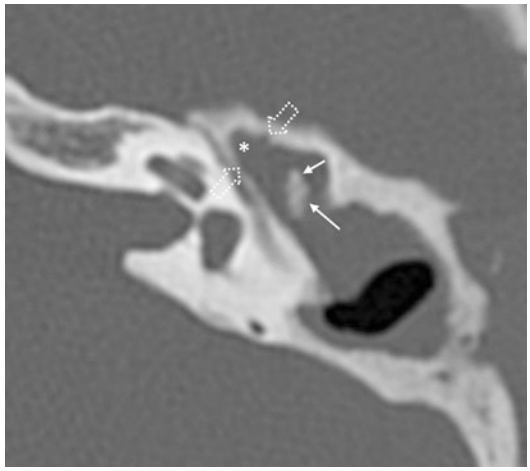

Fig. 6.6 Large atticoantral cholesteatoma also invading the anterior epitympanic recess (asterisk), complete absence of the cog (should be seen between the empty arrows). Lytic ossicular chain: short arrow—lytic malleus head, long arrow—lytic incus

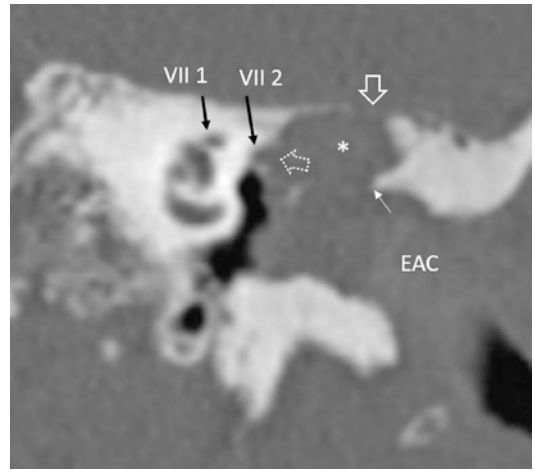

Fig. 6.8 Left coronal CT image, showing a huge cholesteatoma in the attic (asterisk), with lyses of the tegmen (empty arrow), lyses of the facial nerve canal (tympanic portion, dotted empty arrow), and lyses of the scutum (thin arrow). *EAC* external auditory canal

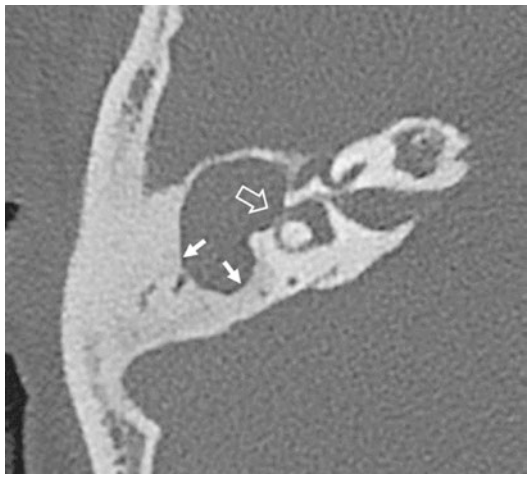

Fig. 6.7 Right side cholesteatoma with labyrinthine fistula secondary to erosion of the anterior limb of the lateral semicircular canal (empty arrow). See also smooth borders of the antrum (arrows) in favor of cholesteatoma

6.10 MRI in Cholesteatoma

MRI permits an almost specific diagnosis of cholesteatoma in the middle ear cleft with diffusion-weighted imaging, especially non-EPI-DWI (see Fig. 6.9), with differentiation from other soft tissues (Table 6.1). It is generally not indicated for the primary diagnosis of cholesteatoma, but rather used in the follow-up with patients postoperatively before second-look indication. In addition, MRI can be considered as a complementary imaging tool when the clinical presentation or CT films suspect complications (see below).

6.11 Management of Cholesteatoma

There is no medical management yet available for cholesteatoma. Surgery of cholesteatoma implies the following:

1. Total eradication of cholesteatoma to obtain a dry and safe ear.
2. Maintain the best condition for wound healing and preserve normal anatomy of the ear.
3. Maintain the best functional status of hearing.

