Inner Ear Infections (Labyrinthitis)

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Introduction

Infection of the inner ear, or labyrinthitis, can be caused by a variety of pathogens. The diagnosis is clinical and based on the findings of and/or vertigo in the setting of a current or recent infection, particularly otitis media or meningitis. Physical exam findings are largely determined by the underlying cause of the infection; findings that specifically suggest involvement of the inner ear are spontaneous nystagmus and sensorineural hearing loss. It should be determined whether the causative agent is bacterial or viral so that appropriate treatment may be administered. Audiometric testing should be obtained at presentation and resolution of the infection. Laboratory tests such as white blood cell count and differential, C-reactive protein, erythrocyte sedimentation rate, and lumbar puncture with cerebrospinal fluid (CSF) analysis are unreliable as indicators of labyrinthitis, though these may be abnormal in cases of severe infection. Imaging with computed tomography (CT) or magnetic resonance imaging (MRI) is not required to diagnose labyrinthitis, but is often performed to evaluate the extent of the underlying infection. Imaging findings that support a clinical diagnosis of labyrinthitis may be bony erosion through the otic capsule on CT, or enhancement of labyrinthine structures on MRI with contrast.

The treatment of labyrinthitis depends on the etiology. In general, once an infection has reached the inner ear, aggressive treatment is warranted to try to prevent permanent and complete loss of cochleovestibular function and spread to intracranial structures. Treatment consists of anti-infective and anti-inflammatory medications, surgical drainage of abscesses, and supportive care for associated symptoms such as vertigo, nausea, vomiting, dehydration, and pain. Acute suppurative labyrinthitis can progress to intracranial infectious complications and requires prompt treatment. The inner ear is exquisitely sensitive to insults such as infection, and in many cases the patient is left with permanent hearing loss and vestibular dysfunction following an inner ear infection.

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Anatomy

The inner ear, or labyrinth, is contained within the dense otic capsule of the temporal bone, and consists mainly of the cochlear and vestibular systems with their corresponding sensory organs for detecting sound and movement, respectively. The cochlea, vestibule, semicircular canals, and intracranial subarachnoid space are in continuity, with CSF flowing from the subarachnoid space through the cochlear aqueduct to the labyrinth. The oval and round windows are interfaces between the inner and middle ears, and allow for sound pressure to be transduced to electrical signals in the cochlea. The oval window contains the stapes footplate, a thin bone surrounded by ligament, and the round window is membranous. Normal labyrinthine anatomy and histology is shown in Fig. 7.1.

Pathophysiology of Labyrinthitis

The structure of the inner ear, lying deep within the temporal bone and surrounded by dense otic capsule bone, renders it relatively well protected from infection. When infection does occur, routes of entry for the infectious agents are typically direct spread from the middle ear, via the oval or round window, or through CSF. Less frequently, infection may enter through erosion of the otic capsule bone from chronic otitis media with cholesteatoma.

The auditory and vestibular sensory organs contained in the inner ear are exquisitely sensitive to insults such as infection and trauma. Inflammation of the inner ear, or labyrinthitis, typically manifests with symptoms of hearing loss and dizziness. The severity of these symptoms is

