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Primary Cholesteatoma of the External Auditory Canal with Adjacent Structure Invasion: a Report of Three Cases and Literature Review

Primarni holesteatom zunanjega sluhovoda s širjenjem v sosednje strukture: trije klinični primeri in pregled literature

ABSTRACT

KEY WORDS: cholesteatoma, external auditory canal, tissue invasion, imaging, otoscopy, mastoidectomy, comorbidities

External auditory canal cholesteatoma is a rare condition. In persons with no significant history of trauma, surgery or pre-existing ear canal stenosis of the affected ear, it is termed primary/idiopathic/spontaneous. While the majority of outer ear canal cholesteatomas are limited to the external ear canal itself, the masses have the potential to spread and destroy adjacent tissues. The aim of our study is to present clinical findings in three patients with primary external auditory canal cholesteatoma spreading to the surrounding structures. This clinical entity is often misdiagnosed, which leads to a delay in adequate treatment and possible complications. External auditory canal cholesteatoma should be considered as a differential diagnosis by otorhinolaryngologists in any case of otitis externa maligna, otomycosis non-responsive to medication, keratosis obturans, neoplasm of the outer ear canal etc. In patients with prolonged non-specific symptoms (such as otorrhea and otalgia), thorough otoscopic examination and appropriate imaging are crucial for a timely diagnosis. Tissue biopsy is necessary, especially in advanced stages of the disease, to exclude malignancies and to plan surgical treatment accordingly. The discrepancy between symptom severity and local extent of the disease in our patients stresses the importance of early recognition and regular follow-up, especially in persons with associated risk factors (advanced age and comorbidities).

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IZVLEČEK

KLJUČNE BESEDE: holesteatom, zunanji sluhovod, destrukcija tkiv, slikovna diagnostika, otoskopija, mastoidektomija, komorbidnosti

Holesteatom zunanjega sluhovoda je redka klinična najdba. Pri bolnikih brez poškodbe, operacije, obsevanja ali iz drugih vzrokov znane prisotne zožitve sluhovoda na prizadetem ušesu gre za primarni/idiopatski/spontani holesteatom zunanjega sluhovoda. Kljub temu da je večina holesteatomov te vrste omejena na sam zunanji sluhovod, imajo lezije potencial k širjenju in uničenju prileţnih tkiv. V prispevku smo želeli predstaviti klinične značilnosti in obravnavo treh bolnikov s primarnim holesteatomom zunanjega sluhovoda, ki se širi v sosednje strukture. Ta klinična entiteta je pogosto napačno diagnosticirana, kar vodi v zamudo z ustreznim zdravljenjem in poveča možnosti za področne ali sistemske zaplete. Otorinolaringologi naj na primarni holesteatom zunanjega sluhovoda posumijo pri vsakem primeru malignega vnetja zunanjega sluhovoda, Otomikoze, neodzivne na zdravljenje, primerih keratosis obturans-a in neoplazmah zunanjega sluhovoda. Pri bolnikih z vztrajajočimi nespecifičnimi simptomi (bolečina in izcedek iz ušesa) sta natančen otoskopski pregled in slikovna diagnostika ključna za optimalno obravnavo. Pred načrtovanjem operativnega posega je predvsem pri razširjenih oblikah bolezni za izključitev malignih tvorb pomembna biopsija tkiva. Nesorazmerje med stopnjo težav in razširjenostjo holesteatomov pri preučevanih bolnikih poudarja pomen zgodnjega prepoznavanja in rednih kontrolnih pregledov, še posebej pri osebah z večjim tveganjem (starost, pridružene bolezni).

INTRODUCTION

External auditory canal (EAC) cholesteatoma is a non-neoplastic formation in the outer ear canal. It is histologically considered an epidermoid cyst. It causes osteonecrosis and sequester formation in the bony EAC with its invasion of the keratinizing squamous epithelium. The first researcher to describe this entity was Toynbee in 1850, using the term »specimens of molluscum contagiosum« in the EAC. In 1893, Scholefield described it more accurately as »epithelial debris in the ear canal«. It was defined and distinguished from keratosis obturans, which is the most similar differential, by Piepergerdes in 1980. Researchers Naiberg et al. were the first to describe the disease histopathologically in 1984 *(1–4).* External auditory canal cholesteatoma (EACC) is a rare condition with an incidence rate of around 0.30/100.000 per year, making it 60 times less common than middle ear cholesteatoma *(5, 6).* It is classified as primary or idiopathic or spontaneous when no significant history of trauma, surgery, radiation or other causes of priorly present ear canal stenosis of the affected ear are found. The pathogenesis of the disease is poorly understood. Potential risk factors for its development have been proposed, including microangiopathy (nicotine abuse, diabetes), microtrauma, remnants of the first branchial cleft, and age-related changes in epithelial migration *(9, 10).* The symptoms are non-specific, otorrhea and otalgia being the most common ones *(7).* The majority of EACCs are limited to the outer ear canal. Still, the disease has the ability to spread and destroy adjacent structures – the temporomandibular joint (TMJ), hypotympanum, mastoid cavity, facial nerve, skull base etc. *(8).* Several staging systems of EACCs are available *(11).* The diagnosis lar-

gely relies on recognition upon clinical examination by the otorhinolaryngologist and on appropriate imaging. Tissue biopsy is essential in advanced lesions before definitive surgical treatment to exclude malignancies. Apart from keratosis obturans, the most common diseases mimicking EACC are otitis externa maligna and squamous cell carcinoma *(8, 9)*. Treatment is not standardised, as it depends on the extent of the disease and most commonly includes ear canal curettage *(11)*.

