Complications and Sequelae: Intracranial

Even though the incidence of suppurative intracranial complications of otitis media has dramatically declined since the advent of antimicrobial agents, we still encounter many serious and potentially life-threatening complications, especially in developing countries of the world.1 Today, these complications are associated more often with chronic suppurative otitis media and mastoiditis, with or without cholesteatoma, than with acute otitis media.2

The middle-ear and mastoid gas cells are close to the intracranial cavity, and infection can spread to intracranial structures, including the dura of the posterior and middle cranial fossae, the sigmoid venous sinus of the brain, and the inner ear. Suppuration in the middle ear or mastoid may spread to these structures and produce the suppurative intracranial complications of meningitis, extradural abscess, subdural empyema, focal encephalitis, brain abscess, lateral (sigmoid) sinus thrombosis, and otitic hydrocephalus (Figure 1).3,4

Having more than one intracranial complication occur is common and frequently depends on the route of infection. Thus, a patient may have meningitis, lateral sinus thrombosis, and cerebellar abscess or other combinations of suppurative disease involving adjacent areas.5 In a review from Thailand of 43 children and adults who developed intracranial complications from otitis media, 44% had two or more complications and meningitis was the most common codisease.6 Of 45 patients described more recently from India, 24% had more than one intracranial complication.7

When a child has acute otitis media (AOM) or chronic middle-ear and mastoid disease (eg, chronic suppurative otitis media or cholesteatoma) and then develops one or more of the classic signs or symptoms of possible intracranial spread, especially while receiving medical treatment, a suppurative intracranial complication should be suspected. Signs and symptoms include one or more of the following: persistent headache, lethargy, malaise, irritability, severe otalgia, onset of fever, nausea, and vomiting. The signs and symptoms demanding an intensive search for an intracranial complication are a stiff neck, focal seizures, ataxia, blurred vision, papilledema, diplopia, hemiplegia, aphasia, dysdiadochokinesia, intention tremor, dysmetria, and hemianopia.8 Conversely, in children with intracranial infection, such as meningitis or brain abscess, middle-ear–mastoid disease must be ruled out as the origin of the central nervous system disease or a concomitant disease.

The presence of headache—even though it is a relatively nonspecific symptom—in children who have AOM, chronic suppurative otitis media, or cholesteatoma indicates a potential complication. Irritability, lethargy, or other changes in person-
ality may be secondary to intracranial spread of the infection. Fever is common when acute infection of the ear is present, but persistent or recurrent fever, particularly after apparently appropriate antimicrobial therapy, may be a potentially dangerous sign of spread. Fever is rarely present in children with chronic suppurative otitis media; when it is present, it may be a hallmark of an impending intracranial complication. The presence of both persisting fever and headache should alert the clinician. Albers confirmed persistent fever and headache as the most common early symptoms of an intracranial complication and stressed the need to make an early diagnosis to reduce morbidity and mortality.9 Schwaber and colleagues reviewed 12 cases of neuro-otologic complications of chronic suppurative otitis media, which included epidural abscess, meningitis, petrous apicitis, and lateral sinus thrombosis, and concluded that purulent malodorous otorrhea, headache, and fever were the most significant early findings.10 An altered mental status was a late finding. In a study from India, Rupa and Ramon compared a large group of patients with intracranial complications of otitis media and mastoiditis with patients who had had a mastoidectomy but without a complication.11 They found that those who had a complication were younger, had a shorter duration of ear discharge, and had had a perforation of the pars tensa.

Today, the widespread availability of computed tomography (CT) and magnetic resonance imaging (MRI) has greatly enhanced the diagnosis of intracranial complications. However, when these are not available, arteriography may also be of value. CT can be diagnostic when extradural, subdural, and brain abscesses are present, and adding radiographic contrast material enhances the diagnosis.12,13 MRI, especially with gadolinium contrast enhancement, provides excellent resolution of intracranial suppuration and its consequences, such as edema, thrombosis, and hydrocephalus.14–16

Intracranial extension of infection may be due to any of the following:

- Progressive thrombophlebitis that allows inflammation to spread through the intact bone (osteothrombophlebitis)
- Erosion of the bony walls of the middle ear or mastoid (osteitis)
- Extension along preformed pathways—round window, dehiscent sutures, skull fracture, or congenital or surgically acquired bony dehiscences (mastoidectomy with dura exposure)

We include in this chapter the incidence, pathogenesis, etiology, diagnosis, management, and outcome for each of these complications as they relate to children. The pathology of these disease entities and the specific otologic procedures performed when they occur are described in detail elsewhere.17–19

**INCIDENCE**

Before the introduction of antimicrobial agents, 2.3% of all patients with otitis media developed intracranial complications, and two-thirds of the cases were due to chronic middle-ear disease.20 The rate was even higher in patients with mastoiditis. Kafka reported that 6.4% of 3,225 patients with mastoiditis developed an intracranial complication, and of these, 76.4% died as a result of their infection.21 The effect of antibiotics
for treating otitis media and thus reducing these potentially life-threatening complications was dramatic. Lund reported that the mortality rate from intracranial complications fell from 36% from 1939 to 1949 (preantibiotic and early antibiotic era) to 6% between 1950 and 1960 and to no deaths from 1961 to 1971. A report from Finland in 1953 provided evidence that the dramatic decrease in these complications was due to the use of antibiotics. In this report, in which 629 patients with AOM were studied, 176 were treated with penicillin and 453 received no antimicrobial agent. There were no complications in the penicillin-treated group, but nine patients in the untreated group developed complications: seven had mastoiditis, one had meningitis, and one patient died as the result of otogenic sinus thrombosis and brain abscess. Some have cautioned that withholding antibiotics today, owing to concern about the development of resistant otogenic bacteria, may result in an increase in suppurative complications.