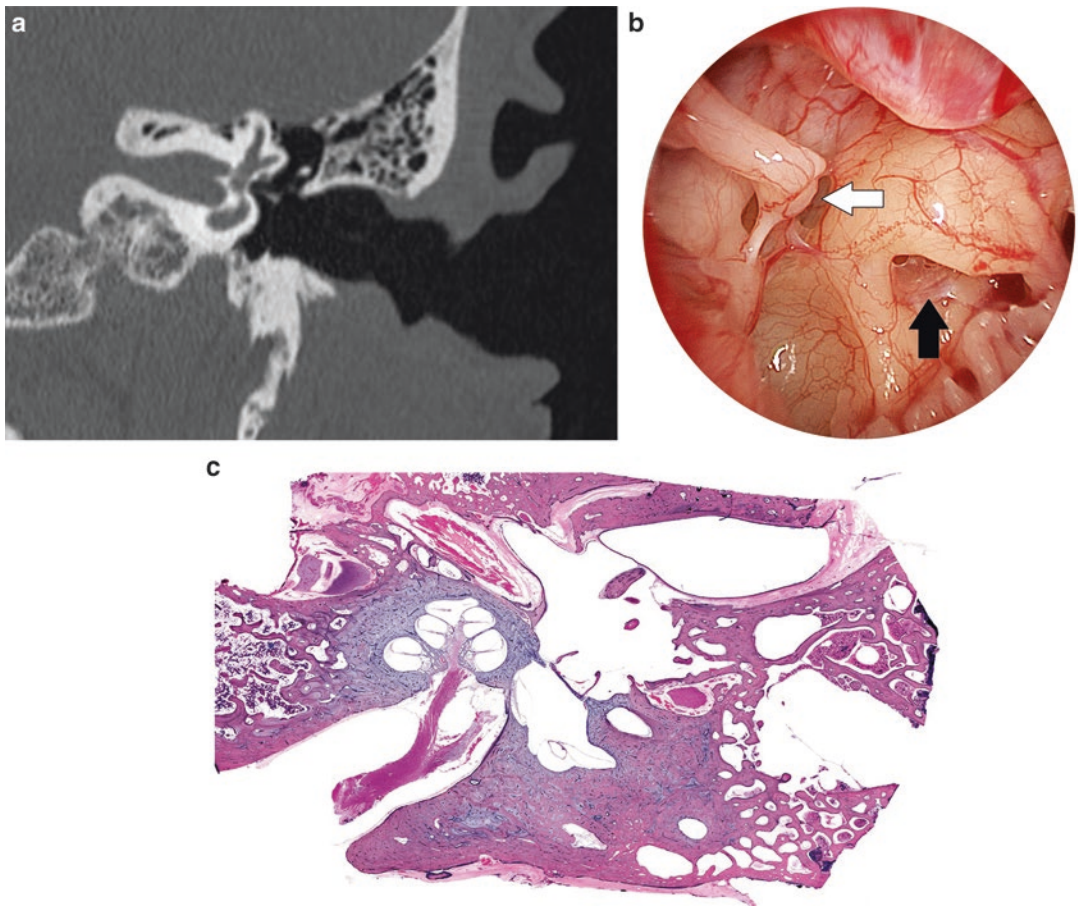

Fig. 7.1 (**a**) CT image in the coronal plane of a normal temporal bone. (**b**) Endoscopic image of the middle ear showing the oval (white arrow) and round (black arrow) windows (Image courtesy of Daniel J. Lee, MD. Unpublished) (**c**) Histopathologic section of a normal cochlea. (Image courtesy of Massachusetts Eye and Ear Temporal Bone Laboratory. Unpublished)

variable, but they often are severe and leave the patient with permanent cochleovestibular dysfunction. Otogenic labyrinthitis may spread to the intracranial space and cause meningoencephalitis, septic thrombophlebitis, and abscesses.

We will discuss specific presentations of infectious labyrinthitis using a classification scheme based on the pathogenesis and clinical presentations of disease.

Bacterial Infections

Serous Labyrinthitis

Serous labyrinthitis is a sterile inflammation within the labyrinth. It is presumed to occur when bacterial toxins or host inflammatory mediators enter the labyrinth, without direct spread of bacteria into the inner ear. This process is not well characterized, but animal studies have demonstrated that pneumococcal proteins applied to the middle ear space result in inflammation and hair cell damage in the inner ear [1–4]. Serous labyrinthitis typically occurs in the context of acute or chronic otitis media (see Chap. 6). In this situation, it is thought that otitis media generates toxins and inflammatory mediators, which then cross the round and oval windows or, rarely, a labyrinthine fistula to reach the inner ear [5]. Although acute otitis media is very common, serous labyrinthitis is rare, reported as complicating <1% of cases of acute otitis media [6, 7]. Serous labyrinthitis can also occur in the setting of meningitis, in which case it may not be noticed due to the more severe symptoms of meningitis.