Our study aims to describe the symptoms, clinical findings, and disease management in three patients with primary EACC spreading to adjacent structures.

METHODS

Medical documentation of three patients (Patient A, B and C) was reviewed.

Medical Cases

All our patients were males over 65 years of age. Patient A presented with progressive otorrhea and ear canal pruritus, persisting for two months. Patient B and C experienced hearing loss and otalgia for three and four weeks, respectively. Patient B also reported aural fullness. All complaints were unilateral, two on the right side and one on the left. All three patients had a positive medical history for comorbidities – arterial hypertension (all patients), diabetes and transitory ischemic attack with neck artery stent placement (patient B), and smoking habit (patient A). Otoscopy and CT scans performed in all patients revealed characteristic lesions in EAC, raising suspicion of cholesteatoma. In patient A, the masses were occupying the inferior anterior portion of the EAC, spreading to the TMJ area and posterior canal wall. In Patient B, the mass invaded the mastoid cavity and the hypo- and mesotympanum. Cholesteatoma in patient C was expanding from the posterior canal wall into the mastoid cavity. All patients underwent surgical treatment under general anaesthesia. Modified canal wall down (CWD) mastoidectomy was performed in patient A. In patients B and C, ear canal curettage was performed to remove cholesteatoma tissue and serve as tissue biopsy, as it was impossible to differentiate between cholesteatoma and possible malignancies with the CT scan alone. With malignancies excluded, patient C, due to mastoid invasion, underwent a CWD mastoidectomy in a separate procedure. All cholesteatomas were removed in total. Histopathological examination confirmed the diagnosis of cholesteatoma in all patients. Pre- and postoperative audiometric testing revealed only minor additional conductive hearing loss in patients with mastoidectomy after surgery, with Patient C already having a known combined hearing loss before surgery. In patient B, a residuum of the disease was found six months after initial treatment, requiring recurettage of the EAC, which was successfully performed. The patients are monitored during regular follow-ups, which periodically include imaging (high resolution computer tomography (HRCT) or MRI), and haven't shown any signs of disease so far (all more than 4 years after surgery).

Detailed clinical presentation and management are described below.

PATIENT A

A 71-year-old male patient presented to the tertiary ENT centre with progressive worsening of otorrhea and external ear canal pruritus on the right ear persisting for two months. The symptoms were not responding to treatment with oral antibiotics, and thorough local cleansing had been performed every second day in the secondary outpatient clinic. The patient's past medical history was significant for tobacco use and allergic rhinitis. There was no history of trauma, stenosis or previous surgery performed on the affected ear. Otoscopic examination revealed a chole-

steatoma-like mass occupying the inferior anterior portion of the right external auditory canal spreading to the temporomandibular joint area and into the posterior canal wall. A fibrose pocket was present laterally to the cholesteatoma. Medially, an intact tympanic membrane was seen. The CT scan demonstrated a cholesteatoma of the outer ear canal with possible growth into the middle ear cavity (figure 1). Microbiological swab testing of the ear discharge was negative for pathogens. Preoperative pure tone audiometry revealed bilateral sensorineural hearing loss in high frequencies without conductive hearing loss. A modified CWD mastoidectomy was performed in general anaesthesia. The posterior upper ear canal was drilled, and the ear canal dilated. The tympanum was left intact, without entry through the atticus, to affect the patient's hearing as little as possible. The TMJ area was affected just up to the capsule, with no direct invasion to the joint. The cholesteatoma mass was removed in total (figure 2). The ear canal was packed with gel foam soaked with antibiotics. A temporalis fascia graft was used to cover the exposed bone before repositioning the meatal skin in the area and below the lifted tympano-meatal flap. Pure tone audiometry postoperatively revealed only minor additional conductive hearing loss (figure 3). An intravenous antibiotic was administered postoperatively on the ward. During regular follow-ups, the denuded bone in front of the TMJ and in the inferior part of the EAC was carefully monitored for appropriate healing. After 15 months, a platelet-rich plasma treatment was administered to aid re-epithelisation, which was visibly improving on every examination. No signs of disease recurrence were evident during follow-ups, four years after initial treatment for the time of this article.

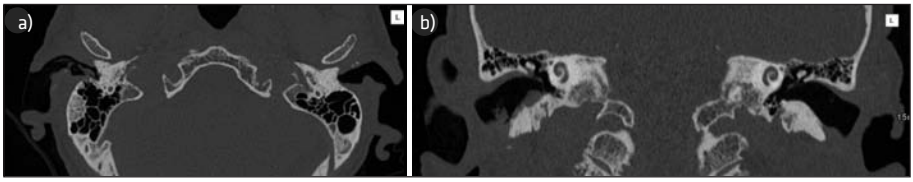

Figure 1. Preoperative CT scan in patient A, both sections showing soft tissue mass in the right EAC with middle ear invasion. A) axial view, B) coronal view.