In the antibiotic era, intracranial complications are uncommon, but nearly two-thirds are still caused by chronic ear disease. Panda and colleagues reported from India that between 1992 and 1995, chronic otitis media was responsible for suppurative complications in children, even when ear drainage was of short duration. However, Dawes reported that most intracranial complications in children were secondary to AOM. In a study from Boston, Friedman and colleagues reviewed the hospital charts of 259 children who had central nervous system infection between 1981 and 1984 and reported that 92 patients (36%) had associated acute middle-ear disease. It is uncertain, however, whether the middle ear was the actual source of the intracranial infection. In a more recent article, Go and colleagues reported that acute mastoiditis, secondary to AOM, progressed into an intracranial complication in 6.8%; sigmoid sinus thrombosis (6), epidural abscess (4), and meningitis (1). In a review from Israel of 12 children treated between 1984 and 2002, all but one was a complication of AOM; meningitis was the most common complication.

Ritter reviewed 152 cases of cholesteatoma, about half of which were present in patients younger than 20 years. The study represented cases between 1965 and 1970 and included four cases with suppurative intracranial complications, two patients with sigmoid sinus thrombosis, and one patient each with extradural abscess and brain abscess. In a review by Sheehy and colleagues of 1,024 operations for cholesteatoma performed from 1965 through 1974 in 949 patients, 17.7% of whom were 15 years old or younger, only 1 patient had meningitis, and in only 2 patients was there an extradural abscess. However, neither of these complications occurred in children. In a study of suppurative intracranial complications of AOM and chronic suppurative otitis media in 37 consecutive children treated at the Children’s Hospital of Pittsburgh from January 1980 through June 1997, meningitis was the most common complication (Table 1). This has also been the case in other reports in the antibiotic era.

In a report from South Africa, Singh and Maharaj found that of 181 patients with intracranial complications (74% of whom were 20 years old or younger), 51% had a brain abscess and only 12% had meningitis. Cholesteatoma caused 57% of the complications.

**MENINGITIS**

Meningitis may be associated with middle-ear infections in three circumstances:

<table>
<thead>
<tr>
<th>Complication</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meningitis</td>
<td>20</td>
</tr>
<tr>
<td>Epidural abscess</td>
<td>7</td>
</tr>
<tr>
<td>Brain abscess</td>
<td>1</td>
</tr>
<tr>
<td>Lateral sinus thrombosis</td>
<td>9</td>
</tr>
<tr>
<td>Otitic hydrocephalus</td>
<td>9</td>
</tr>
<tr>
<td>Cavernous sinus thrombosis</td>
<td>1</td>
</tr>
<tr>
<td>Carotid artery thrombosis</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>48*</td>
</tr>
</tbody>
</table>

*Adapted from Don DM et al.
*Acute otitis media and chronic suppurative otitis media.
*Nine (24.3%) patients had coexisting complications.
1. **Direct invasion.** A suppurative focus in the middle ear or mastoid spreads through the dura, extends to the pia-arachnoid, and causes generalized meningitis.

2. **Inflammation in an adjacent area.** The meninges may become inflamed if there is suppuration in an adjacent area, such as a subdural abscess, a brain abscess, or lateral sinus thrombophlebitis.

3. **Concurrent infection.** Otitis media arises by contiguous spread from an infectious focus in the upper respiratory tract, and meningitis results from invasion of the blood from the upper respiratory tract focus. The infections are simultaneous, but meningitis does not arise from the middle-ear infection.

Hematogenous spread is the most common route of meningitis. Less common is direct extension through congenital preformed pathways or by thrombophlebitis, which usually extends to the middle cranial fossa through the petrosquamous suture or to the posterior cranial fossa through the subarcuate fossa (ie, the first route). In the preantibiotic era, Lindsay examined the histopathologic features of temporal bones of patients who had had AOM and meningitis and found that most of the specimens had evidence of direct spread of infection through the petrous apex. However, since the widespread use of antimicrobial agents, extension of infection from the middle ear to the meninges is thought to be rare in developed nations. Spread of infection from the middle ear and mastoid through the inner ear to the meninges is another pathway but is thought to be rare compared with the other pathogenic mechanisms. In an animal experiment in which *Streptococcus pneumoniae* in the nose and middle ear caused meningitis, a hematogenous route could not be confirmed, which suggested another route of infection into the brain. In a review of 39 Israeli children with intracranial complications from ear and sinus disease, 25 (64%) had meningitis, and 21 of these patients had otitis media as the purported source of their infection. However, Eavey and colleagues examined 16 temporal bones from 8 children who died of meningitis and found otitis media in 14 bones but no evidence that the middle-ear infection had spread to the meninges. Richardson and colleagues provided support for this finding. They could not find any evidence that either AOM or otitis media with effusion was the cause of meningitis that developed in 124 children in Great Britain, especially because 92 (74%) had meningococcal meningitis, which is not caused by an otitic bacterial pathogen. However, meningitis is still a complication of otitis media in developing countries. From South Africa, Singh and Maharaj reported that of 181 patients with intracranial complications, 22 (12%) had meningitis. As shown in Table 2, a review from Thailand by Kangsanarak and colleagues found that meningitis was the most common intracranial complication, either as the only complication or in combination with another one; 51% of 43 children and adults had meningitis.

