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Neurological Complications of Acute and Chronic Otitis Media

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Abstract

Purpose of Review The aim of this study is to discuss the symptoms, diagnosis, and management of the neurologic complications of acute and chronic otitis media.

Recent Findings Antibiotic therapy has greatly reduced the frequency of complications of otitis media. However, it is of vital importance to remain aware of the possible development of neurologic complications. There is a trend toward less severe presenting symptoms including otorrhea, headache, nausea, and fever, with altered mental status and focal neurologic deficits presenting later. In order to reduce morbidity, early deployment of a multidisciplinary approach with prompt imaging and laboratory studies is imperative to guide appropriate management.

Summary Complications of acute and chronic otitis media may present with neurologic signs and symptoms. It is important to recognize the possible otitic origin of such complications to ensure proper management and to decrease overall morbidity and mortality

Keywords Acute otitis media · Chronic otitis media · Neurologic complications

Introduction

The seriousness of otitis media (OM) and its complications was first noted in 460 B.C. when Hippocrates noted that "acute pain of the ear with continued high fever is to be dreaded for the patient may become delirious and die" [1]. During the 5 years preceding the introduction of sulfonamides, 1 out of 40 deaths in the USA occurred from intracranial complications of OM. The most feared of these were generalized meningitis and brain abscess. Ten years later, after the widespread introduction of antibiotics, the mortality rate from otitis media dropped to 1 out of every 400 deaths [2]. Today, the complications secondary to OM occur in approximately 1 out of every 2000 children treated for OM in developed countries and up to 4 out of every 100 children in developing countries [3–7]. The World Health Organization estimates that 28,000 deaths each year worldwide are attributable to complications of OM and that between 65 and 330 million people suffer from chronic suppurative otitis media [8]. It is of vital importance to maintain a high clinical index of suspicion for the possibility of otitic origin when patients present with the neurologic complications described in this chapter in order to properly manage these complications and decrease overall morbidity and mortality.

Acute otitis media (AOM) is usually defined as a history of acute onset of signs and symptoms of middle ear inflammation in the presence of middle ear effusion. Otitis media with effusion (OME) is defined as "the presence of fluid in the middle ear without signs or symptoms of acute ear infection" [9]. Chronic suppurative otitis media (CSOM) is chronic inflammation of the middle ear associated with tympanic membrane (TM) perforation and chronic discharge (otorrhea), although the definition of "chronic" in the entity of CSOM varies somewhat. The World Health Organization defines CSOM as otorrhea lasting at least 2 weeks [8].

The most frequent cause of AOM involves infection from *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*, whereas chronic CSOM is more likely

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to be caused by *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Proteus mirabilis*, or anaerobic bacteria [10–12]. However, in cases of OM with complications, the most common organisms include *S. pneumoniae*, Streptococcus pyogenes, *P. aeruginosa*, and Staphylococcus species [7, 13–15]. Interestingly, no growth has been noted to occur in up to 36% of isolates of AOM [13].

Complications of acute and chronic otitis media are generally separated into extracranial (intratemporal) and intracranial categories. Intratemporal complications include hearing loss, mastoiditis, subperiosteal abscess, facial paralysis, petrous apicitis, labyrinthitis, and labyrinthine fistula. Intracranial complications include meningitis, epidural and subdural empyema, brain abscess, cerebral venous sinus thrombosis, otitic hydrocephalus, cerebrospinal fluid (CSF) leak, and encephalocele. Each complication will be presented below with a focus on the symptoms, diagnosis, and treatment.

Intratemporal Complications

Hearing Loss

The middle ear is integral in the acoustic transmission of sound and speech from the external world to the cochlea. Types of hearing loss include conductive, sensory, neural, and mixed patterns. Conductive hearing loss involves the interference of sound transmission to the cochlea, sensory hearing loss involves dysfunction of the hair cells within the cochlea, and neural hearing loss generally occurs with dysfunction of the auditory nerve [16]. Sensory and neural hearing loss are often combined as sensorineural hearing loss (SNHL).

The accumulation of fluid and inflammation in OM will almost always include a component of conductive hearing loss. While a mild temporary hearing loss in an older child or adult is inconsequential, a mild-to-moderate conductive hearing impairment in a younger child can be significant, as the first 2–3 years of life are considered a critical period for speech and language development [16]. This can lead to diminished academic achievement and attention/behavioral issues which can often manifest as neurologic and cognitive delay.