In serous labyrinthitis, patients suffer SNHL and vestibular symptoms of variable severity. Mild cases may return to normal function following treatment. Severe cases may be lethal to the sensory cells and cause permanent hearing loss and vestibular dysfunction (Fig. 7.2). In the acute period, serous and suppurative bacterial labyrinthitis cannot be differentiated. A diagnosis of serous labyrinthitis is presumed retrospectively if there is some recovery of auditory and vestibular function.

Treatment requires drainage of the middle ear effusion by myringotomy if a tympanic membrane perforation has not already occurred. A tympanostomy tube may be placed, which ensures that a drainage and ventilation route remains patent. This tube also facilitates delivery of antibiotic and corticosteroid ear drops to the middle ear space. Systemic broad spectrum antibiotics with CSF penetration should be used initially, and then narrowed based on culture and sensitivity results. This is because even though serous labyrinthitis is sterile, the condition cannot be differentiated from suppurative (bacterial) labyrinthitis. Systemic corticosteroids should be used in an attempt to decrease damage to the audiovestibular sense organs and reduce subsequent labyrinthitis ossificans [8, 9]. Vestibular symptoms are treated symptomatically.

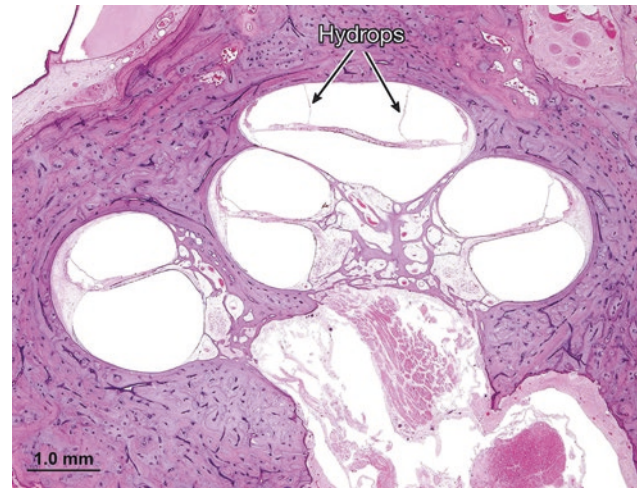

Fig. 7.2 Histopathology of a patient with serous labyrinthitis. (Image courtesy of Massachusetts Eye and Ear Temporal Bone Laboratory. Unpublished)

Otogenic Suppurative Labyrinthitis

Otogenic suppurative labyrinthitis is caused by contiguous spread of bacterial infection into the inner ear from surrounding spaces in the temporal bone, most frequently the middle ear. The most common situation is for cholesteatoma in the middle ear to erode through the otic capsule bone overlying the horizontal semicircular canal, producing a pathway for direct bacterial spread into the labyrinth (Fig. 7.3). Suppurative labyrinthitis tends to cause severe hearing loss and vertigo with permanent auditory and vestibular function loss. After the infection resolves, the labyrinth fills with fibrous and bony tissue, a process called labyrinthitis ossificans (Fig. 7.4). If left untreated, otogenic suppurative labyrinthitis frequently leads to intracranial complications.

Diagnosis and treatment are similar for suppurative and serous labyrinthitis, with the exception of surgical approaches. Empiric broad-spectrum antibiotics should be started as soon as the diagnosis of acute suppurative labyrinthitis is suspected. Most otogenic suppurative labyrinthitis results from cholesteatoma, and surgical removal of the cholesteatoma is critical for definitively treating the inner and middle ear infections. Myringotomy with or without tympanostomy tube should still be performed promptly to drain the middle ear effusion and allow antibiotic and corticosteroid ear drops to reach the middle ear space. Tympanomastoidectomy with the removal of cholesteatoma should occur urgently to prevent intracranial spread of the infection. If cochlear implantation is a possibility, early implantation, before labyrinthitis ossificans begins to ablate the cochlear lumen, should be considered [10].