As recently reported, recipients of cochlear implants had had meningitis in the past, causing their profound sensorineural hearing loss, which, in some cases, could be attributed to an antecedent attack of otitis media. These children most likely had an underlying congenital inner or middle ear malformation that provided a pathway for the bacterium to enter the brain. Early identification of these children could prevent this serious life-threatening complication of otitis media.

### Table 2. INTRACRANIAL COMPLICATIONS OF OTITIS MEDIA IN 43 PATIENTS FROM THAILAND BETWEEN 1983 AND 1990

<table>
<thead>
<tr>
<th>Complication</th>
<th>Number of Cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meningitis</td>
<td>22</td>
<td>51</td>
</tr>
<tr>
<td>Brain abscess</td>
<td>18</td>
<td>42</td>
</tr>
<tr>
<td>Lateral sinus thrombosis</td>
<td>8</td>
<td>19</td>
</tr>
<tr>
<td>Extradural abscess</td>
<td>7</td>
<td>16</td>
</tr>
<tr>
<td>Perisinusus abscess</td>
<td>5</td>
<td>12</td>
</tr>
<tr>
<td>Cerebellitis</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Internal jugular vein thrombosis</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Oticc hydrocephalus</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Encephalitis</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Cavernous sinus thrombosis</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

Adapted from Kangsanarak J et al. *Some patients had more than one complication.*
Symptoms of meningitis caused by any of the three mechanisms include fever, headache, neck stiffness, and altered consciousness. Examination of cerebrospinal fluid reveals pleocytosis and an elevated protein concentration in all cases. Depression of glucose is common only in cases of direct invasion and concurrent infection. Polymorphonuclear leukocytes are the predominant cell type in the early phase of meningitis caused by those two mechanisms. When infection occurs by inflammation in an adjacent area, it is likely to be chronic, and lymphocytes usually predominate in the cerebrospinal fluid. Organisms are usually isolated from the spinal fluid when meningitis is caused by direct invasion or concurrent infection but not when it is caused by inflammation in an adjacent area. Thus, meningitis from this last cause may be defined as an aseptic meningitis (clinical signs of meningitis associated with cells in the cerebrospinal fluid but without bacteria isolated by usual laboratory techniques).

The organisms associated with meningitis arising from AOM are the common agents of meningitis: \textit{S. pneumoniae} and \textit{Haemophilus influenzae} type b. About 20% of all cases of AOM are due to \textit{H. influenzae}, but less than 10% of these are type b. Some children with otitis media owing to \textit{H. influenzae} type b show toxic symptoms, and up to one-quarter have concomitant bacteremia or meningitis.\cite{42,43} Fortunately, with the widespread availability of \textit{H. influenzae} type b conjugate polysaccharide vaccine during the 1990s in developed countries, this bacterium is rarely isolated from middle-ear effusions of children with AOM. The development of \textit{H. influenzae} type b meningitis is likewise rare. In developing nations, however, these infections are still prevalent because of the lack of the vaccine. Pneumococcal meningitis may be caused by antibiotic-resistant organisms,\cite{44} but it is hoped that with the advent of new vaccines for the prevention of pneumococcal meningitis, the incidence of this organism as the cause will decrease in the future.\cite{45}

Meningitis as a complication of otitis media should initially be treated with high doses of appropriate antimicrobial agents. If the causative agent is unknown, a third-generation cephalosporin (ceftriaxone or cefotaxime) or a combination of ampicillin and chloramphenicol is administered (see Chapter 8). Because of concern about multidrug-resistant \textit{S. pneumoniae}, vancomycin (with uniform efficacy for \textit{Pneumococcus}) should be added to the cephalosporin regimen in communities where resistant strains are prevalent. The regimen may be modified after the results of cerebrospinal fluid cultures are known. If the cultures are negative and there is concern that the aseptic process may be caused by a suppurative focus, diagnostic tests should be performed to identify the focus, obtain material for culture, and clear the local infection, usually by incision and drainage. If an AOM or otitis media with effusion is present, tympanocentesis and myringotomy (for drainage) should be performed immediately to identify the causative organism within the middle ear. If otorrhea is present, a culture should be obtained from the middle ear, if possible. Likewise, if chronic suppurative otitis media is present, the purulent material from the middle ear should be aspirated and sent for Gram stain, culture, and susceptibility tests (see Chapter 7).

If an acute mastoiditis with osteitis is present, a complete simple mastoidectomy is indicated as soon as the child can tolerate a general anesthetic. If chronic suppurative otitis media or cholesteatoma is present, tympanomastoidectomy is frequently required and should be performed when the patient is stable. If there is bilateral middle-ear disease and the offending side is uncertain, bilateral tympanomastoidectomy is a reasonable procedure today.\cite{46} Most otologic surgeons attempt to perform hearing preservation surgery for these patients today, instead of the radical or modified radical mastoidectomy recommended in the past. However, appropriate management of any of the suppurative intratemporal complications (eg, petrositis, labyrinthitis) or intracranial complications (eg, extradural abscess) may require surgery and consultation with a neurologist, a neurologic surgeon, or both.
On occasion, after trauma to the temporal bone, an AOM develops that is complicated by meningitis. Tympanocentesis and myringotomy should be performed immediately for culture and drainage, and any otorrhea should be cultured. However, exploration of the middle ear and mastoid may be necessary later to search for and repair possible defects in the dura, especially if otorrhea or cerebrospinal fluid is present.