In developed countries, approximately 90% of children have at least one episode of AOM before school age, most often between the ages of 6 months and 4 years [17]. Hearing impairment secondary to OM, defined as a persistent hearing loss for the past year of greater than 25 dB, has an overall incidence of approximately 30/10,000 (ranging from a low of 2/10,000 in Western Europe, Australasia, North America, and the Asian Pacific regions to a high of 97/10,000 in South Asia) [18]. In young children, it is especially important to monitor language development due to the concern for early onset SNHL or hearing loss from OM. Well-standardized tools for providing speech assessment such as the *Early Language Milestone Scale* are widely used [19]. A useful screening tool for expressive language milestones which the authors employ in clinical practice is 3–5 words by age 1, 25–30 words and several 2–3 word phrases by age 2 and 200+ words, and simple sentences by age 3 (A. Hotaling).

Diagnosis of hearing loss secondary to OM involves a multidisciplinary approach with otolaryngologic consultation for otoscopic examination to evaluate for the presence of a middle ear effusion and audiogram to identify the type of hearing loss. If a conductive hearing loss is noted, bilateral myringotomy with pressure equalization tube placement (BM&T) may be indicated to decrease the frequency of infections and, most importantly, improve sound conduction and overall hearing.

Acute Mastoiditis

Mastoiditis is a term that describes a number of suppurative complications of both AOM and CSOM, involving a suppurative infection of the mastoid air cells located within the temporal bone. Because the middle ear and mastoid air cells are freely connected via the valveless aditus ad antrum, inflammation or infection of AOM may involve the middle ear with opacification of the mastoid air cells [20].

Acute mastoiditis (AM) is a common complication of AOM presenting with postauricular pain, erythema, tenderness, and/or swelling causing anterior displacement of the pinna. Symptoms of AOM may present 1–2 weeks prior to the symptoms of AM [20]. Otoscopy typically demonstrates a purulent middle ear effusion with or without a perforation.

Acute mastoiditis may also present as a subperiosteal abscess (SA), occurring when infection spreads to the periosteum of the temporal bone along the lateral wall of the mastoid or via the erosion of mastoid cortical bone with extrusion of purulence beneath the periosteum [7, 21–23]. Defining symptoms of a SA include postauricular pain and erythema, protuberance of the upper half of the auricle, and an area of fluctuance postauricularly [20]. A Bezold's abscess is a rare complication of AM involving suppuration breaking through the mastoid tip resulting in a fluctuant mass along the sternocleidomastoid muscle in the posterior cervical triangle [23].

It is important to appropriately manage mastoiditis to prevent the progression to subsequent intratemporal and intracranial complications of AOM and CSOM. Most clinicians today advocate for a more conservative approach to management with BM&T and aggressive intravenous (IV) antibiotic therapy [24•, 25]. If coalescent mastoiditis (breakdown of bony septae within the mastoid cavity) occurs, mastoidectomy may be indicated [26].

Facial Paralysis

Facial nerve paralysis is an uncommon but serious complication of OM with functionally, esthetically, and emotionally devastating consequences. While the incidence of facial nerve

paralysis has significantly declined from the pre-antibiotic era where it occurred in up to 2 out of 100 cases of OM to approximately 1 in 2000 in the post-antibiotic era, prevention and management can be a challenging problem [27–29]. Facial paralysis may result from either AOM or CSOM with or without cholesteatoma (trapped squamous epithelium in the middle ear or mastoid). In children, facial paralysis is more commonly seen in AOM, whereas in adults, CSOM is the more likely culprit occurring in 1–3% of patients with facial paralysis [30, 31].

The etiology of facial nerve paralysis in OM is not well understood, but possible mechanisms include direct neurotoxic effects, inflammation, and edema of the nerve and ischemia [32]. In CSOM, facial paralysis is attributed to erosion of the bony canal by infection or by cholesteatoma compressing the nerve.

Diagnosis of facial paralysis is made based on physical examination. All branches of the facial nerve will be affected. Paralysis can be either gradual in onset as often occurs in CSOM, or sudden onset, more often seen in AOM. When associated with OM, symptoms may include a history of otalgia, fever, headaches, or otorrhea. Otoscopic examination is required to determine active infection.