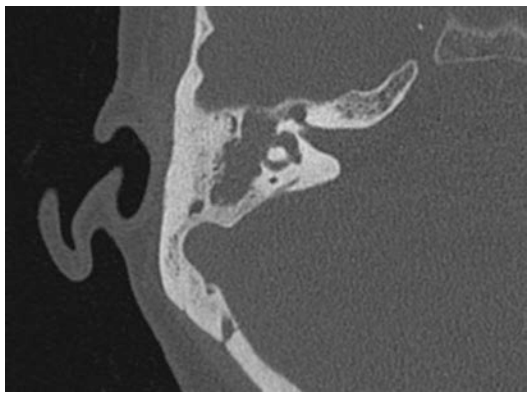

Fig. 7.3 CT image in the axial plane showing chronic otitis media with cholesteatoma that has eroded into the horizontal semicircular canal. The labyrinthine fistula is a route of bacterial spread from the middle ear to the inner ear

Meningogenic Suppurative Labyrinthitis

Sensorineural hearing loss is a common sequela of bacterial meningitis. There is a higher incidence of SNHL following pneumococcal than meningococcal meningitis (14–69% versus 3–40%, respectively) [11]. The route of spread seems to be through the cochlear aqueduct and internal auditory canal, based on post-mortem temporal bone histopathology [12]. Meningitis can result in partial or complete fibro-ossification of the bilateral cochleae and vestibular systems. Aside from pneumococcal meningitis, the protective effects of administering adjuvant corticosteroids in acute bacterial meningitis are unknown. A Cochrane Review reviewed 25 studies (4 high quality, 14 intermediate quality, 7 low quality) and concluded that the high quality studies found no benefit of corticosteroids in reducing the incidence of severe hearing loss [8]. A small retrospective study (ten pediatric patients) undergoing cochlear implantation for SNHL occurring after meningitis (pneumococcal in 9) concluded that corticosteroids may prevent the development of labyrinthitis ossificans [9]. Early bilateral cochlear implantation should be considered in cases with bilateral profound sensorineural hearing loss [10].

Viral Labyrinthitis

A broad group of viruses are known to affect the inner ear. Viral infections of the inner ear may affect the labyrinthine organs or their peripheral nerves. In addition to the clinical presentations listed below, there are clearly many acute disorders of the inner ear that are characterized by sudden hearing loss and/or vertigo, such as sudden idiopathic sensorineural hearing loss, laby-

