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Case Study

The chronic ear: A case report of bilateral cholesteatoma in a 10-year-old boy

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Key Learning Points

- Cholesteatoma is a rare condition affecting 9-12.6 adults and 3-15 children per 100,000 per annum[1–4], with a more aggressive presentation in the paediatric population[5].
- Intermittent otorrhea (ear discharge) is the presenting complaint in over half of cholesteatoma patients[6, 7]. The peak incidence of cholesteatoma is 5-15 years of age[8] which overlaps significantly with a period of high incidence in otitis media[9] and externa [10], diseases that often present the same way as cholesteatoma. This results in diagnosis that may take several years.
- Left untreated, cholesteatoma can cause significant lasting damage in the form of deafness, vertigo, facial paralysis, meningitis, and brain abscesses which may prove fatal[11].
- Current treatment options are limited to surgical excision with the aim to establish a safe and manageable ear, while maintaining hearing is secondary. Improving surgical instrumentation has allowed a better success rate, however, revision surgeries remain a mainstay of practice. In practical terms, this means that those affected by bilateral disease often undergo surgery 4 or more times[12]. This represents a significant burden for patients.
- The decision about the exact surgical approach (canal wall up vs canal wall down) is a careful balancing act of safety versus functionality, and the pros and cons must be weighed in light of available evidence and the skill of the surgeon[13].

Introduction

Cholesteatoma is a rare disease with potentially life-threatening complications

Cholesteatoma (chole = cholesterol; steat = fat; oma = tumor) is the non-cancerous locally invasive growth of keratinising squamous epithelium in the middle ear and mastoid air cells, where such tissue is not normally found[14]. The name cholesteatoma is a misnomer since the characteristic growth does not consist of cholesterol or fat, nor is it neoplastic in nature. Often simply described as
"skin in the wrong place"[15,16], the condition can be much more sinister than this label may suggest.

Extension of skin tissue into the middle ear and mastoid air cells may be associated with complications that may ultimately prove life-threatening[11]. To start, the enzymatically active nature of the cholesteatoma matrix can contribute to the erosive destruction of inner ear structures. In addition, the abnormal accumulation of dead tissue promotes an environment of chronic infection, further amplifying the osteolytic effects of cholesteatoma[17]. This can result in conductive deafness if ossicles are affected, while exposure of inner ear structures may lead to sensorineural hearing loss and vertigo. In severe cases, cranial nerve VII injury may result in facial paralysis in a lower motor neuron pattern[11]. Finally, if left untreated, cholesteatoma has the potential to erode through the tegmen (roof) of the middle ear and cause intracranial complications, such as meningitis or brain abscesses in an estimated 1.6-7.5% of patients[18,19]. This constitutes a significant paediatric cause of morbidity and death in developing regions with limited access to advanced health care[20–22].

Interestingly, paediatric cases progress more aggressively, resulting in more extensive disease which, at the same time, is more prone to infection than adult forms of the disease, leading to a more destructive phenotype[5]. Therefore, children are disproportionately affected by the side-effects of cholesteatoma. Furthermore, this group is particularly sensitive to hearing impairment resulting from the disease, causing delayed speech development and learning difficulties[13]. This highlights children as a subset of the patient population in need of special attention in order to achieve timely diagnosis and curtail lasting damage.

Aetiology and pathogenesis

In its aetiology, cholesteatoma is known to be either congenital or acquired, with the latter affecting both

adults and children. The rarer congenital cholesteatoma (CC) is characterised by a white mass that forms before birth behind an intact ear drum. CC is thought to be a persistent foetal epidermoid (squamous inclusion), although definitive evidence for its origin is lacking[23]. It is distinguished from acquired cholesteatoma (AC) in that it tends not to be associated with otitis media.

There are several competing theories that describe AC formation, and their relative contribution is still up for debate. The first description of AC is attributed to Du Verney's report of a temporal bone tumour from 1683[24]. An oncological origin was indeed suspected for two centuries by several leading physicians including Virchow, who considered the condition to be the result of mesenchymal-to-epidermal metaplasia[25]. The neo- and metaplastic theories have, however, largely fallen out of favour. Current leading theory of the development of AC is via the disruption of the normal migratory pattern of skin cells, secondary to collapse of the ear drum due to infection or trauma[23]. Histologically, the thin fibrous structure of the tympanic membrane is lined by a single layer of cuboidal epithelium towards the middle ear and keratinizing squamous epithelium on the external ear side. The squamous epithelium migrates radially from the centre out to the annulus and then longitudinally along the external auditory canal[26]. This flow of the external epithelium aids the self-cleansing of the ear and ensures that the keratinous material that constantly sloughs off does not accumulate. Disruption of the ear drum interferes with normal cell migration patterns. Damage from repeated infections and iatrogenic causes or retraction pockets due to the obstruction of the eustachian tube therefore result in the accumulation of dead skin and can progress to inappropriately localised squamous cells[23].

