Intracranial complications of acute otitis media and Gradenigo’s Syndrome

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Abstract. Intracranial complications of acute otitis media and Gradenigo’s Syndrome. We describe the case of a 12-year-old girl with acute otitis media complicated by acute mastoiditis, epidural empyema, thrombosis of the sigmoid sinus and paralysis of the abducens nerve. The patient underwent a mastoidectomy on the left side combined with drainage of the epidural empyema through an extended burr hole and received intravenous antibiotics for 6 weeks and anticoagulation for 12 weeks. This report discusses the intracranial complications of acute otitis media, which were a common problem before the advent of adequate antibiotic drugs but have become rare since their introduction.

Introduction

Acute otitis media is a common disease, with the highest incidence during the first 6 years of life. The disease is characterised by purulent inflammation of the middle ear resulting in otalgia, fever, and hearing loss. Extensive mucosal oedema in the middle ear can, however, block the aditus ad antrum, preventing the mastoid air cells from draining, and initiating a cascade of inflammation, osteitis and necrosis resulting in acute mastoiditis.1

The incidence of intracranial complications is 0.36% and there is a tendency to increase, which is probably attributable to resistant organisms favoured by the availability of antibiotics and vaccinal influence.2,3

Intracranial complications caused by otitis media are meningitis, epidural empyema, intracranial abscess, subdural empyema, sigmoid sinus thrombosis or thrombophlebitis, and hydrocephalus. The mortality rate for these complications is still 8-26.3%.4,5 There are three pathways through which otitis media can provoke these intracranial complications: 1) by direct spread of the infection through osteitic bone to the middle fossa and posterior fossa dura mater, 2) by haematogenic spread or thrombophlebitis, 3) by infectious spread through the labyrinth via the round and oval window or congenital malformations.4

Case report

A 12-year-old girl was admitted to the intensive care unit of the Antwerp University Hospital (UZA) after being transferred from a secondary-referral hospital. For the previous two months, she had been experiencing recurrent acute otitis media. One week before hospital admission she underwent an adenoidectomy and bilateral placement of tympanostomy tubes. Except for the recurrent acute otitis media, she had no significant medical history. Several days after the surgery she was admitted to the referring hospital with complaints of back pain and an infectious clinical appearance with nausea, vomiting and diplopia. There was no ophthalmic pain. The clinical examination revealed signs of meningeal irritation. Computed tomography (CT) scanning revealed a complicated otomastoiditis of the left ear in combination with an epidural empyema and partial thrombosis of the sigmoid sinus. Intravenous antibiotic therapy was started (cefotaxim) but the symptoms did not subside. Because of progressive somnolence, she was transferred to our tertiary university hospital.

The clinical examination revealed an ill, pale child with normal blood pressure, normal pulse rate, an oxygen saturation of 96%, a score of 14 on 15 on the Glasgow Coma Scale and absence of fever (37.3°C). The cardiac examination was normal.
as were the pulmonary and abdominal examinations. ENT examination showed bilateral otorrhoea. On audiometric tests, bilateral conductive hearing loss was noted, with a Fletcher index of 37 dBHL on the right ear, and 60 dBHL on the left ear. Ophthalmic investigation was deemed necessary because of mydriasis, and bilateral normal eye fundus was found. A left-sided abducens palsy was diagnosed (Figure 1) on the ipsilateral side, explaining the diplopia. Blood laboratory results revealed elevated inflammatory markers with leukocytosis, CRP rising to 21.54 mg/dl and a strongly positive titre on mycoplasma serology.

An MRI scan was taken, confirming the diagnosis of otomastoiditis on the left side with a breakthrough to the external auditory meatus and posterior fossa with empyema posterior to the cerebellar hemispheres on the left more than the right side (Figure 2). The empyema on the left side surrounded the sigmoid sinus and jugular bulb with venous sinus thrombosis (Figure 2).