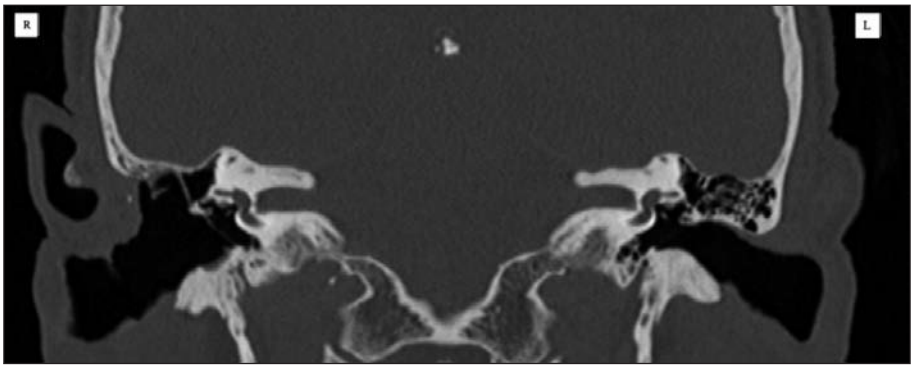

Figure 2. Postoperative CT scan in patient A, coronal view, post-canal wall down mastoidectomy showing no cholesteatoma on the right ear.

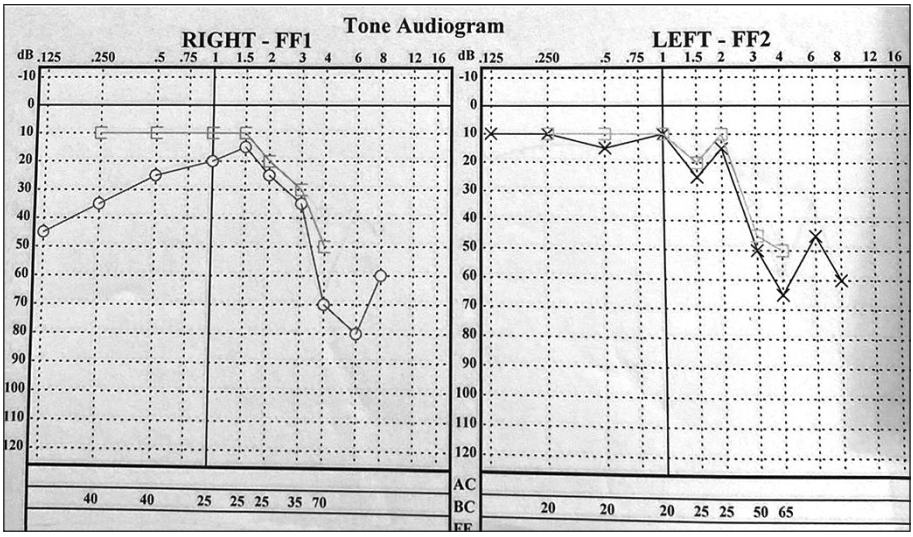

Figure 3. Postoperative pure tone audiometry testing in patient A, two months after surgery (image of preoperative testing is not available, based on written documentation, the test revealed sensorineural hearing loss up to 55 dB at 4000 Hz on the right ear, and sensorineural hearing loss up to 60 dB at 4000 Hz, 30 dB at 6000 Hz and 65 dB at 8000 Hz on the left ear, with no conductive hearing loss bilaterally).

PATIENT B

A 67-year-old man presented to the tertiary centre due to persistent otalgia and hearing loss on the left ear starting three weeks before referral. His comorbidities were diabetes mellitus on metformin and hypertension. His past medical history was significant for a transitory ischemic attack 20 years prior, along with the placement of a stent in the right neck artery. No evidence of trauma or previous surgery on the affected ear was reported. An expanded left external ear canal was evident upon otoscopic examination. In the inferior canal, wall granulations and sequesters of dead bone were seen. The diagnosis of EACC was suggested. Audiometric testing revealed a symmetrical sensory-neural loss bilaterally. Microbiological swab samples were obtained prior to intravenous antibiotic administration (Ciprofloxacin) on the ward. They were positive for *Turicella otidis*, sensitive to the selected antibiotic. The CT scan demonstrated demineralization and a defect of the bony area of left ear canal, filled with accumulated bone spurs and dense tissue (figure 4). The mass undermined the lower part of the tympanic membrane, and locally invaded the tympanic cavity into the hypo- and mesotympanic area, cranially up to the epitympanum and minimally invaded the latter as well. The auditory ossicles were not destructed, only mildly demineralized due to associated inflammation. The mastoid cells contained a thick collection without significant changes of the mastoid cell walls. External ear canal curettage and biopsy were performed in general anaesthesia. Histopathological examination confirmed the diagnosis of cholesteatoma – fragments of necrotic bone tissue and keratin scales. Postoperatively, an MRI was performed, showing no remnants of the cholesteatoma. After six weeks of parenteral antibiotics and meticulous cleansing of the EAC, the patient was discharged. The inflammation was in regression, and an intact tympanic membrane was seen with no signs of epithelium growth. Appropriate healing of the ear canal was

evident. Antibiotic treatment for another four weeks after discharge was prescribed. The patient had regular check-ups postoperatively. A control MRI after two months revealed no cholesteatoma masses. Contrast build-up superficially in the medial EAC and the inferior part of tympanic membrane was observed, possibly due to inflammation or postoperatively. Careful observation was indicated. Another MRI was later obtained in four months, which showed new unspecific thickening in the lower and anterior portion of the ear canal. Accumulation of epithelium debris towards the anterior canal wall was seen otoscopically. The patient was admitted for re-curettage in general anaesthesia. The cholesteatoma recurrence was removed in total along with the cholesteatoma sac. The tympanic membrane was unchanged, as well as the middle ear. No remnants of cholesteatoma or epithelium debris were seen postoperatively.