When facial paralysis occurs in the setting of AOM, it is an otolaryngologic emergency. Urgent myringotomy with or without tube insertion and fluid culture is recommended along with aggressive IV antibiotic therapy. The effectiveness of IV corticosteroids in this setting is controversial but continues to be routinely used in management [32]. If facial paralysis fails to improve within 7 days of conservative management, a temporal bone CT may be indicated. Electroneurography (ENoG) is a useful prognostic tool to identify patients who are likely to have poor functional outcome and it should be performed 3–4 days after the onset of complete facial nerve paralysis to determine the extent of nerve injury. If ENoG is positive, a surgical decompression of the facial nerve may be indicated. In the majority of pediatric patients with acute onset facial paralysis secondary to AOM, paralysis rarely lasts longer than 3 weeks [33].

In CSOM, management includes aggressive antibiotic therapy and mastoidectomy to eradicate the infection within the temporal bone.

Eye care is critical in the management of facial palsy if incomplete eye closure is noted. Ophthalmologic consultation may be indicated if the patient complains of any eye pain, vision changes, or redness.

In the setting of AOM, greater than 95% of patients will have complete recovery. Patients with complete facial paralysis due to CSOM generally have worse outcomes with complete recovery in only 58–70% of patients [27, 30, 33, 34].

Petrositis–Gradenigo's Syndrome

Petrositis is similar to mastoiditis but involves a different area within the temporal bone. It was first described in 1904 by Giuseppe Gradenigo as a triad of unilateral periorbital pain, diplopia from abducens palsy as the nerve passes through Dorello's canal, and otorrhea caused by a bacterial OM with involvement of the petrous portion of the temporal bone (petrous apicitis). CT temporal bone with contrast is the imaging modality of choice to correlate with clinical symptoms in the diagnosis of petrositis. Initial management is similar to that of other intratemporal complications of OM with initiation of broad-spectrum antibiotics [7, 35].

Labyrinthitis and Labyrinthine Fistula

The bony labyrinth houses the cochlea and vestibular system of the inner ear. *Labyrinthitis* describes an infection or inflammation of these inner ear components from acute or chronic otitis media. The routes of transmission typically include either direct spread from the middle ear to the inner ear or progression of bacterial meningitis to the inner ear [23]. It can also spread through a congenital perilymphatic fistula or through acquired defects following head trauma, previous otologic surgery, or from CSOM.

Labyrinthitis can be serous or suppurative. Serous labyrinthitis from OM is believed to arise secondary to inflammation, whereas suppurative labyrinthitis involves direct bacterial invasion of the labyrinth [36].

Symptoms of acute serous labyrinthitis include ipsilateral hearing loss, vertigo, and nystagmus with nausea and vomiting in an otherwise non-toxic appearing patient. There may also be symptoms of acute mastoiditis with otorrhea. Audiometry will differentiate the SNHL characteristic of labyrinthitis to the conductive hearing loss commonly noted in AOM. Patients with suppurative labyrinthitis will present with much more severe signs and symptoms and will typically be febrile and toxic-appearing. Diagnosis is typically made clinically.

Management of both serous and suppurative labyrinthitis involves aggressive antibiotic therapy because differentiation between the two is often made based on response to treatment and audiologic improvement in patients with serous labyrinthitis [7]. Patients with suppurative labyrinthitis must be monitored closely. If patients fail to respond to broad spectrum IV antibiotic therapy, tympanostomy with tube placement is indicated. Additionally, mastoidectomy is often performed if coalescent mastoiditis is noted on imaging [23]. Patients will typically develop permanent, profound ipsilateral SNHL in suppurative labyrinthitis.

A labyrinthine fistula is seen in CSOM with or without cholesteatoma [37]. The fistula develops when bony erosion secondary to chronic infection or cholesteatoma creates an abnormal communication between the inner ear and surrounding structures [38]. Similar to suppurative labyrinthitis, patients typically present with vertigo, spontaneous nystagmus,

and severe to profound SNHL. Management involves mastoidectomy.

Intracranial Complications

Penido et al. stated that "it is an erroneous but commonly held belief that intracranial complications of acute and chronic otitis media are diseases of the past or are only seen in developing countries. These problems remain, despite improvements in antibiotic care" [39]. In general, time is of the essence in managing these patients to minimize morbidity and mortality. Once an intracranial complication is identified, the multidisciplinary approach includes neurology, otolaryngology, infectious disease, radiology, and neurosurgery.