An urgent mastoidectomy was performed on the left side. The mastoid was completely filled with granulation tissue and purulent secretions. The mastoid cavity was rather small because of a low tegmen. The sigmoid sinus was skeletonised without opening it. There were no signs of surrounding inflammation. There were two pearls of cholesterol granuloma, which were removed completely. The granulation tissue in the mastoid was removed as far as possible. The mastoid was closed with a drain being left in place. After this procedure a small trepanation of the epidural space was performed just beneath the left transverse sinus by the neurosurgeon in order to evacuate the epidural empyema.

The child was treated postoperatively with intravenous antibiotics (cefotaxim, metronidazol and clarithromycin). Clarithromycin was added because of the positive Mycoplasma serology, which had already been identified at the time of referral. The day after surgery, therapeutic doses of low molecular weight heparine (nadroparine) were started, accompanied by close monitoring of the anti-fac-tor-Xa plasma levels. The day after the surgery, a control CT scan showed the postoperative state after mastoidectomy on the left side with a drain in the mastoidectomy cavity (Figure 4). The empyema was diminished by comparison with the previous MRI investigation (Figure 4).

Over subsequent days, the overall clinical status of the patient improved, with a fall in inflammatory markers on blood sample. Low-molecular-weight heparin was continued for 12 weeks in total.

The patient had one more episode of fever, rising to 38.4°C, with a leucocytosis but a CT scan identified no changes by comparison with the previous scan. Microbiological examination and culture revealed a growth of *Streptococcus Viridans*. Antibiotics were changed to amoxicillin-clavulanic acid. Intravenous antibiotics were continued for 6 weeks.

One month after these events, the patient reported a marked hearing improvement. A mild residual bilateral conductive hearing loss at the low frequencies was observed on audiometry (Fletcher index of 7 dBHL for the right ear, and 8 dBHL on the left). The left abducens nerve palsy resolved partially within 2 months and resolved completely after 4 months.

**Discussion**

Intracranial complications of otitis media were a common problem in the past; nowadays, they are rare because they can be treated with antibiotics.\(^5\)
Complications of acute otitis media

The most common complication is meningitis (46%), followed by brain abscess (21%); subdural empyema and sinus thrombosis are relatively rare. The most frequent clinical symptoms of intracranial complications are symptoms of meningeal irritation: headache, fever, nausea and vomiting. Seizures, personality disorders, impairment of consciousness and meningeal irritation are also possible in severe cases.

The clinical signs of lateral sinus thrombosis include severe headache, otalgia, otorrhoea, postauricular oedema (Griesinger sign) and fever. Typical picket-fence fever caused by the release of beta-haemolytic streptococcus into the circulation is rarer nowadays. Since these clinical symptoms do not always indicate an otogenic cause, it is important to perform an otoscopic examination in every ill child. It should be noted that antibiotic treatment may mask significant clinical signs, causing a delay in diagnosis.

If the acute otitis media/mastoiditis extends to the petrous apex, patients can present with deep facial pain resulting from trigeminal involvement and ipsilateral abducens nerve palsy. The combination of these symptoms is called Gradenigo’s syndrome, and it was first described in 1907. The syndrome occurs as a complication of otitis media due to the extension of the infection to the petrous apex. Irritation of the ophthalmic branch of the trigeminal nerve and of the sixth nerve contributes to lateral rectus palsy and resultant diplopia and facial pain. Different investigators have demonstrated that only a small number of patients present with the classical triad. Our patient did not have ophthalmic pain. Infections in the petrous apex may be life-threatening because of the propensity to spread medially toward the meninges, cavernous sinus, and brain. During surgery there was granulation and inflammation in the mastoid in direct contact with the tegmen. In our patient, it was likely that the spread of infection occurred through reactive inflammation of the dura since there was no apical petrositis on imaging.
Mastoiditis in combination with intracranial complications such as lateral sinus thrombosis and acute petrositis is treated at three different levels: surgical treatment, intravenous broad-spectrum antibiotics and anticoagulants. Recent literature has found no beneficial effect resulting from the exploration of the sinus and evacuation of the blood clot by comparison with (attico)mastoidectomy.