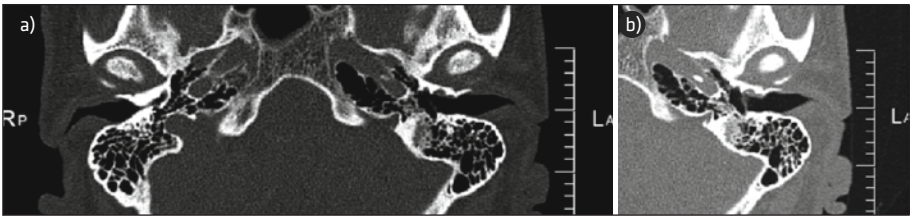

Figure 4. Preoperative CT scans in patient B, axial view, showing: A) bone erosion of the left external auditory canal; B) a soft tissue mass in the left external auditory canal.

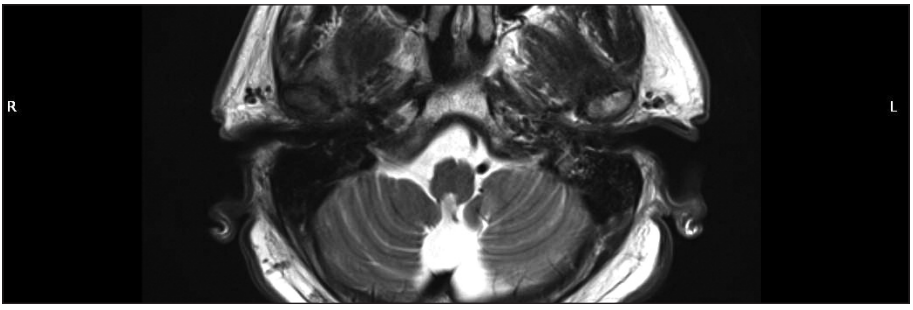

Figure 5. Postoperative MRI in patient B, T2-weighted sequence, axial view, upon follow-up (five years after treatment) without a cholesteatoma mass in the left external auditory canal.

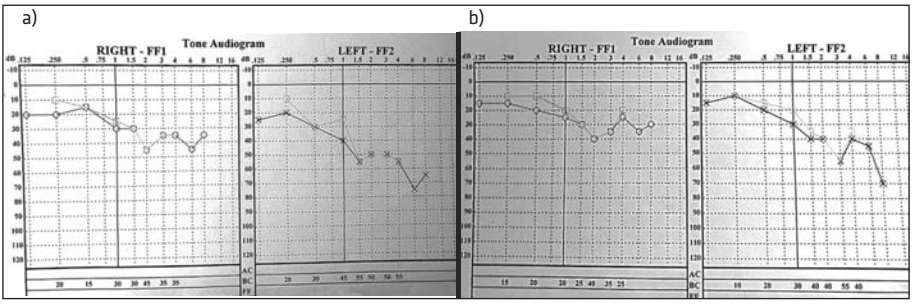

Figure 6. A) preoperative pure tone audiometry testing; B) postoperative pure tone audiometry testing in patient B.

A postoperative MRI showed diminished contrast build-up in the area where it was previously described. During follow-ups, appropriate reepithelization of the exposed bone was seen. The patient reported unchanged hearing postoperatively. No changes in hearing were observed during audiometric testing (figure 6). Regular cleansing was necessary postoperatively with regular follow-up MRI, which showed no cholesteatoma recurrence up to this point, over five years after surgical treatment.

PATIENT C

81-year-old male presented with otalgia and hearing loss of the right ear gradually worsening in the past month. He had a known bilateral symmetric combined hearing loss for 15 years and was wearing a hearing aid on the left ear. His comorbidities were arterial hypertension, clinical depression and prostate enlargement. No history of trauma, surgery or prolonged infection of the affected ear was reported. Otoscopy revealed an obstructed right outer ear canal in two-thirds with white epithelial masses, which were removed by aspiration. Dry and hardened cerumen was seen behind the masses with only partially removable granulated epithelium. Suspicion of possible bone sequestra and outer ear canal cholesteatoma was raised. In the microbiological swab, *Escherichia coli* was isolated and treated accordingly. A CT scan demonstrated osteomyelitis of the temporal bone. Bone fragments and cholesteatoma masses were seen in the right EAC with the destruction of the posterior ear canal wall and a defective bone barrier between the EAC and the mastoid (figure 7). The tympanic membrane was intact. An ear canal curettage and biopsy were performed under general anaesthesia. Using the endaural approach, the EAC was dilated, and bone fragments with the cholesteatoma sac were removed. The sac was present inferiorly to the tympanic membrane. No invasion of the middle ear was evident, however, the invasion in the mastoid could not be assessed. The posterior canal wall and the area below the tympanic membrane were drilled. The removed tissue was sent for pathological examination, confirming the cholesteatoma diagnosis. Osteomyelitic bone fragments were microbiologically inspected, demonstrating several pathogens. Targeted antibiotic treatment was administered in the ward. Due to the poor visibility of the mastoid and the suspected invasion of the cells, a CWD mastoidectomy was performed in another surgery under general anaesthesia with lat. *n. facialis* monitoring. Retroauricularly. The mastoid was trepanned, demonstrating dense liquid in the mastoid cells. The cholesteatoma sac along with thick mucosa were removed