The surgical procedures can be divided into major groups

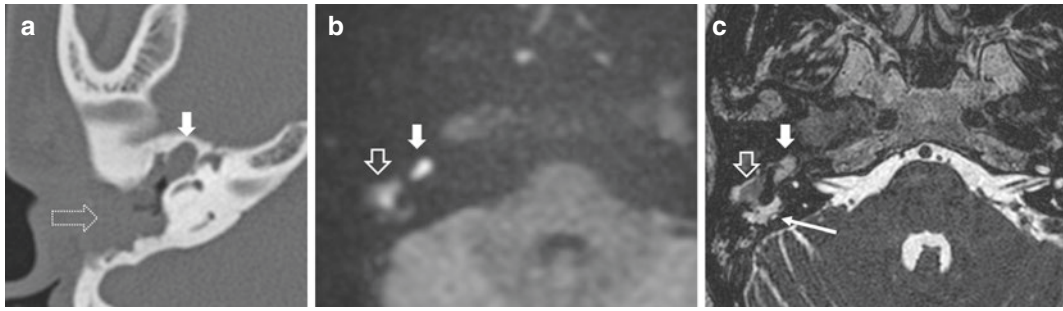

Fig. 6.9 Recurrent cholesteatoma of the right ear: (**a**) axial CT showing non-specific condensations in the cavity of mastoidectomy (open arrow), and oval-shaped condensation of the AER (white arrow). (**b**) Axial diffusion image at B 1000 shows two foci of pathologic restriction corresponding to cholesteatoma in the cavity of mastoidectomy (empty arrow) and in the AER (plain arrow). (**c**) Axial T2 HR Drive image showing the hypointense cholesteatoma in the cavity of mastoidectomy (empty arrow), surrounded by hyperintense effusion (long arrow). Second focus of cholesteatoma in the AER (plain arrow), of intermediate non-specific intensity in this sequence

Table 6.1 Differential diagnosis by MRI [6]

	T1	T2	Diffusion	Gado
Cholesteatoma	Hypointense	Hyperintense	Restriction	No early uptake
Cholesterol granuloma	Hyperintense	Hyperintense	No restriction	No uptake
Granulation tissue	Hypo/intermediate	Hyperintense	No restriction	Uptake
Scar tissue	Hypointense	Hypointense	No restriction	Uptake

1. A closed technique: like canal wall up (CWU) procedure, canal wall down (CWD) with a reconstruction of the ear canal, or CWD with mastoid obliteration.
2. An open technique: CWD, atticotomy without reconstruction or obliteration.

6.11.1 Surgical Procedures

See Table 6.2.

6.11.2 Endoscopy in Cholesteatoma

Otoendoscopy offers better visualization of a disease hidden in areas like sinus tympani, anterior epitympanic recess, and retrotympanum. It permits, better than the microscope, to rule out peroperative residual. In many cases, micro-endoscopic surgery prevails to ensure adequate surgical procedure.

Wet Ear Cavity is the most common reason for revision surgery after CWD mastoidectomy (troublesome mastoid cavity). It is due to the following [10]:

1. Incomplete eradication of the mastoid aircells disease or inadequate lowering of the facial ridge (85%).
2. A very large cavity or/and inadequate meatoplasty (10%).
3. Recurrent or residual cholesteatoma (5%).

6.11.3 Hearing Rehabilitation in Cholesteatoma Surgery

1. Ossiculoplasty done either by autologous ossicular graft or by prosthesis (partial or total ossicular replacement prosthesis). In extended cases, it is recommended to control the disease process first and do the ossicular reconstruction later. Safe ear prevails on hearing restauration.
2. Bone anchored hearing aid (BAHA) can provide a viable option to improve hearing outcome.