Broad-spectrum antibiotics for at least six weeks are indicated. Third-generation cephalosporins, aminoglycosides, metronidazole and chloramphenicol are most frequently used as the antibiotic treatment for complicated otitis media. A combination of two or more antibiotics is preferred to monotherapy since they cover the pathogens that provoke acute mastoiditis in most cases: Streptococcus pneumoniae, Streptococcus pyogenes, Staphylococcus aureus and Haemophilus influenzae. In our case, the provoking pathogen was Streptococcus viridans. The antibiogram found sensitivity to amoxicillin-clavulanic acid and vancomycin and so the antibiotic regimen was changed and administered for six weeks.

The difficult clinical diagnosis makes radiological evaluation very important in the determination of diagnosis and management. Nowadays, CT scan, MRI and MR venography are the most important approaches to identifying intracranial complications (Figure 2). In most cases, CT scan is the first-line investigation because it is more readily available than MRI scanning. The literature indicates a sensitivity of 97% and a positive predictive value of 94% for CT scanning in detecting intracranial complications. In the case of lateral sinus thrombosis, CT scan shows the classic ‘delta’ sign, which is the absent contrast enhancement of the thrombosed sigmoid sinus. In cases where CT scan does not show a sinus thrombosis, MRI may reveal increased signal intensity in the throbsum in T1 and T2 images. MRI is more sensitive in recognising lateral sinus thrombosis. In the case of Gradenigo’s syndrome, CT and MRI scanning can reveal inflammatory changes in apical petrositis. But the interpretation of imaging studies of the petrous apex is complicated by normal anatomical variation in the degree of pneumatization of this region. Even though all the clinical signs were present, the CT and MRI examinations of our patient did not show any apical petrositis and the petrous apex had a dense bone structure. Furthermore, there was not even any obvious inflammatory process visible around the abducens nerve (Figure 3).

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In the treatment of lateral sinus thrombosis, the role of anticoagulants is still unclear. The advantages of anticoagulants are: 1) prevention of thrombus progression or embolisation; 2) resolution of thrombus, improving intracranial venous drainage. These effects are intended to improve the neurological
Complications of acute otitis media

We continued therapy for 12 weeks. Our patient did not show any adverse effects.

Gradenigo’s syndrome as a single entity can be treated conservatively by intravenous antibiotic therapy and anticoagulation. In our patient the Gradenigo’s syndrome was an additional finding alongside the more aggressive intracranial empyema.

Conclusion

The combination of acute mastoiditis with intracranial complication and Gradenigo’s syndrome caused by acute otitis media is rare. An otoscopy examination is mandatory in a seriously ill child, as antibiotics may mask significant clinical signs. In addition, imaging techniques, preferentially MRI, are very important in the diagnosis and management of intracranial complications. In the case of Gradenigo’s syndrome, imaging techniques can be challenging. The mainstay of treatment is a combination of surgical intervention (mastoidectomy) and the long-term administration of antibiotics. Anticoagulation therapy should be considered in selected cases. Gradenigo’s syndrome can resolve completely with this combined medical and surgical approach and the abducens nerve palsy may disappear.

References


outcome and should be considered in the light of possible risks. These risks depend on the duration, intensity, agent used and specific patient characteristics and include bleeding, drug interactions, thrombocytopenia, osteoporosis and haemorrhagic skin necrosis. Anticoagulation is most important when patients have multiple intracranial complications, as in our case. We suggest using anticoagulants in cases of thrombus progression, when the thrombus extends to other sites on initial examination (jugular vein, transverse sinus, cavernous sinus), and in cases of neurologic changes, persistent fevers or embolic events. The importance of serial imaging to monitor for thrombus progression was also noted. Traditionally, intravenous unfractionated heparin (UFH) has been the standard anticoagulant. Nowadays, low-molecular-weight heparin (LMWH) derivates are preferred. They are easy to administer — a subcutaneous injection twice daily — and less likely to cause thrombocytopenia and osteoporosis. Anti-factor-Xa plasma levels should be monitored. The duration of anticoagulant treatment is another area of discussion. Recanalisation of the sinus is generally considered to indicate interrup-

Figure 4
Axial CT image of the head. It shows a reduction of the empyema in the posterior fossa behind the left cerebellar hemisphere. The burr hole is visible in the retrosigmoid area (white arrow).

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