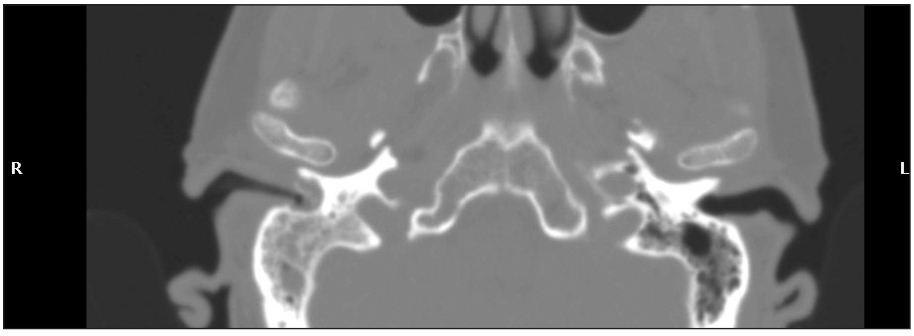

Figure 7. Preoperative CT scans in patient C, axial view, showing a soft tissue mass in the right EAC with destruction of the posterior ear canal wall.

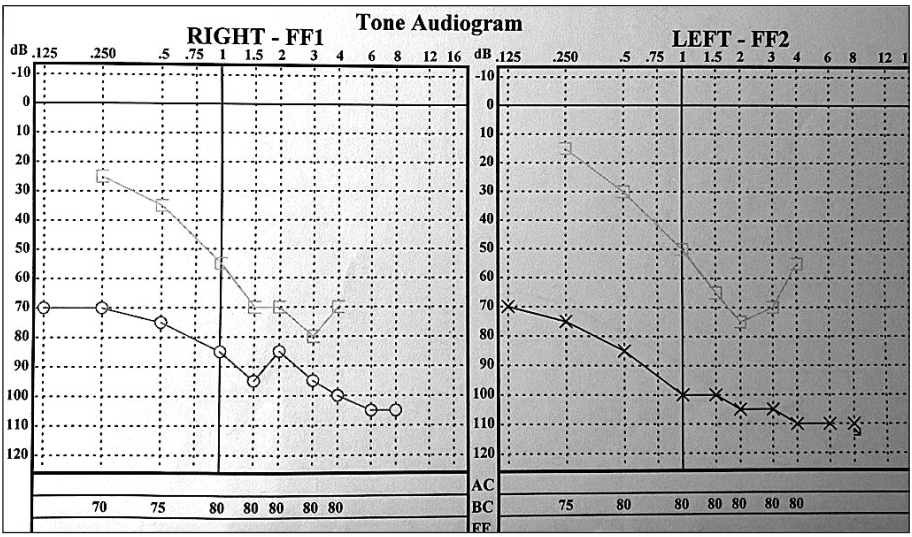

Figure 8. Postoperative pure tone audiometry testing in patient C, four months after surgery – priorly known bilateral combined sensory loss (preoperative testing picture is not available, based on written documentation).

entirely. Less than expected post-CWD conductive hearing loss in high frequencies was documented with audiometric testing postoperatively (figure 8). After six weeks of intravenous antibiotic application, the patient was discharged and regularly examined during follow-ups at the outpatient clinic. Successful epithelisation of the radical cavity was observed. No cholesteatoma recurrence was seen upon regular examinations four years after cholesteatoma removal.

DISCUSSION

Incidence and Demographics

EACC is a term describing a cystic lesion lined by keratinizing stratified squamous epithelium in the external auditory canal. It is a rare finding, accounting for 1/1000 otological patients *(12)*. The annual incidence rate of EACC in the general population is between 0.19 and 0.3 per 100,000 inhabitants in Switzerland, and Denmark and Greenland *(5, 15)*. In comparison, the annual incidence of middle ear cholesteatoma is around 9.2/100,000 individuals *(8)*. In a study in 2018, Herz et al. described a significantly higher incidence in Europe than previously reported: 0.97 per year per 100,000 inhabitants. The researchers assumed that previous studies only included patients treated in tertiary centres, without mild cases treated by general practitioners and without possible asymptomatic cases *(14)*. In another recent Chinese study by He et al. in 2021, an even higher incidence was reported, 23.2 per one million residents. Underestimating the incidence in previous studies was similarly attributed to only taking into account intermediate, advanced, or surgically treated lesions. The study could not exclude regional or ethnic specificity of the incidence *(11)*. EACC has been described in all age groups, but more commonly occurs in older patients with comorbidities. No unanimous gender predilection of the disease has been concluded, however, in our study the patients were all males *(5, 6, 13, 14)*.

Pathogenetics and Predisposing Factors

Embryologically, the EAC is formed from the pharyngeal groove between the first and

second branchial arches, i. e. ectoderm, lined by the squamous epithelium. Epithelial skin from the tympanic membrane (TM) migrates towards the ear canal and carries keratin debris for removal. The basic mechanical characteristic of the EACC is found to be the narrowing or obstruction in the outer ear canal that blocks this epithelium migration. The obstruction contributes to cholesteatoma formation by creating an entrapment or isolation pockets of keratin debris *(8, 9)*. Bunting et al. proposed that the close contact between the skin and the bone of the canal leads to epithelial abnormality with increased keratotic activity, which can result in cholesteatoma *(20)*. According to the study by Brookes and Graham, the obstruction of the EAC causes cholesteatoma through its involvement in epithelial desquamation, which leads to a collection of squamous epithelial debris *(21)*.