Appropriate management of both the meningitis and the suppurative focus within the temporal bone should result in a favorable outcome, although many studies still report considerable mortality associated with otitic meningitis. Kessler and colleagues reported a mortality rate of 33% in the 51 patients with otitic meningitis they studied.47

**EXTRADURAL ABSCESS**

Extradural (epidural) abscess usually results when cholesteatoma or infection destroys bone adjacent to the dura.48 This occurs when granulation tissue and purulent material collect between the lateral aspect of the dura and the adjacent temporal bone. Dural granulation tissue within a bony defect is much more common than an actual accumulation of pus. When an abscess is present, a dural sinus thrombosis or, less commonly, a subdural or brain abscess may also be present. If extensive bone destruction has occurred when acute mastoid osteitis is present, an extradural abscess may develop in the area of the sigmoid dural sinus.

The most common symptoms of an extradural abscess are severe earache, low-grade fever, and headache in the temporal region with deep local throbbing pain, or there may be no signs or symptoms. An asymptomatic extradural abscess is frequently found in patients undergoing elective mastoidectomy for cholesteatoma.

Otorrhea that accompanies an extradural abscess is characteristically profuse, creamy, and pulsatile. Compressing the ipsilateral jugular vein may increase the rate of discharge and the degree of pulsation. Malaise and anorexia are present, there is usually no fever, and there are no specific neurologic signs. Cerebrospinal fluid cell count and pressure are normal unless meningitis is also present. CT may demonstrate a sizable extradural abscess (Figure 2).

Treatment of an extradural abscess consists of surgical drainage, and identification of the infecting organism and appropriate antimicrobial therapy can help prevent an intradural complication from developing. A tympanomastoidectomy is indicated in which an attempt should be made to preserve hearing and to avoid a radical or modified radical mastoidectomy.

**SUBDURAL EMPYEMA**

A subdural empyema is a collection of purulent material within the potential space between the dura externally and the arachnoid membrane internally.48 Because the pus collects in a preformed space, it is correctly termed empyema rather than abscess. A subdural empyema may develop as a direct extension or, more rarely, by thrombophlebitis through venous channels. It is a rare complication of otitis media, but it is not an uncommon intracranial complication of paranasal sinusitis.49
Children with subdural empyema are febrile and extremely toxic. There are usually signs and symptoms of a locally expanding intracranial mass, and severe headache in the temporoparietal area is often present. Central nervous system findings can include seizures, hemiplegia, dysmetria, belligerent behavior, somnolence, stupor, deviation of the eyes, dysphagia, sensory deficits, stiff neck, and the presence of Kernig's sign. Hemiplegia and recurrent seizures in a child with suppurative middle-ear and mastoid disease also indicate a subdural empyema. Diagnosis is often made by CT results. The peripheral white blood cell count is high. Cerebrospinal fluid pressure is high, pleocytosis is present with increased numbers of polymorphonuclear leukocytes, glucose concentration is normal, and no microorganisms are seen on smear or culture.

Treatment of subdural empyema includes intensive intravenous antimicrobial therapy and neurosurgical drainage of the empyema through bur holes, craniectomy, or, in infants, possibly only percutaneous aspiration. Main Mastoid surgery to locate and drain the source of infection is usually delayed until after neurosurgical intervention improves the neurologic status. The condition still has a high mortality rate, and more than half of those children who recover will have some neurologic deficit.

FOCAL OTITIC ENCEPHALITIS

Focal areas of the brain can become edematous and inflamed as a complication of acute or chronic otitis media or of one or more of the suppurative complications of these disorders, such as an extradural abscess or dural sinus thrombophlebitis. This localized inflammation is called focal otitic encephalitis or cerebritis, and its signs and symptoms may be similar to those characteristic of a brain abscess, except that there is no suppurative within the brain. Ataxia, nystagmus, vomiting, and giddiness indicate a possible cerebellar focus, whereas drowsiness, disorientation, restlessness, seizures, and coma indicate a cerebral focus. In both sites, headache may be present. However, because these signs and symptoms are also commonly associated with a brain abscess or a subdural empyema, needle aspiration may be necessary to rule them out. CT or MRI can also help make the distinction.

If an abscess is not thought to be present, focal encephalitis should be treated by administering antimicrobial agents and by an appropriate otologic surgical procedure to remove the infection from within the temporal bone. Failing to control the source of infection can cause a brain abscess to develop. Anticonvulsive medication is given when there is cerebral involvement.