A paediatric case of cholesteatoma

Ethan Lewis (pseudonym), a 10-year-old boy with bilateral cholesteatoma, was seen with his mother at a large tertiary hospital in March 2021 for stage 1 combined approach tympanoplasty (CAT) of the right ear.

Ethan has had a long history of ear disease with significant effect on his daily life. From the age of two, Ethan has been suffering from frequent ear infections, oozing (otorrhea), perforations, and glue ears (otitis media with effusion). The resulting reduced hearing acuity and occasional tinnitus impacted his school performance and lead to him having to sit closer to the teacher, something he found embarrassing at the time. Originally from New Zealand, flying to and from the UK or travelling for holidays has also caused him significant discomfort. In addition, as Ethan is a huge fan of swimming, the medical advice to refrain from water meant that his condition limited his life both in terms of school attainment as well as hobbies.

Previous interventions to relieve his symptoms included three grommets (ventilation tubes) and adenoidectomy, all of which aimed to ensure an adequate drainage and prevent fluid build-up. His diagnosis was later made following otoscopic observation of whitish mass behind his tympanic membrane on the left ear, while the right ear showed a posterior retraction pocket. Previous curative treatments included combined approach tympanoplasty on the more severely affected left ear in September 2019, with revision surgery carried out in October 2020. He takes no regular medication, only post-operative antibiotic ear drops as necessary. He has a penicillin allergy manifesting in a rash.

Management

Diagnosis of cholesteatoma

Ethan's case is not at all uncommon. Indeed, most patients who are ultimately diagnosed with cholesteatoma have a long-standing history of ear disease. While it may be asymptomatic in early stages of the condition, it presents as recurrent or chronic infection in over 50% of patients[6,7]. Non-cholesteatoma related infections of the middle ear and external auditory canal, however, are several orders of magnitude more prevalent than cholesteatoma[9,10]. Therefore, an average primary care physician may see hundreds of these cases every year, but only one cholesteatoma every 10 years. As a result of this, cholesteatoma is usually not even suspected as a diagnosis, delaying appropriate treatment. Furthermore, the peak incidence of both otitis media[9] and externa[10] overlap significantly with the age of occurrence of cholesteatoma at 5-15[8], contributing to an increased risk of late diagnosis specifically in children.

Certain elements of the history may help raise the index of suspicion for cholesteatoma. Unlike otitis media and externa, which mainly present sporadically, recurrent or chronic infections are more likely in cholesteatoma. Additionally, these infections are often associated with a malodorous discharge that may prove refractory to antibiotic treatment[27]. Tinnitus and hearing loss are also among the more common presentations, although the latter may go unnoticed by some patients. In addition, some of the less frequent symptoms include otalgia, vertigo, or even facial nerve involvement in more advanced disease[28]. Ultimately, correct diagnosis is often not found until several years have passed and the disease has progressed.

An accurate diagnosis may be aided by taking relevant risk factors into consideration alongside history. In line with its suspected aetiology, one of the best documented risk factors for cholesteatoma is history of previous ear disease and interventions[29]. This includes prior infections, Eustachian tube dysfunction leading to retraction pockets, surgery, or trauma to the ear. Male gender also increases risk 3:2 relative to females[30]. While there is some indication of familial clustering of cholesteatoma, its strongest genetic link is with conditions that result in craniofacial abnormalities, like Turner's or Down's syndrome[31]. In the United Kingdom, cholesteatoma is also correlated with social deprivation[32]. Finally, although less relevant for the paediatric populations, osteoporosis treatment with bisphosphonates is also associated with higher incidence of disease[33].

Careful examination visualising the entire tympanic membrane is the gold standard for cholesteatoma diagnosis (Figure 1). This might be complicated in the primary care setting is by otorrhea and swelling leading to poor visibility. Adequate visualisation may therefore require aural toilet to clear any discharge. This could, however, prove difficult: if children do not cooperate with otoscopic assessment, an examination under anaesthesia may become necessary, contributing an additional layer of complexity.

During examination, crusting or keratin on the superior tympanic membrane, retraction pockets with or without debris, or granulation tissue can all be taken as signs of cholesteatoma[27]. These most commonly affect pars flaccida and posterior superior segments of the eardrum (Figure 1). The subtlety of these signs makes them rather challenging for non-specialists to notice.