This close contact or obstruction may occur in the ear canal caused by surgery, trauma, radiation, stenosis following osteoma, exostosis, congenitally, inflammation or years of bisphosphonate treatment. In those cases, it is termed secondary EACC *(14)*. In 1992, Holt divided EACCs in five categories based on different aetiologies – congenital, posttraumatic, iatrogenic, spontaneous, post-obstructive or post-inflammatory *(10)*. The simple division into primary/idiopathic/spontaneous EACC and secondary EACC has later been well established and most commonly used. Primary EACC therefore develops in the absence of known prior processes occurring in the affected ear. According to recent studies, it may be more common than secondary EACC *(5, 22)*. None of our patients had any known identifiable aetiological factors and were therefore considered primary EACCs.

The etiopathogenetic events of primary EACC are unclear, as well as the predisposing factors for its development. It has been priorly suggested that underlying local periosteitis causes the stenosis in primary EACC through the mechanisms of a reactive process *(12)*. More recently, the hypothesis of abnormal epithelium migration and proliferation in individuals developing primary EACC has been proposed by Makino and Amatsu. Their study has shown that the migratory rate of the epithelium in the inferior wall of the external ear canal is slower in patients with primary EACC than in those without EACC *(18)*. This theory is debatable, since it has recently been challenged by a study, which showed no difference in the rate of epithelial migration between normal ears and those affected by EACC *(32)*. This reduction or loss of normal epithelial migration, however, does occur in the aging process, which is probably the reason for higher EACC occurrence rates in the elderly *(19)*. Other predisposing factors have been suggested, such as the disruption of local microcirculation due to repeated microtrauma from the use of cotton swabs, smoking, diabetes mellitus, hearing aids etc. The dehiscence of the petrotympanic fissure, the persistence of first branchial cleft epithelium and other branchial arch anomalies also result in the retention of epithelial masses and are possible risk factors for EACC *(13–17, 23)*.

Recent immunohistochemical studies have given researchers additional insight into EACC development. Increased levels of various growth factors in patients with EACC have been reported, such as an elevated vascular endothelial growth factor and hepatocyte growth factor. These indicate tissue hypoxia and increased apoptosis of epithelial cells and debris formation, respectively, and are a step further in understanding this clinical entity *(24, 25)*.

In our study, the patients were all over 65 years old and had a positive medical history for comorbidities, one of the patients was wearing a hearing aid. These anamnestic facts are consistent with the literature describing the EACC risk factors and could contribute to disease development in our patients.

Location in the ear canal and extension to the surrounding tissues

The most common location of idiopathic EACC is known to be the posterior inferior canal wall. Relatively poor blood supply to the skin along the inferior aspect of the canal, the effect of gravity and chewing movements have all been found to promote the invasion of cholesteatoma in this part of the EAC *(11, 13).*

While most EACCs remain limited to the external canal, the disease can spread to surrounding structures. Cholesteatoma extension is often larger than suggested by clinical examination *(26).* It can invade the structures anteriorly to the TMJ, inferiorly to the hypotympanum, posteriorly to the mastoid, where it can cause damage to the facial canal, semicircular canals, or sigmoid sinus. The mass can spread superiorly to the facial nerve or to the base of the skull. The tympanum and the TM are usually not affected, except in advanced lesions of middle ear invasion, when it is difficult to differentiate it from middle ear cholesteatoma. However, the TM may be inflamed and sometimes perforated. In less extended lesions of the middle ear, the distinction between middle and external ear cholesteatoma can be made based on the location of the main body of the lesion and the direction of TM destruction (inside out). *(8, 22, 27).* According to He et al., EACCs have five direction of expansion pathways: lesions can spread downward or forward within the temporal bone adjacent to the inferior or anterior wall of the EAC and are found to be less destructive. The other two invasion pathways are backward or upward. These invade into the mastoid air cells or through the lateral attic wall upward into the epitympanum. They can invade the temporal bone air cells and can spread rapidly. The last pathway is the inward invasion, which means lesions extend medially to the TM, resulting in invagination, ischemia, or perforation. These can invade through the TM into the tympanic cavity *(11).*

Owen et. al reported that the most common adjacent structure involvement of the EACC is the fibrous capsule of the TMJ, followed by the mastoid and the middle ear *(5).* In a study by Heilbrun et al., disease extension was found in all their 13 subjects; in five cases, into the middle ear, in four cases, as erosion of mastoid air cells, and in two cases, erosion of the facial nerve canal. Consistently with similar studies, they reported it was rare for lesions themselves to break inward through the TM into the tympanic cavity. Shadows on CT scans around the ossicular chain were common according to their study, which they attributed to infections rather than EACC involvement. They concluded that the TM appeared to be a resilient natural barrier to cholesteatoma invasion. As the disease seems to easily destroy bone structures, TM tissues are more difficultly impacted by cholesteatoma destructive mechanisms *(14, 17, 22).*

The invasion of the EAC can result in complications, such as facial palsy, ossicular erosion, or labyrinthine fistula. A case of EACC presenting as a cerebellar abscess has been reported, despite the extremely rare occurrence of intracranial complications *(8, 28).*

Consistent with the recent literature, in all our cases the inferior portion of the EAC was involved, which is the most commonly described location. In the first patient, the mass was occupying the anterior inferior portion of the right EAC spreading to the TMJ area and into the posterior canal wall. The cholesteatoma and dead bone tissue in the second patient undermined the lower part of the TM and locally invaded the tympanic cavity into the hypo- and mesotympanic areas, cranially up to the epitympanum and minimally invaded the latter. In the last patient, cholesteatoma with osteomyelitis and destruction of the posterior ear canal

wall was described. The mass was spreading from the posterior canal wall into the mastoid cavity. The mild and unspecific clinical signs and symptoms may explain the reason our patients presented in the tertiary centre relatively late after the disease onset (three weeks minimum), when the cholesteatoma had already invaded the neighbouring structures.