BRAIN ABSCESSION

Of all age groups, infants and children have the highest incidence of brain abscess. However, the incidence of brain abscess has decreased significantly in the antibiotic era. From 1930 to 1960, there were 89 cases of otogenic brain abscess at the Otolaryngological Hospital of the University of Helsinki, whereas between 1961 and 1969, there were only 3 cases. Kraus and Tovi described 39 children with intracranial complications of ear and sinus disease in an Israeli hospital between 1972 and 1990 and found that 7 (18%) had an otogenic brain abscess. Several studies reported that infection of the middle ear and mastoid was the predominant source of infection when brain abscess occurred in children. This suppurative complication of otitis media and mastoiditis remains a prevalent disease in developing countries, such as in Turkey, but still occurs in more developed nations around the world. In a review from Costa Rica and Dallas of 101 infants and children with brain abscess, meningitis (24%), chronic otitis media and mastoiditis (22%), and congenital heart disease (14%) were the most common predisposing factors. Jadavji and colleagues reviewed 74 cases of brain abscess diagnosed at The Hospital for Sick Children in Toronto between 1960 and 1984 and found cyanotic congenital heart disease (24%) to be the most common cause; 10 children (14%) had chronic otitis media with or without mastoidi-
tis.61 Indeed, in the United States today, the etiology of brain abscess is primarily due to congenital heart disease, but an otogenic cause still is potential underlying etiology.62 A review of 45 patients in Syracuse between 1975 and 1990 revealed that only 5 individuals had brain abscess with an otologic origin; 2 were children, and the abscess originated from an attack of AOM in both patients.63 Otogenic brain abscess is still a persistent and prevalent complication in developing nations (see Table 2).7,35,53 In a recent review of intracranial complications of otitis media in 33 Brazilian patients (66% younger than 25 years of age) diagnosed between 1987 and 2002, 26 (46%) had a brain abscess (Table 3).1

Cholesteatoma with chronic suppurative otitis media is thought to be the most common cause of brain abscess, but Browning reviewed 26 consecutive patients with brain abscess and found that 10 of them had chronic ear disease without cholesteatoma.64

Otogenic brain abscess can directly follow an acute or chronic middle-ear and mastoid infection, or it can follow the development of an adjacent infection, such as lateral sinus thrombophlebitis, petrosis, or meningitis. The dura overlying the infected mastoid is invaded either along vascular pathways or when the dura adheres to underlying infected bone. Chronic otitis media or mastoiditis with or without cholesteatoma can cause the tegmen tympani to erode by pressure necrosis and perforation of the bone, resulting in inflammation of the dura and invasion by pathogenic organisms. An extradural abscess occurs with subsequent infiltration of the dura and spreads to the subdural space, and a localized subdural abscess or leptomeningitis ensues. Invasion of brain tissue follows, and the various stages of abscess formation take place: inflammatory reaction, suppuration, necrosis and liquefaction, and development of a fibrinous capsule. If delimitation of the abscess does not occur, infection may extend to the meninges or may rupture into the ventricles.

The site of the abscess is the area closest to the primary source of infection. Thus, temporal lobe abscesses occur after invasion through the tegmen tympani or petrous bone. Cerebellar abscesses occur when the infectious focus is the posterior surface of the petrous bone or thrombophlebitis of the lateral sinus. An abscess in the temporal lobe occurs more commonly than does one in the cerebellum, and multiple abscesses are frequent.65,66 However, in a review from India of 10 children with otogenic brain abscess, the site of the abscess was the cerebellum in 8 children and the temporal lobe in 2 children.67

The natural history of brain abscesses includes resorption and healing through gliosis and calcification, spontaneous rupture through a fistulous tract, or spillage into the ventricles or subarachnoid space, producing encephalitis or meningitis.

The bacterial pathogens responsible for brain abscesses include the virulent invasive strains associated with acute disease or the more indolent strains associated with chronic disease54:

- Gram-positive cocci: *Streptococcus pyogenes*, *S. pneumoniae*, *Streptococcus viridans*, and *Staphylococcus aureus*
- Gram-negative coccobacilli: *H. influenzae* and *Haemophilus aphrophilus*
- Gram-negative enteric bacilli: *Escherichia coli*, *Proteus* species, *Enterobacter aerogenes*, *Enterobacter cloacae*, and *Pseudomonas aeruginosa*
- Anaerobic bacteria: *Eubacterium* species, *Bacteroides* species, *Peptostreptococcus* species, and *Propionibacterium acnes*68

In a review of 101 children from Costa Rica and Dallas with brain abscess, *S. aureus* was the
most common causative organism overall, but in the 22 who had an otogenic brain abscess, anaerobes such as *Bacteroides* species and *Bacteroides fragilis* were most commonly isolated. Brook described 23 children in California with intracranial abscess, 4 of whom had chronic otitis media; 2 of those children also had mastoiditis. The most common organisms were anaerobic and gram-positive cocci and gram-negative bacilli. In a study from Greece, anaerobic bacteria were also the predominant bacterial pathogens in 21 patients with brain abscess. However, the common bacterial pathogens that cause AOM may also be isolated from a brain abscess. Grigoriadis and Gold reported a case from Toronto and found 23 other case reports in the literature of *Pneumococcus* as the bacterial agent of brain abscess.

Signs that the central nervous system has been invaded usually occur about a month after an episode of AOM or an acute exacerbation of chronic otitis media. Systemic signs, including fever and chills, are variable and may be absent. Signs of a generalized central nervous system infection include severe headache, vomiting, drowsiness, seizures, irritability, personality changes, altered levels of consciousness, anorexia and weight loss, and meningismus. In addition to these signs of an expanding intracranial lesion, there may be specific signs that the temporal or cerebellar lobes are involved, including vertigo, focal seizures, visual field defects, and nystagmus. These signs indicate that the cranial nerves are involved. Temporal lobe abscesses may be silent. There may be persistent purulent ear drainage, suggesting this as the primary site of infection. Terminal signs include coma, papilledema, and cardiovascular changes.

Diagnosis is based on clinical signs and symptoms and the results of imaging the brain by CT scan, MRI, or both (Figure 3). The results of MRI can be abnormal when focal encephalitis or a brain abscess is present. Of particular concern is the sudden appearance of signs of acute disease—fever and headache—in a patient with chronic middle-ear disease.