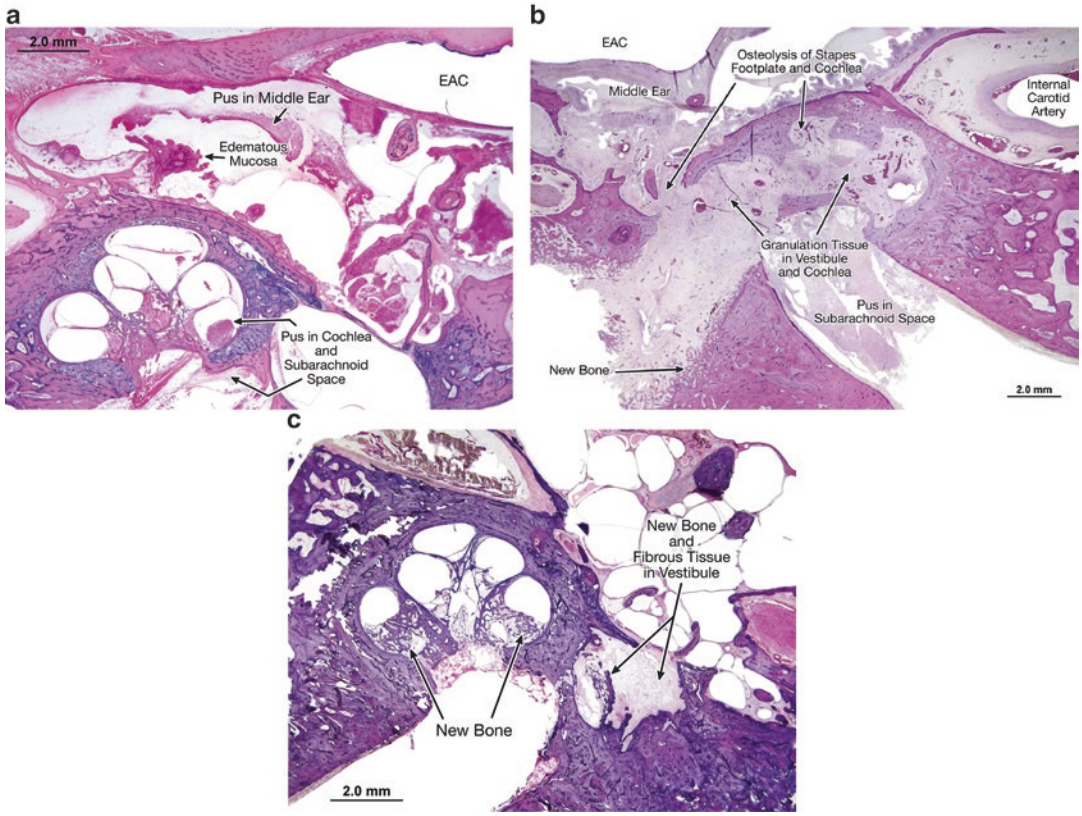

Fig. 7.4 Histopathology of patients with suppurative labyrinthitis and the resulting labyrinthitis ossificans (All images courtesy of Massachusetts Eye and Ear Temporal Bone Laboratory. Unpublished). (**a**) Image shows active otogenic suppurative labyrinthitis. (**b**) Section from a patient with chronic suppurative otitis media and mastoiditis. He died of spread to an epidural abscess and purulent meningitis. (**c**) Image shows labyrinthitis ossificans many years after a patient suffered hearing loss from a febrile illness

rinthitis, or vestibular neuritis, that are attributed to viral causes but lack definitive pathologic or clinical evidence.

Herpes Zoster Oticus (Ramsay Hunt Syndrome)

Herpes zoster is caused by the varicella zoster virus (VZV) that also causes chickenpox and shingles. The virus remains latent in the central nervous system and possibly the geniculate ganglia. Reactivation often occurs years later in settings of biologic stress or immunosuppression. When reactivation occurs in nerves that innervate the ear, this is termed herpes zoster oticus (also called Ramsay Hunt syndrome).

Frequently, the first symptom is burning pain in the region of the ear. This is followed by a vesicular eruption of the external auditory canal and concha, and sometimes surrounding dermatomes. Facial paralysis, hearing loss, and vertigo may occur after the onset of pain, and before or after vesicular eruption. Other cranial neuropathies may also develop. Diagnosis is made clinically and may be confirmed by testing scrapings of the base of the vesicular lesions for the presence of VZV.

About half of the patients with herpes zoster oticus retain some permanent facial motor disturbance and a few have permanent complete paralysis [13]. Prognosis is poorer for patients with complete paralysis, age over 50, or incomplete eye closure with a dry eye [14–16]. For hearing loss, some recovery is expected with resolution of the infection; however, with severe losses the

recovery is rarely complete [17]. Studies suggest that early treatment with an antiviral medication (e.g., acyclovir or valacyclovir) and corticosteroids improves the outcome of facial paralysis, though high-quality evidence is lacking [18]. Consultation with an ophthalmologist should be pursued if there is any concern about ocular involvement. Surgical decompression of the facial nerve for facial paralysis in this setting is not indicated.