Bacterial Meningitis

Bacterial meningitis is the most common intracranial complication of acute and chronic otitis media [23, 26, 40]. Meningitis resulting from OM in children is commonly from a bacteremia seeding the meninges, while in adults, it is due to CSOM [23, 37, 39]. Symptoms include severe headache, high fever, neck stiffness, irritability, altered mental status, and malaise [23]. Common organisms involved are *S. pneumoniae*, Group A streptococcus, and *H. influenzae* Type B [4].

Diagnosis begins with history and physical examination. In early localized meningitis, examination may reveal a patient in mild discomfort with fever and tachycardia. As the infection spreads, the patient will develop more severe restlessness, delirium, and confusion. Otoscopy may reveal signs of acute or chronic otitis media including a bulging hyperemic tympanic membrane; however, signs may be subtle, especially with recent antimicrobial treatment. Kernig and Babinski's signs may be positive. Lumbar puncture (LP) is diagnostic but should be performed only after ruling out elevated intracranial pressure [23]. It will reveal an elevated opening pressure, decreased glucose, and elevated protein content as well as elevated white blood cell count and organisms on Gram stain.

Treatment is high-dose IV antibiotics with CSF penetration. Duration of therapy is 7–21 days, dictated by clinical response, imaging studies, and results of repeat lumbar puncture when needed. In AOM, BM&T with culture is recommended. In the setting of CSOM with cholesteatoma, mastoidectomy should be performed to remove the source of infection once the patient is stable. Long-term sequelae of bacterial meningitis include SNHL in up to 14% of patients, so serial audiograms are indicated as the hearing loss may be delayed [36, 41]. Adjuvant therapy with dexamethasone has been shown to decrease overall risk of mortality and subsequent neurologic sequelae including a significant reduction in hearing loss [42•]. Current clinical practice guidelines recommend its administration 10–20 min prior the first dose of antibiotic therapy [43–45].

Brain Abscess

Brain abscess is the deadliest complication of OM with a 4–47% mortality [20]. OM and AM were the most common predisposing conditions for brain abscess (32% of cases) in a systematic review of studies from 1970 to 2013, primarily from contiguous spread of infection or retrograde thrombophlebitis [46]. Headache, fever, nausea, vomiting, neurologic deficits, and altered consciousness are the most common symptoms [46]. Only 20% of patients in a large systematic review presented with the "classic" triad of fever, headache, and focal neurological deficits [46]. Cultures from otogenic brain abscesses grow Streptococcal species (aerobic, anaerobic), Bacteroides, Prevotella species, and Enterobacteriaceae [47]. These brain abscesses are located adjacent to the temporal bone in either the temporal lobe or cerebellum [39]. A temporal lobe abscess generally develops via spread through the roof of the mastoid (tegmen tympani, tegmen mastoideum), and a cerebellar abscess is associated with lateral sinus thrombosis. Left untreated, such brain abscesses may expand, rupture into the ventricle or subarachnoid space, and cause fulminant meningitis, brainstem compression, and cerebellar tonsillar herniation.

Emergent contrast CT brain will confirm the diagnosis of brain abscess with a false negative rate of 6% [46]. Secondarily, MRI may be required to clarify the pathology, particularly to differentiate between multiple abscesses and metastatic disease. Emergent neurosurgical consultation is imperative. With current modern stereotactic neurosurgical techniques, the majority of brain abscesses can be safely aspirated or drained through a burr hole. Intravenous antimicrobial therapy is administered for 6–8 weeks. Mortality from brain abscess has decreased from 40 to 10% worldwide over the past half century, while the rate of full recovery has improved from 33 to 70% [46].

Epidural and Subdural Empyema

Epidural and/or subdural empyema may develop in the setting of either AOM or CSOM. An epidural empyema develops when purulent material and granulation tissue accumulates between the mastoid bone and dura. Often seen in CSOM with or without cholesteatoma, infection can break through the mastoid to the intracranial fossae [36]. An additional pathway for the spread of infection is by localized thrombophlebitis. An epidural empyema can occur with sigmoid sinus thrombosis due to the proximity of the epidural space to the sigmoid sinus [1, 24•].

A subdural empyema forms in a similar fashion but involves erosion through the dura. Once established, it may lead

to multiple cerebral abscesses via thrombophlebitic spread. Symptoms can be non-specific, but signs of meningismus (symptoms of meningitis without pathology of the meninges) as well as hemiplegia and aphasia are often seen [36]. Contrast-enhanced CT or MRI is diagnostic. Urgent neurosurgical evaluation is mandatory [6]. Long-term IV antibiotics and interval mastoidectomy are indicated.