Clinical Presentation

EACC usually presents with non-specific symptoms. The most common symptoms reported in the literature are otalgia and otorrhea. Otalgia has not been consistently described, ranging from cases of vague, mild discomfort to chronic dull pain and severe pain *(9, 10, 12)*. Owen et al. propose that otalgia is a symptom already related to advanced cases of cholesteatoma with the invasion of surrounding structures, as it was significantly present only in patients with EACC invading the TMJ and the mastoid. Otorrhea is another symptom they found inconsistently described and were unable to relate it to the extension of the EACC or coexisting symptoms. Subjective symptoms such as »fullness« or »occlusion feeling«, which diminishes after ear cleansing, were found to be more consistently reported by patients. Researchers in the study also found a relatively large share of patients presenting as asymptomatic: 24% of all patients. This is consistent with the previously reported rate in literature, between 25 and 31% *(5)*. Hearing loss is traditionally not a common symptom in EACC, unless described as a blockage of the ear canal or in cases of middle ear invasion *(5, 6)*. In a study by Vrabec and Chaljub, they reported cases of 12 patients with spontaneous EACC and no hearing loss until late in the course of the disease *(29)*. Conversely, in a study by He et al., the most common symptom they found was hearing loss, or sense of blockage, in 78.7%, followed by acute or chronic otalgia in 73.4% and otorrhea in 28.2%, others being tinnitus, pruritus; in one case, they also found facial paralysis. They proposed the patients mostly seek treatment with acute symptoms, such as otalgia or otorrhea, whereas hearing loss described as blockage is also present in this disease before, tracing retrospectively *(11)*. It can be proposed that these additional unspecific symptoms are often not reported as the main complaints as they develop more gradually and are, therefore, noted to a lesser extent.

In this paper, we only report advanced cases of EACC. Our findings are consistent with the existing literature, which describe additional symptoms in advanced lesions, apart from the most common ones. Two of our cases reported hearing loss and otalgia, while the other presented with otorrhea and ear canal pruritus. All the symptoms persisted for minimally 3 weeks and were unspecific for this disease. The patients' complaints were subjectively not as severe as one would have expected in an advanced stage of the disease. These facts stress the importance of early suspicion of EACC in patients with prolonged unspecific symptoms.

Importance of Imaging

To obtain more information about a mass presenting in the EAC following thorough clinical examination and suspicion of EACC raised in otoscopy, appropriate imaging is essential. Often the extent of the disease is clinically underestimated. To delineate any soft tissue in the temporal bone, HRCT is the imaging modality of choice when suspecting cholesteatoma. A CT scan aids to confirm the diagnosis to assess the extension of the disease and to plan the treatment. In 50% of cases, it usually shows eroded contact surface between the cholesteatoma and the ear canal and osteolysis. A soft tissue mass in the absence of osteolysis, however, is unspecific on HRCT to exclude other differentials. An MRI with

diffusion weighted imaging (DWI) should be conducted in that case. An MRI without DWI is non-specific as granulation tissue (otitis maligna externa) and shows similar patterns of signal through this imaging modality *(13, 17, 22, 27)*.

Differential Diagnosis

Especially in the early stages of the disease, EACCs are often misdiagnosed. This is due to their unspecific clinical appearance with erosions, inflammation and keratin accumulation, while yielding non-specific complaints from patients. Physicians need to differentiate EACC from conditions such as malignant otitis externa, keratosis obturans, post-inflammatory medial canal fibrosis, Langerhans' acromegalic disorder, malignant tumours and otomycosis non-responsive to medication *(9)*. A soft tissue plug in the EAC is seen in keratosis obturans and in post-inflammatory medial canal fibrosis. The latter is usually differentiated by patient history of recent EAC inflammation *(8)*.

Keratosis obturans (KO) is a disease, where the accumulation of desquamated keratin in the external canal without bone erosion occurs. KO is more commonly observed in younger individuals and presents bilaterally with acute severe pain with conductive hearing loss. Otorrhea is rarely reported. On imaging, smooth enlargement of the ear canal is observed without bone destruction or sequestrum formation. The TM is usually affected by the pathological process, contrary to EACC, where it is mostly normal. The differentiation between the two entities is clinically important because the management of KO is usually conservative *(4, 5, 8, 27)*.

Malignancies must also be ruled out in cases of EACC. On imaging, malignant otitis externa and squamous cell carcinoma (SCC) of the EAC both show osteolysis and can appear as EACC. Clinical features usually distinguish these entities from one another. Malignant otitis externa is an infection of the EAC that typically affects older diabetic patients. It is a rapidly progressing disease with observable granulation tissue with diffuse osteolysis in the EAC presenting with severe otalgia, otorrhea and hearing loss. On the contrary, EACC progresses in a slower manner. In SCC, the lesions usually involve the ear canal as part of tumour dissemination, rather than being the originating location. Despite this fact, biopsy is usually the only definite distinction tool to differentiate the two conditions *(12–14, 17)*. Another differential is an EAC osteoma, which is a rare benign tumour. It usually starts at the tympanomastoid or tympanosquamous suture near the osteocartilaginous junction as a small bony mass. Patients remain asymptomatic unless there is obstruction of the EAC *(30)*. Langerhans acromegalic disorder is also a disease with similar manifestations in the ear canal, especially due to the most common symptom of otorrhea. It is a condition that occurs in children; retroauricular edema in the mastoid is additionally seen with a typical laboratory finding of an increased erythrocyte sedimentation rate, which is usually normal in younger patients with EACC *(17, 30)*.