Congenital Cytomegalovirus (CMV)

Cytomegalovirus is a DNA virus that belongs to the Herpesviridae family. Congenital CMV produces symptomatic infection at birth (e.g., petechiae, hepatomegaly, splenomegaly, hepatitis, chorioretinitis, central nervous system abnormalities) in a minority of infected infants. Asymptomatic congenital CMV presents without any of the above findings, but may include undetected SNHL. Some children may have normal hearing at birth but suffer progressive hearing loss. Importantly, the risk of SNHL from congenital CMV is decreased with early antiviral therapy, so high awareness and vigilance by clinicians is critical.

Congenital CMV infection is the most common cause of non-syndromic SNHL in children. Cytomegalovirus affects approximately 0.6% of live births in developed countries, and 85–90% of congenital CMV infections are asymptomatic at birth [19]. However, approximately one-third of infants born with symptomatic CMV and 6–25% of infants with asymptomatic CMV will develop SNHL [19, 20]. The onset of hearing loss may be delayed. A recent meta-analysis estimates the prevalence of hearing loss due to CMV as approximately 20% in children with hearing loss of unknown origin [19].

There is no pathognomonic pattern of SNHL from CMV. It may be unilateral or bilateral, with variable frequency, severity, and progression characteristics. Sixty percent of children with CMV-related hearing loss will have passed their newborn hearing screening, and hearing loss may present at any time from birth up to 9 years of age [20, 21]. The exact mechanism of CMV-induced hearing loss is not known, but inflammation of the labyrinth in response to the infection appears to play some role [22].

Congenital CMV is diagnosed by testing urine or saliva for CMV in the very early neonatal period. Polymerase chain reaction (PCR) and viral cultures are the test methods used. After 2–3 weeks, postnatal and congenital CMV cannot be distinguished based on saliva or urine samples, so diagnosis is based on retrospective testing of a dried blood spot sample drawn within the first week of life. Sensitivity and specificity of urine or saliva PCR is reported at >97% [23]. Dried blood spot testing has poor sensitivity (34%) but excellent specificity (99.9%) [24].

A randomized, controlled trial published in 2003 evaluated the effect of 6 weeks of ganciclovir, an intravenous antiviral agent, on change in audiometric thresholds in neonates with symptomatic CMV involving the central nervous system [25]. This trial demonstrated that treatment with ganciclovir significantly improved or stabilized hearing at 6 months compared with controls. However, almost two-thirds of the infants treated with ganciclovir developed significant neutropenia (all reversible on cessation of the drug). A more recent randomized prospective trial (published 2015) compared audiometric and neurodevelopmental outcomes in neonates with symptomatic congenital CMV who received 6 weeks versus 6 months of oral valganciclovir [26]. Valganciclovir is a prodrug of ganciclovir. The longer administration led to modestly better hearing and neurodevelopmental test scores at 24 months [26]. At 24 months, hearing remained normal or was improved in 77% of the 6-month group versus 64% of the 6-week group. Approximately 20% of the infants developed grade 3 or 4 neutropenia during the first 6 weeks of the trial (when both the groups received valganciclovir), but only 3% required a temporary cessation of the drug. The incidence of neutropenia during the remaining 4.5 months of the trial was similar between the two groups, and no child required temporary cessation of the drug. Treatment of congenital

CMV with valganciclovir is currently limited to infants born with symptomatic congenital CMV as no prospective trial has evaluated the efficacy or safety of this medication in infants whose only manifestation is SNHL.

Measles (Rubeola)

Measles is caused by a paramyxovirus and is highly contagious. A live virus vaccine against measles was licensed in the U.S. in 1963, and since then the disease has become very rare in the U.S. However, measles still occurs in unvaccinated populations worldwide (36 cases per million population annually). Of infected patients, 0.1% develop acute encephalitis and 0.2% die from respiratory or neurologic complications [27]. Measles has been implicated as a cause of bilateral moderate to profound loss of auditory and vestibular function [17, 28]. Persistent measles virus within the otic capsule has been proposed as a cause of otosclerosis, supported by findings of viral-like particles and measles virus gene products in active otosclerotic lesions [29–37].