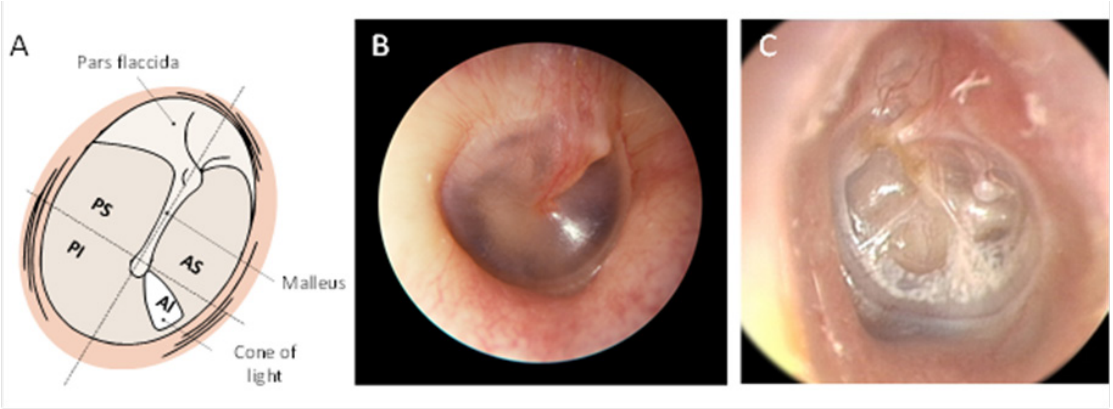

Figure 1: Otoscopic investigation of normal and retracted tympanic membrane. (A) Schematic view of the ear drum demonstrating key anatomical features. (B) Normal tympanic membrane. (C) Retracted ear drum PS – posterior superior, PI – posterior inferior, AS – anterior superior, AI – anterior inferior (modified from Wikimedia Commons, panel A Madhero88 under CC BY 3.0, panel B Michael Hawke MD under CC BY-SA 4.0, panel C Adrian L James under CC BY-SA 3.0)

Once cholesteatoma is found, further examination may include CT scanning to assess the extent of disease with a particular focus on mastoid involvement, while audiometry is used to establish a baseline, pre-surgical hearing level[29]. Overall, chronic, and recurrent ear complaints deserve thorough examination and referral to ear, nose and throat specialists.

Symptomatic treatment of cholesteatoma

Due to difficulties in identification, first-line treatment options mostly provide symptomatic relief following guidelines aimed at ear infections. Otitis media and externa tend to resolve on their own within a week, therefore mild analgesia using paracetamol or ibuprofen is usually sufficient. Otitis media with effusion (fluid accumulation behind the tympanic membrane) is often treated with myringotomy and the insertion of grommets. Adenoidectomy is sometimes performed in combination with grommet insertion as there is evidence of improved outcomes compared to ventilation tubes alone[34,35]. Finally, systemic antibiotic therapy is usually not indicated unless patients are generally unwell, but topical antibiotic-steroid drops are often used[27]. The latter play an important role even after correct diagnosis of cholesteatoma is made in reducing peri-operative infection and inflammation.

Curative intervention

Surgical excision is the only definitive treatment for cholesteatoma. The procedure aims to achieve a hierarchy of three main goals:

1. Make the ear safe.
2. Create a dry, manageable ear.
3. Restore hearing.

Therefore, hearing may be sacrificed in order to realise the primary objectives of the operation.

There are two main alternative surgical approaches to cholesteatoma treatment – canal wall up (CWU) and canal wall down (CWD) mastoidectomies[12]. The main distinction between the two techniques is whether the bony posterior ear canal wall is retained (Figure 2A). Historically, CWD has been the most widely used approach, and depending on available instrumentation, it is still done routinely in developing nations[21]. CWD allows better access and hence reduces the chance of residual disease. It does, however, create a common cavity between the mastoid and the ear canal, leading to an aesthetically less pleasing result and introducing a number of lasting side effects. For instance, patients may develop caloric stimulation vertigo, where exposure to hot or cold air causes dizziness. Exposure to water post intervention must also be limited, which may interfere with recreational activities and regular cleaning of the area. Furthermore, due to the extensive change to the resonant chambers of the middle ear, hearing is often negatively impacted. This is not helped by the fact that the enlarged cavity may result in ill-fitting hearing aids. Finally, patients also frequently have to return for debridement and drainage, further limiting their quality of life[12].