![Figure 3. Computed tomographic scan of a 10-year-old boy showing a right cerebellar brain abscess (arrow) as a complication of right acute mastoiditis with osteitis. The child had a 3-week history of headache and vertigo 1 day following the onset of fever and presented with increasing lethargy, vertigo, slurred speech, nausea, and head-tilting to the left. Examination revealed ataxia, nystagmus, slow speech, mild confusion, and right-sided weakness but no otalgia or otorrhea. Otoscopic examination revealed left middle-ear effusion, which was confirmed by tympanocentesis. The brain abscess was drained, and cortical mastoidectomy (and tympanostomy tube insertion) was performed. Purulent material was found within the mastoid at the time of mastoid surgery, and culture of the abscess revealed *Streptococcus pneumoniae*, which was susceptible to penicillin. The child made a complete recovery, without any sequelae, following the brain and mastoid surgery and 6 weeks of intravenous penicillin therapy.](image)
the meninges have been invaded by bacteria. Cultures of spinal fluid are usually negative if there is no suppurative meningitis. Lumbar puncture should be withheld if there are signs of increased intracranial pressure.

Brain abscess treatment includes use of antimicrobial agents and surgical débridement of the primary focus, the middle ear and mastoid, or adjacent infected tissues, such as in cases of thrombophlebitis of the lateral sinus. Brain abscess management has undergone an evolution from drainage or resection of the brain abscess, or both, to intensive parenteral long-term antibiotic treatment and withholding of a neurosurgical procedure. Brain abscess, especially in the early phase of cerebritis, may respond to antimicrobial therapy without surgical drainage, emphasizing the need for early diagnosis.

The choice of antimicrobial regimen is difficult because of the varied bacteriologic characteristics of otogenic brain abscess. Aspiration of the abscess to define its origin may be helpful. Initial therapy should include administration of a penicillin for gram-positive cocci, an aminoglycoside for gram-negative enteric pathogens, and chloramphenicol to combat gram-negative organisms and anaerobic bacteria (see Chapters 8 and 9). A penicillinase-resistant penicillin should be substituted as the penicillin if the Gram stain suggests a staphylococcal infection. The use of a β-lactamase agent combined with chloramphenicol or metronidazole for 2 months has also been recommended; the parenteral route of administration is advised for the first 2 weeks. Even when antimicrobial agents are administered, the mortality caused by brain abscess has been approximately 30%. In a report from Israel, brain abscess had a 40% mortality rate, the highest of all of their intracranial complications. The best results, a mortality rate of zero, were reported in brain abscesses in children treated by catheter drainage. In a review of 122 patients in Taiwan who developed brain abscess from several sources, the mortality rate was 3.8% when the infection was caused by an otolaryngologic focus compared with 24% when the abscess was from other sources.

**LATERAL SINUS THROMBOSIS**

Lateral and sigmoid sinus thrombosis, or thrombophlebitis, arises from inflammation in the adjacent mastoid. Although the superior and petrosal dural sinuses are intimately associated with the temporal bone, they are rarely affected. The mastoid infection is in contact with the sinus walls and produces inflammation of the adventitia followed by penetration of the venous wall. A thrombus forms after the infection has spread to the intima. The mural thrombus may become infected and may propagate, occluding the lumen. Embolization of septic thrombi or extension of infection into the tributary vessels may produce further disease.

Lateral sinus thrombosis is still a relatively common suppurative complication of otitis media and mastoiditis in children even in developed countries, but it is more frequently encountered in developing nations (see Table 2). Of 13 patients who had otogenic lateral sinus disease at the Groote Schuur Hospital in South Africa from 1967 to 1970, 9 were younger than 20 years, 3 children had acute ear infection, and 6 had chronic ear infection. In a review from Iran, 13 children had a diagnosis of sigmoid sinus involvement secondary to chronic mastoid infection from 1978 to 1985. From 1972 to 1990, there were 39 Israeli children with intracranial infection secondary to either ear or sinus disease, and of these, 10 (26%) had a lateral sinus thrombosis from acute or chronic otitis media. In a study from Israel, otogenic lateral sinus thrombosis was diagnosed in 13 children during the 15-year period from 1982 to 1997; 5 (38%) of these cases were complications of AOM, whereas the remaining 8 (62%) were due to chronic otitis media.

Garcia and colleagues reviewed the world literature from 1960 to 1995 and found 58 children with lateral sinus thrombosis as a complication of ear disease; 57% had middle-ear and mastoid infection, and 43% had only
otitis media. Acute and chronic mastoiditis is not an uncommon cause of sinus thrombosis today. Many patients with this suppurative complication of otitis media have one or more other intracranial complications, such as brain abscess, otitic hydrocephalus, and epidural abscess. Marzo recently reported a child who had a sinus thrombosis who also had a contralateral abducens palsy.

The clinical signs of lateral sinus thrombosis may be grouped as follows:

1. Systemic: fever, headache, and malaise. If an infectious mural thrombus forms, the patient may have spiking fever and chills.
2. Signs of increased intracranial pressure: altered states of consciousness, headache, papilledema, and seizures
3. Signs of intracranial complications: meningitis, cavernous sinus thrombosis, and brain abscess
4. Signs of disease resulting from metastases of infected thrombi: pneumonia and empyema, bone and joint infection, and, less commonly, thyroiditis, endocarditis, ophthalmitis, and abscess of the kidney
5. Spread to overlying soft tissue and skin may produce cellulitis or abscess.