Mumps

Mumps is a highly contagious viral illness that is discussed in depth in Chap. 23. Mumps may cause meningoencephalitis and/or SNHL. The hearing loss tends to be unilateral and of variable severity. Vestibular symptoms are also frequently present.

Maternal Rubella

Rubella infection during pregnancy can result in significant teratogenic effects to the fetus, with SNHL being the most common manifestation [38–40]. The pattern of hearing loss tends to be flat (i.e., pure tone thresholds are elevated to a similar degree at all frequencies) and considerably different between the two ears [41]. The mechanism of hearing loss seems to be from both direct cytopathogenic effects from virus-induced apoptosis and inhibition of cell division [40]. The characteristic otopathologic finding is cochleosaccular dysplasia [17]. Treatment is similar to other forms of sensorineural hearing loss, with listening strategies, amplification, and cochlear implantation as indicated.

Infectious Causes of Facial Paralysis

Although the facial nerve is not properly part of the inner ear, it does pass through the temporal bone in close proximity to the cochlea and labyrinth. Infectious causes of facial paralysis without suppuration are discussed here. For a discussion of facial paralysis with otitis media or mastoiditis, see Chap. 6.

Herpes Simplex Type 1

The cause of idiopathic facial palsy, or Bell's palsy, is unknown, but a theory is that it may be caused by *Herpes simplex* virus type 1 [42–44]. The diagnosis of Bell's palsy is made clinically. Treatment is with oral corticosteroids, with or without oral antivirals. The current American Academy of Otolaryngology—Head and Neck Surgery (AAO-HNS) guideline on Bell's palsy recommends treatment of adults (age ≥16) with oral corticosteroids, starting within 72 h of symptom onset [45]. Early corticosteroid treatment results in recovery of normal facial function by 9 months in approximately 12% more patients than those given placebo (94% versus 82%) [46]. No benefit has been demonstrated for treating Bell's palsy with antiviral therapy versus placebo, however, and the AAO-HNS guideline strongly recommends against antiviral treatment alone [45]. The guideline also notes that large randomized trials have found no benefit of corticosteroids plus antivirals over corticosteroids alone, but suggests combination therapy as an "option" because the published trials could not exclude a small, non-significant benefit [45]. A survey of neurotologists showed that most prescribe both corticosteroids and antivirals, and conclusions from a 2015 Cochrane Review support this practice [47, 48].

The prognosis for complete recovery of facial function in Bell's is excellent if paralysis is incomplete. For complete paralysis with axonal degeneration of >90%, measured by electroneuronography (ENoG) and absence of muscle activity on volitional electromyography (EMG), middle fossa craniotomy and surgical decom-

pression of the facial nerve may be considered within a 14-day window of symptom onset [48–50], although this is controversial because of the poor quality of available evidence (graded as "D" by the AAO-HNS) [45]. Randomized controlled trials are not available. A case series by Gantz et al. retrospectively combined the experience of three U.S. centers (Iowa, Michigan, Texas) over many years (≤15 years) in treating a total of 31 patients with surgical decompression [49]. The study was initially designed in 1982 as a prospective trial involving 22 centers, but only three enrolled more than one patient. The study allowed patients who met criteria (complete paralysis with axonal degeneration of >90% plus absence of muscle activity) to "self-select" for surgery versus corticosteroids. The early years of the study allowed surgery for up to 21 days after symptom onset but this was later revised to 14 days. The results favored surgery within 14 days versus corticosteroids, and noted that patients who underwent surgery 14–21 days after symptom onset had the same outcomes as the corticosteroid group. A retrospective case series by Cannon et al. evaluated outcomes in 14 patients who met the Gantz criteria and who were treated with surgery at a single center over a 12-year period [50]. The study had no control group. The majority (73%) regained normal (27% with House-Brackmann 1) or near-normal (47% with House-Brackmann 2) return of facial nerve function.