In our patients, CT scans demonstrated an extended disease pattern guiding the clinician to the diagnosis of EACC, but biopsy was necessary to undoubtedly differentiate lesions from malignant conditions.

Staging and Treatment

Several staging systems are available for EACC. On the basis of histopathology and clinical symptoms, Naim (2005) classified EACC into four stages: Stage I meaning canal epithelium hyperplasia, stage II meaning periosteitis, Stage III meaning canal erosion, and Stage IV meaning erosion of the adjacent structure *(31)*. The Shin (2010) staging system, based on both clinical and imaging findings, is more convenient for

clinical application. It differentiates between four stages. Stage I indicates that the EACC lesion is limited to the external auditory canal, stage II means that the EACC lesion invades the tympanic membrane and middle ear, in stage III the cholesteatoma creates a defect of the EAC and involves the mastoid air cells, and stage IV indicates that the EACC lesion is in the TMJ and beyond the temporal bone. This staging system describes treatment used in their study for each stage. In stage I, they recommend local care or canaloplasty, stage II recommends canaloplasty and tympanoplasty, stage III canaloplasty with mastoidectomy with or without tympanoplasty, and removal of mass by various approaches is recommended for stage 4 *(32)*. A newer staging system has been proposed in 2021 by He at al. as the Shin system for them fails to illustrate the severity of the disease in more advanced lesions. Stage I contains invasion without bony lesions, stage II invasion within the EAC and possible bone erosion seen as a rough edge or localized defect of the bone, Stage III invasion beyond the EAC involving the mastoid air cells or tympanic cavity but within the temporal bone, with subtypes A: backward invasion into the mastoid air cells, B: inward or upward invasion into the tympanic cavity, C: invasion into the tympanic cavity and mastoid air cells. Stage IV means invasion beyond the temporal bone or complications caused by the involvement of structures adjacent to the temporal bone. They suggest treatment plans for separate stages as follows: conservative treatment with ear canal curettage of the EAC for stage I. For Stage II lesions, which are limited to the EAC and do not invade the tympanic cavity or mastoid cells, curettage with additional canaloplasty, or EAC wall reconstruction in larger defects. In lesions that involve the mastoid (IIIA), a mastoidectomy or partial mastoidectomy may be the treatment of choice. If the lesion invades the tympanic cavity (IIIB), tympanoplasty may be necessary in large TM perforations. For Stage IV lesions, the surgical approach and technique depend on the extent of the invasion *(11)*.

All of our patients underwent surgical treatment under general anaesthesia. In patient A, a canal wall down (CWD) modified mastoidectomy was performed due to disease extension. Ear canal curettage was performed in patients B and C to confirm the diagnosis prior to extensive surgical treatment in patient C and as a removal tool in patient B. In a separate further procedure, Patient C had a modified CWD mastoidectomy performed due to mastoid invasion. The posterior canal was removed, but the tympanic cavity was not punctured or altered. All cholesteatomas were removed in total, and histopathology confirmed the diagnosis of cholesteatoma in all patients. Pre- and postoperative audiometric testing was conducted, showing only minor additional conductive hearing loss in patients with a CWD mastoidectomy. This can be attributed to the mentioned surgical modification, which left the patients without significant conductive hearing loss. It needs to be noted that Patient C had severe bilateral combined hearing loss prior to surgery.

The treatment of EACC is, therefore, not standardized and depends on the extent of the condition. This needs to be assessed clinically, by biopsy and imaging modalities. To prevent further disease progression and restore normal epithelial migration in the EAC, the lesions as well as necrosed bone tissue must be fully removed, leaving the canal wall as smooth as possible. Regular follow up with debris cleansing is important to prevent the re-accumulation of keratin.

There is little known information on the recurrence rates in patients with EACS. In one of our patients, a residuum of the disease was found 6 months after initial treatment, requiring re-curettage of the EAC,

which was successfully performed. After surgery, a DWI is the most appropriate imaging option to exclude disease recurrence even in asymptomatic patients with fully removed lesions *(13)*. Our patients are monitored during regular follow-ups and have not shown any signs of disease for at least 4 years.

CONCLUSION

Despite recent reports of a higher incidence of EACC cases, EACC remains a rare disease. Most lesions are limited to the ear canal, but can invade the surrounding tissues. Clinical examination usually underestimates the disease progression. Apart from thorough otoscopic examination, appropriate imaging is crucial for a timely and correct diagnosis. Tissue biopsy is necessary in surgical planning to exclude malignancies. In our patients, the discrepancy between symptom severity and local extent of the disease was evident. This stresses the importance of early disease recognition, especially in persons with associated risk factors, such as advanced age and other comorbidities. Recognizing it as a distinct entity is important as its management is different from that of its differential diagnoses. Ear, nose, throat physicians should consider this a differential in any case of otitis externa maligna, otomycosis non-responsive to medication, keratosis obturans, neoplasm of the EAC and in patients with prolonged non-specific symptoms, such as otalgia and otorrhea. The case of EACC reoccurrence in one of our patients demonstrates the significance of regular follow-ups with imaging even in fully removed lesions.

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