In the UK, CWU procedures, specifically the combined approach of working through the ear canal and an enlarged mastoid aditus followed by the reconstruction of the tympanic membrane, referred to as combined approach tympanoplasty (CAT), is the preferred intervention for cholesteatoma[29]. CAT is usually performed in two (or occasionally more) stages separated by 9-12 months. Hearing is often worse after the first surgery which aims to remove squamous cells. During revision, comprehensive ossicular chain reconstruction is performed, leading to improved results. A piece of conchal cartilage is often used in children to reinforce the eardrum and avoid recidivism[36]. Overall, CWU retains more of the original anatomy relative to CWD, ensuring that all three goals of surgical intervention are achieved.

Complications of cholesteatoma operations

Cholesteatoma surgery-associated complications range from general surgical sequelae, like bleeding, incision scars and post-operative infections, to ones that are unique to the surgical site. In this case, the middle ear is a restrictive space densely packed with sensitive anatomical features (Figure 2). A branch of the facial nerve, the chorda tympani, supplies taste sensation to the anterior two thirds of the tongue. It passes directly behind the ear drum, which is removed during surgery to provide access[37]. Evidence shows that by the time most patients get to surgery, the nerve has sustained considerable damage, and most patients experience little to no change in their taste sensation[37–39]. As a result, preservation of the chorda tympani is not a priority. Damage to the facial nerve itself is a less frequent, but more serious complication that can lead to facial weakness or paralysis. Facial nerve monitoring has been suggested as an invaluable tool to guide the procedure[40]. Secondly, the middle ear communicates with the mastoid antrum, which is particularly well-pneumatised in children (Figure 2). This means that children

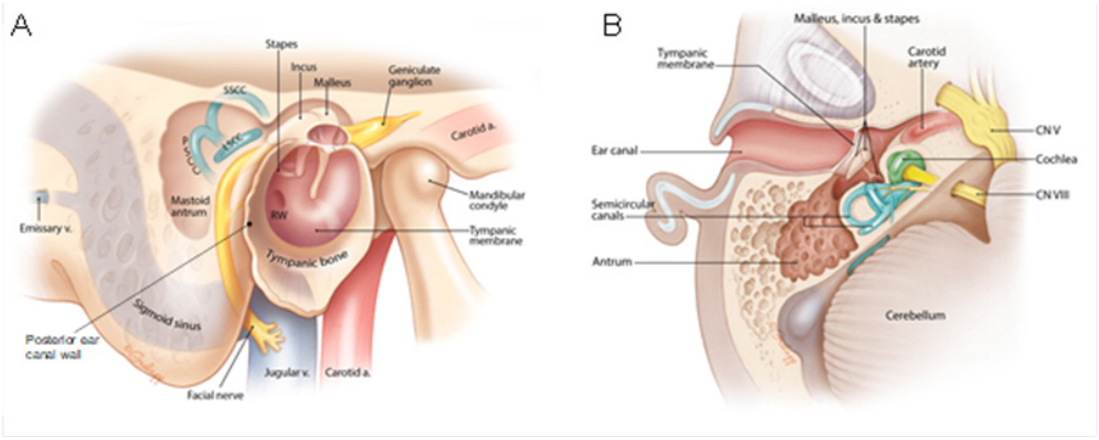

Figure 2: Overview of the anatomy of the temporal bone. (A) Lateral and (B) axial view of the ear. LSCC – lateral semicircular canal, PSCC – posterior semicircular canal, RW – round window, SSC – superior semicircular canal (modified from Stanford Medicine Otologic Surgery Atlas; © Christine Gralapp)

with highly proliferative cholesteatomas can have disease progress into their mastoid air cells. Adequate clearance of this abnormal tissue necessitates the removal of parts of the temporal bone, which can potentially expose or damage inner ear structures, causing vertigo or tinnitus. Finally, recesses in the middle ear may harbour residual disease not removed by surgery. Incomplete clearance may therefore result in disease recurrence, making revision surgeries commonplace[12].

Ancillary devices in cholesteatoma management

Cholesteatoma surgery aims to remove all squamous epithelial cells from the middle ear and mastoid air cells. It is a careful balancing act between safety and functionality. Several new techniques such as fibre-guided lasers and endoscopic approaches have been proposed as tools that may help tip the balance towards improved outcomes both in terms of reduced recurrence and greater hearing retention[17].

Clearance of the temporal bone cavities is conventionally achieved by mechanical means, mostly using diamond burrs. Such techniques are associated with increased risk of iatrogenic complications, but due to their imperfect nature, are also frequently plagued by recurrence of residual disease. Fibre-guided, laser-assisted surgery aims to resolve the apparent conflict between hearing preservation and disease eradication. The fine control allowed by the fine optic fibre means that disease in close proximity to ossicles can be targeted with high accuracy without damaging the hearing chain[12]. Indeed, preliminary results based on the limited data currently available point to laser-assisted surgery as a safe and effective way to reduce recurrence with good hearing outcomes[41].