Lyme Disease

Lyme disease is caused by the spirochete *Borrelia burgdorferi*, transmitted by tick bite. The clinical presentation and progression varies significantly. A subset of patients with Lyme disease may develop meningoradiculitis and neuropathies of multiple cranial nerves. Of patients who develop meningoradiculitis, it is estimated that 60% will have facial palsy, with 30% of these being bilateral [51]. Patients who live in or visit Lyme-endemic areas and who present with unilateral facial palsy or other symptoms of Lyme disease, including multiple cranial neuropathies or bilateral facial paralysis, should be tested for Lyme disease. Treatment is with doxycycline.

Otosyphilis

Syphilis is caused by the spirochete *Treponema pallidum*, and may be congenital or acquired. Otosyphilis, or syphilitic involvement of the labyrinth and temporal bone, is a common feature in both congenital and acquired syphilis. In both forms, hearing loss may be sudden or progressive, is usually bilateral, and may or may not include vestibular symptoms. Frequently, the symptoms of otosyphilis mimic those of Meniere's disease. Pathologically, otosyphilis is characterized by progressive endolymphatic hydrops, degeneration in the sensory and neural structures, and inflammation and resorption of the bony labyrinth (Fig. 7.5). Otosyphilis is treated with high-dose intravenous penicillin. Corticosteroids are often given as well, although no randomized controlled trials have been performed to evaluate the value of this adjunctive therapy. Treatment often halts progression of hearing loss, and in some cases hearing may improve [52].

Conclusion

Labyrinthitis is characterized by sensorineural hearing loss and/or vestibular dysfunction. It can be caused by viruses or bacteria, and determination of the pathologic agent is important for directing treatment. Treatment is often with a combination of antibiotics and empiric corticosteroids. If suppuration is present, it should be drained to expedite resolution of the infection and prevent intracranial spread. Labyrinthitis often leaves patients with permanent hearing loss and vestibular dysfunction. Labyrinthitis ossificans complicates later cochlear implant placement, and early cochlear implantation should be considered in patients with profound sensorineural hearing loss from labyrinthitis.

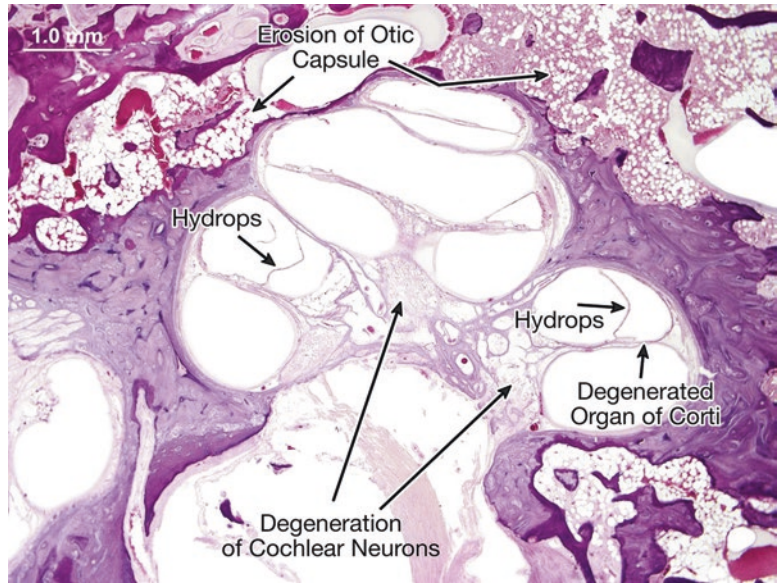

Fig. 7.5 Histopathology of a patient with otosyphilis. (Image courtesy of Massachusetts Eye and Ear Temporal Bone Laboratory. Unpublished)

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