Bacteremia is frequent. In Rosenwasser’s series of 100 patients published in 1945 (the specific years of the cases are not mentioned, but with only 19 patients receiving sulfonamides, most were presumably evaluated before 1935), 80 had presurgery blood cultures that were positive for bacteremia, and the cultures of 8 of 17 patients that were negative preoperatively were positive postoperatively. Bacteremia persisted after the operation in 36 cases for a median of 4 to 5 days (range 1–24 days). The predominant organisms were β-hemolytic streptococci (68 patients), S. pneumoniae type 3 (3 patients), Bacillus proteus (Proteus species) (2 patients), S. aureus (1 patient), and Bacillus pyocyaneus (P. aeruginosa) (1 patient).

Singh and Maharaj reported the microbiology of 36 patients diagnosed from 1985 to 1990 with lateral sinus thrombosis and found similar organisms isolated from the blood, including ampicillin- and penicillin-resistant Proteus mirabilis and Enterobacter species. In a more recent report, Syms and colleagues isolated several bacteria from the ears of six patients with this complication, such as Bacteroides fragilis, Peptostreptococcus species, Proteus species, and Pseudomonas species. Recently, Agarwal and colleagues reported on a child who had sinus thrombosis, secondary to an attack of AOM, caused by a multidrug-resistant S. pneumoniae.

CT and MRI are invaluable aids in diagnosing lateral sinus thrombosis and should precede a lumbar puncture whenever it is suspected. MRI and magnetic resonance angiography are recommended diagnostic procedures. An MRI that reveals high signal intensity on T1- and T2-weighted images and absence of flow within thrombosed sinuses on gradient echo images indicates this complication. A normal CT scan or MRI result does not rule out the presence of lateral sinus thrombosis. Holzman and colleagues preferred contrast-enhanced CT in their review of six children who had lateral sinus thrombosis as a complication of otitis media and mastoiditis. The Queckenstedt test, which measures changes in cerebrospinal fluid pressure with compression and release of the jugular vein, can show variations in cerebrospinal fluid pressure. If the sinus is occluded, there is no rise in pressure when the jugular vein of the affected side is compressed, whereas compression of the contralateral jugular vein results in a brisk rise and fall in pressure. However, if the intracranial pressure is increased, the brain may herniate. In addition to this potential danger, the Queckenstedt test may give falsely negative or inconclusive results. There are usually no other abnormalities in the cerebrospinal fluid, although leakage of red cells and subsequent xanthochromia may occur in some cases.

Management includes use of appropriate antimicrobial agents; penicillin, an aminoglycoside, and clindamycin (or metronidazole) are recommended for management of brain abscess. Some clinicians advocate use of anticoagulant medication, but there is no consensus on this
treatment today. Those who advise against anticoagulation medication cite the fear that septic emboli could be released from a lateral sinus that has septic thrombophlebitis. The role of anticoagulation remains uncertain today, and it has been suggested that withholding them is a reasonable alternative to administering these agents.

The decision to perform middle-ear and mastoid surgery depends on the disease status in these anatomic sites. If only otitis media is present, myringotomy and tympanostomy tube insertion may be effective without the need for mastoid surgery. With acute mastoid osteitis, chronic suppurative otitis media, cholesteatoma, or a combination of these conditions, tympanomastoidectomy is usually indicated. When mastoidectomy is required, the sinus should be uncovered and any perisinuous abscess drained. Some surgeons recommend opening the lateral sinus and removing any thrombus. Others recommend only needle aspiration, and still others recommend neither procedure.

Today, the internal jugular vein rarely requires ligation. The timing and team approach for management of this otogenic complication were described by Brackmann and colleagues, Seven and colleagues, and Manolidis and Kutz.

For a complete description of the surgical technique, see the discussions by Glasscock and colleagues, Harris and Darrow, and Brackmann and colleagues.

The mortality in the Rosenwasser series (before 1945) was 27%, with an increased risk in patients older than 30 years. In a review of the world literature by Garcia and colleagues, of 58 children in the antibiotic era (1960–1995), only 3 patients died (5%), all of whom were from South Africa and had other intracranial complications, such as brain abscess, sepsis, and cavernous sinus thrombosis. In a report from Israel in which 13 children had a thrombosis, only 1 child died who also had a brain abscess. Today, with appropriate and adequate management, children who develop lateral sinus thrombosis should have a favorable outcome. Approximately 25 to 33% of patients with lateral sinus thrombosis will have otitic hydrocephalus.

**OTITIC HYDROCEPHALUS**

The term otitic hydrocephalus was introduced by Symonds in 1931 to describe a syndrome of increased intracranial pressure without abnormalities of cerebrospinal fluid as a complication of acute otitis media. The pathogenesis of the syndrome is unknown, but because the ventricles are not dilated, the term benign intracranial hypertension also seems appropriate. The disease is usually associated with lateral sinus thrombosis that can be diagnosed with the aid of MRI.

Symptoms include headache (often intractable), blurred vision, nausea, and diplopia. Signs include vomiting, a draining ear, abducens paralysis of one or both lateral rectus muscles, and papilledema.

If otitic hydrocephalus is suspected, lumbar puncture should be performed after MRI, with a neurologic surgeon in attendance. The cerebrospinal fluid pressure can be high, sometimes above 300 mm H2O, but protein and glucose concentrations and cell counts are normal, and the ventricles are of normal or small size. MRI can be used to diagnose otitic hydrocephalus by showing thrombosis in the sigmoid and transverse sinus. Also, magnetic resonance venography has been shown to be a valuable diagnostic aid. Although thought of as benign, otitic hydrocephalus in some cases has proceeded to loss of vision secondary to optic atrophy.