Another source of tension is between the two alternative surgical approaches. CWU procedures achieve better functionality, but at the cost of higher residual and recurrent disease rates relative to CWD. At its core, this difference is due to the different levels of access and visibility the two procedures offer. Endoscopy, especially lateral vision endoscopy at angles of 30° or 45°, reduces residual disease rates of CWU operations to be on par with CWD by allowing surgeons to examine hidden areas, such as the supratubal recess and sinus tympani, during surgery[12].

Some newer approaches eliminate open surgery and instead rely entirely on a trans-canal endoscopic ear surgical (TEES) approach. Using the ear canal as a natural port of access TEES better aligns surgical access with the underlying anatomy, thereby minimising invasiveness[42]. Somewhat counterintuitively, TEES often offers a better surgical field than what can be achieved using microscopic surgery via a post-auricular transmastoid approach, which would normally involve extensive clearing of the mastoid cavity. This is especially true for recesses of the tympanic cavity – the most frequent source of residual disease[12,42]. TEES is therefore associated with reduced rates of recurrence[43].

The use of TEES in children may be constrained by several factors. For example, the diameter of the external auditory canal orifice is directly correlated with age in paediatric patients[44], making its applicability in children uncertain. To this end, a study investigating the applicability of TEES found that more than 4 out of 5 participants had ear canal orifice larger than 4 mm, providing adequate clearance for a 3 mm endoscope[44]. Nevertheless, greater concern stems from the frequent involvement of mastoid air cells in children, access to which is limited in TEES. Treatment of advanced disease may therefore necessitate the use of conventional techniques involving mastoid ablation[45]. Overall, endoscopy is a valuable tool that can be used either exclusively or in combination with conventional techniques, depending on specific patient requirements, such as in the case of mastoid involvement.

Adequate follow up after surgery is just as important as the procedure itself, given cholesteatoma's high rates of recidivism[12]. Historically, high resolution computed tomography (CT) served as the gold standard for pre-operative imaging of cholesteatoma[12,46,47]. Its post-surgical use, however, was limited by CT's inability to accurately distinguish between various structures with soft-tissue density, such as granulation tissue, effusion, or indeed, recurrent disease[47–49]. Furthermore, imaging modalities that rely on high doses of radiation are less desirable, especially in children, who are considerably more radio-sensitive and have a longer life-expectancy than adults[50]. Diffusion-weighted magnetic resonance imaging (DW-MRI) is one of the more recent additions to the MRI contrast generation repertoire that solves most problems associated with CT. DW-MRI allows for a more accurate differentiation between soft-tissues without the use of X-rays, making it a go-to tool in paediatric cholesteatoma management[49,51,52]. In fact, there is evidence that DW-MRI is sensitive enough in the post-

operative setting to forgo invasive second-look surgeries[52,53], which constitute a significant burden for patients and a considerable expense to healthcare services[54]. That said, not all reports agree that imaging is in a position to replace surgery[55,56]. A change in clinical practice will have to rely on the development robust protocols and large prospective randomised-control trials to validate these findings.

Conclusion

Paediatric cases of cholesteatoma pose a challenge both at the diagnostic and treatment stages and therefore require special attention. Better awareness of this disease by primary care physicians may reduce the delay from first presentation to surgery. While NICE does reference cholesteatoma as a differential diagnosis for a subset of conditions that have a significant overlap of symptoms, such as chronic middle ear infection, it does not mention it in others, like otitis media with or without effusion. Complete visualisation of the tympanic membrane, with particular attention to the attic and posterosuperior quadrant, is recommended for all patients with recurrent ear disease[27,57], as early detection of cholesteatoma is associated with better outcomes[17]. Additionally, current NICE and BMJ Best Practice guidelines make no distinction between adult and paediatric cases[29,58]. This is despite the fact that cholesteatoma in children is more prone to infections, is more extensive, and is associated with poorer prognosis[5,12]. Furthermore, mastoid involvement also limits the use of less invasive surgical approaches once the disease is identified[45]. This presents somewhat of a controversy regarding the ideal treatment approach in this population. Overall, patients and parents must have sufficient understanding of risks and benefits of different surgical approaches, as well as factors that may predispose to complications. In the context of potentially severe complications, guideline recommendations need to be revised in order to expedite the treatment of those most at risk.

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Consent

The patient's guardian has consented to the publication of this case study.

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