Table 6.2 Comparison between CWU and CWD procedures

	Canal wall down (CWD) procedure	Canal wall up procedure
Indications	1. Cholesteatoma of an only hearing ear. 2. Major erosion of the posterior bony canal wall. 3. History of vertigo due to a labyrinthine fistula. 4. Poor Eustachian tube function. 5. Sclerotic mastoid with limited access to the epitympanum. 6. Patient non-compliant for follow-up.	Indicated in most cases of cholesteatoma, especially for cases with a large pneumatized mastoid and in children *Contraindications* 1. Only hearing ear. 2. A long-standing ear disease after multiple previous procedures and persistent extended pathology. 3. Extensive lysis of the bony ear canal.
Advantages	1. The relatively short duration of the surgery. 2. Attic and the facial recess are well exteriorized; easier surgical in toto removal of the extended disease. 3. Any postoperative cholesteatoma regrowth can readily be seen and removed as an office procedure.	1. More rapid healing. 2. Better quality of life for the patient and normal ear contours. 3. Better fit of hearing aids when needed.
Disadvantages	1. Hearing reconstruction is less successful. 2. Open cavity: the mastoid bowl maintenance can be a lifelong problem. Unpleasant appearance of the meatoplasty. 3. Secondary reconstruction would be less successful. 4. Difficulty fitting of hearing aid because of meatoplasty.	1. Long duration of the surgical procedure in extended pathologies. 2. Unsatisfactory exposure and high rate of residual disease. 3. Staging and multiple surgical looks. It may require a second look after 12 months in adults and 6–9 months in children.

Table 6.3 Complications of chronic otitis media with cholesteatoma (Fig. 6.10)

	Extratemporal	
Intratemporal	Intracranial	Extracranial
Labyrinthine fistula	Lateral sinus thrombosis	Sub-periosteal abscess
Facial paralysis	Meningitis	Bezold's abscess
Petrositis	Extradural abscess	
Labyrinthitis	Subdural abscess	
	Cerebral abscess	

6.11.4 Follow-Up

The rate of recurrence and residual disease is higher in children (30%) than in adults. It is important to ensure as long as possible the follow-up with the patient postoperatively. For children, follow-up should continue until adulthood and longer. MRI imaging can be considered as the first-line follow-up imaging tool to search for disease recurrence.

Otologist should consider the following choices during patients' follow-up, especially in children:

1. Second-look surgery should be offered when complete surgical removal of cholesteatoma was uncertain to the surgeon and the patient has a positive MRI image. (It is to note that MRI is a difficult tool in children because it requires general anesthesia.).
2. When the surgeon was sure of complete removal of cholesteatoma, and when an unequivocal normal microscopic examination is observed in the first 6 months, then MRI can be a substitute for second-look surgery.

6.12 Complications of Chronic Otitis Media with Cholesteatoma [6]

Possible intra- and extratemporal complications are enumerated in Table 6.3 and illustrated by Fig. 6.10.

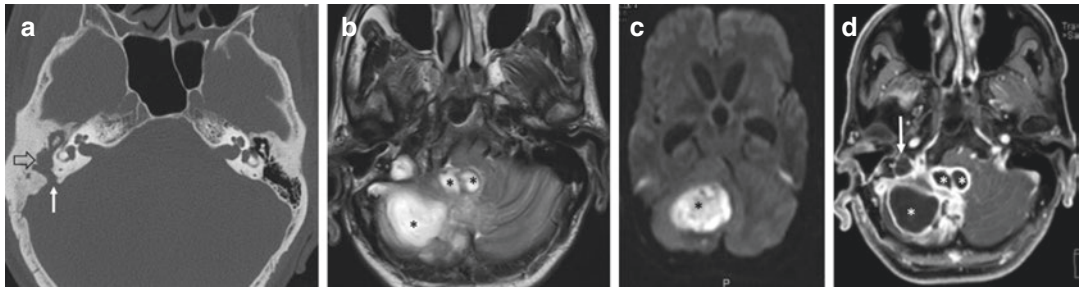

Fig. 6.10 (**a**) Axial HRCT, (**b**) Axial T2-WI MRI, (**c**) Axial DWI MRI, and (**d**) Axial Contrast enhanced tT1-WI MRI. (**a**) Showing CT features of right sided otomastoiditis/cholesteatoma (black empty arrow) with focal bony erosion along the posterior wall (white arrow). (**b**) Multiple right cerebellar abscesses, hyperintense in Flair (asterisk) that show diffusion restriction in **c**, and a typical ring enhancement after Gadolinium in **d**, also subdural empyema (arrow)

Take-Home Messages

- Despite advances in diagnosis and surgery, deficiencies exist worldwide with access to health care facilities, meaning cholesteatoma remains a serious and challenging entity to manage when found within the pediatric or adult population.
- Proper diagnosis and management of each type of cholesteatoma must be achieved through a strict methodology and long-life follow-up.

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