Management is similar to that for lateral sinus thrombosis: antimicrobial agents, myringotomy and tympanostomy tube insertion, and possible tympanomastoid surgery; also recommended are medication (acetazolamide or furosemide), repeated lumbar punctures, and a lumboperitoneal shunt to normalize intracranial pressure. An aggressive surgical approach is warranted because of the possibility of optic atrophy.
PREVENTION

The life-threatening complications of middle-ear disease in children are relatively uncommon. The goal should be to reduce the incidence of these complications still further by effectively managing acute and chronic otitis media with effusion and preventing chronic suppurative otitis media and cholesteatoma. Multiple factors can influence whether infection from the middle ear and mastoid extends to the intracranial cavity. These include virulence of the bacteria, defects in anatomy, and altered host immunity. An impending complication can be prevented from developing into a life-threatening condition if tympanocentesis and myringotomy are performed to identify the causative organism and provide adequate drainage when children with AOM have persistent or recurrent fever, otalgia, or other signs and symptoms of toxicity that do not respond to medical management. In such cases, the results of the middle-ear effusion culture should guide the clinician in selecting the appropriate antimicrobial agent. If persistent or recurrent discharge through a perforation is present, a culture should be obtained by aspirating the purulent material in the middle-ear cavity. The antimicrobial agent chosen should be administered in a dosage schedule that is high enough to prevent a suppurative complication.

In children who have had meningitis as a complication of AOM, the presence of a perilymphatic fistula (eg, a cerebrospinal fluid fistula) must be ruled out, especially if more than one episode of meningitis has occurred. The fistula may be in the area of the oval or round window, or both, and it may be congenital or due to an acquired defect. Suppurative labyrinthitis is usually present, and the fistula must be repaired to prevent the intracranial complication from recurring. Acute mastoid osteitis and petrositis are other possible intratemporal complications of AOM in which the infection may spread to the intracranial cavity. Early diagnosis and appropriate management of these conditions can prevent intracranial complications.

A suppurative complication should be suspected in children who have the signs and symptoms of acute infection when preexisting chronic suppurative otitis media with or without a cholesteatoma is present. An acute exacerbation in a chronically infected ear may destroy bone and permit bacteria to enter the intracranial cavity. A persistent aural discharge can indicate the presence of this type of disease.

In children with chronic suppurative otitis media and in whom ear discharge is persistent despite medical treatment (such as ototopical medication and orally administered antimicrobial agents), hospitalization may be required to provide more aggressive therapy. A parenterally administered antimicrobial agent may be necessary, depending on the results of culture of the discharge, and direct instillation of an appropriate ototopical medication through the tympanic membrane perforation after thorough aspiration of the middle ear may be warranted. This procedure is best performed with the use of an otomicroscope. If the suppurative process continues, surgical intervention is indicated. A cholesteatoma that cannot be identified by inspection of the tympanic membrane even with an otomicroscope is frequently found in the middle ear and possibly the mastoid. Nevertheless, if a cholesteatoma is not present, middle-ear and mastoid surgery is still indicated to drain the ear and decrease the possibility of further complications. Tympanoplasty surgery, which may be performed at the time of the initial procedure or as a second-stage operation, may be required to prevent subsequent episodes of discharge (see Chapter 9).

When a cholesteatoma is present, the diagnosis should be made promptly. Surgery is indicated because structural damage to the middle ear and mastoid is usually progressive, and suppurative complications are an ever-present danger. The most important goals of surgery on such ears are complete eradication of the cholesteatoma (or its exteriorization), elimination of the infection, and prevention of potential intratemporal or intracranial complications. If these goals are met, the ear is “safe.” Children who have
had a cholesteatoma must have a prolonged follow-up because recurrence is common. Surgical intervention may again be necessary in patients who have had middle-ear and mastoid surgery and in whom infection in the middle-ear or mastoid cavity, or both, persists despite medical management. When a radical mastoidectomy has been performed, the middle-ear–mastoid discharge may be the result of reflux of nasopharyngeal secretions through a patent eustachian tube into the middle ear. Surgical closure of the eustachian tube at the middle-ear end may be required to eliminate the reflux and chronic infection. Likewise, identifying an extradural abscess can prevent the infection from spreading farther into the intracranial cavity. During surgery, the tegmen tympani should be thoroughly examined because such an abscess may be present as a result of cholesteatoma or infection in the area. If the cholesteatoma is in the region of the lateral semicircular canal, the possibility of a labyrinthine fistula must be ruled out. Juselius and Kaltiokallio reported that of 42 patients with labyrinthine fistula, 5 had suppurative labyrinthitis and meningitis.

The incidence of intracranial complications from middle-ear and mastoid infections has dramatically declined since the advent of the widespread use of antibiotics for otitis media. In underdeveloped areas of the world, however, where the availability of medical facilities is still limited, complications occur, with significant morbidity and mortality. Clinicians in developed countries should be especially watchful for possible intracranial complications of otitis media because they are less commonly encountered than in developing nations. Early diagnosis is important in reducing morbidity and mortality. The physician must remain alert to the possibility of these relatively rare but ever-present complications of otitis media, a highly prevalent disease.

REFERENCES