Cerebral Venous Sinus Thrombosis/Otitic Hydrocephalus

Historically, cerebral venous sinus thrombosis (CVST) ranked second to meningitis in the pre-antibiotic area as the most frequent fatal complication of OM [1]. The lateral cerebral venous pathway travels along the transverse sinus through the sigmoid sinus to the jugular bulb and ultimately becomes the internal jugular vein. Thrombosis of the transverse or sigmoid sinus may occur by direct progression of infection from an epidural empyema or true thrombophlebitis of the mastoid emissary veins which drain into the transverse sinus. The thrombus may propagate along the venous sinus pathways causing bacteremia, septicemia, or septic venous embolization including the potential for pulmonary embolus. A dangerous sequela of otogenic CVST is otitic hydrocephalus (OH). Most cases of OH are associated with transverse and/or sigmoid sinus thrombosis.

Transverse and/or sigmoid sinus thrombosis typically presents with a recent history of AOM or CSOM, otalgia, headache, nausea, and vomiting. Spiking high fevers (so-called *picket fence* fever) is less frequently seen in the antibiotic era [48, 49]. Griesinger's sign (edema over the posterior mastoid) or abducens nerve palsy may be seen. Often, otoscopic examination is the only indication of underlying otologic disease [50]. The majority of patients with CVST will exhibit cranial neuropathies and increased intracranial pressure, but may deny fevers and otologic symptoms [50].

OH typically occurs with CVST in children and adolescents with a several week history of OM [20]. Symptoms include protracted headache, sometimes with diplopia and vomiting. There may be bilateral papilledema and possible abducens nerve palsy. MRI/magnetic resonance venography (MRV) should be performed in all pediatric patients with cranial neuropathies and increased ICP to rule out CVST [51]. LP is diagnostic with opening pressure greater than 300 mm of water with normal CSF cytology. Evaluation for an underlying hypercoagulable state is pediatric patients with CVST is strongly recommended [52, 53].

The pathophysiology remains controversial. Symonds, in 1937, suggested non-obstructing mural thrombi extending from the transverse and/or sigmoid sinus thrombosis into the sagittal sinus, interfering with CSF resorption [54, 55]. An alternate mechanism suggests that transverse and/or sigmoid sinus thrombosis causes impeded cerebral venous drainage into the neck [56, 57]. The wide range of anatomical variation of cerebral venous drainage is put forth to explain why all cases of otogenic CVST do not lead to OH [58, 59].

Treatment universally involves early administration of broad-spectrum IV antibiotic therapy. Recent studies advocate a conservative surgical approach involving myringotomy with or without tympanostomy tube placement and mastoidectomy [49–52, 60•]. While anticoagulation is generally the standard of care, it remains controversial [55–57, 62, 63]. A Cochrane database review concluded that the use of anticoagulation was safe and led to a reduction in the risk of mortality. However, these results did not reach statistical significance [61]. The American Heart Association currently advocates for the initiation of anticoagulation for CVST, but there remains a lack of statistical significance with large-scale randomized controlled trials to advocate for or against the use of anticoatulation [60•, 62]. MRV is the standard imaging modality to monitor the course of resolution of the CVST and assess for recanalization [24•, 49, 51, 52]. In cases of CVST with OH, neuro-ophthalmology consultation is indicated.

Encephalocele and Cerebrospinal Fluid Leak

Encephalocele (brain hernia or meningoencephalocele) and CSF leak may be associated with AOM or CSOM. Spontaneous CSF leaks may occur due to bony erosion of the tegmen tympani or the tegmen mastoideum [12]. With a large bony defect, brain may herniate. In adults, CSF leak and encephalocele typically occur in CSOM [12]. Management requires otolaryngologic, and potentially neurosurgical consultation.

Conclusion

In this chapter, we have reviewed the extracranial and intracranial complications of acute and chronic otitis media. While these complications have become uncommon in the post-antibiotic era, it is of vital importance to consider the possible otitic origin of the aforementioned signs and symptoms when a patient first presents in the clinic or hospital setting.

Compliance with Ethical Standards

Conflict of Interest Michael J. Hutz, Dennis M. Moore, and Andrew J. Hotaling declare no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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