



## Foudroyant middle-ear pneumococcal inflammation with meningoencephalitis in a six-year-old girl

Fudroajantno pneumokokno zapaljenje srednjeg uva sa meningoencefalitisom kod šestogodišnje devojčice

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### Abstract

**Introduction.** Intracranial complications of *otitis media* still occur, despite great progress in the treatment of all forms of inflammation. These are serious conditions which are still life-threatening and require a fast and accurate diagnosis and an adequate treatment. We present an illustrative case of an acute, foudroyant, pneumococcal, suppurative *otitis media* with infection spreading into endocranium and development of meningoencephalitis and otic hydrocephalus. **Case report.** A 6-year-old girl was admitted to the University Children's Clinic in Belgrade, Serbia, because of fever, headache, vomiting and disorder of consciousness. Computed tomography scan of the endocranium and temporal bone revealed brain edema and hypodense content in the left mastoid and tympanic cavity. The diagnosis of acute *otitis media* with meningoencephalitis was made and we started with intensive antibiotic treatment. Lumbar puncture and hemoculture confirmed a pneumococcal infection. Otosurgical treatment was conducted,

too, due to an inadequate reaction to the conservative treatment. Firstly, left mastoidectomy with the implantation of a ventilation tube was performed, followed by a radical tympanomastoidectomy, because there was no improvement. Three weeks after the second operation, a magnetic resonance imaging of the endocranium was performed and an otic hydrocephalus was diagnosed. A neurosurgical operation was performed on the same day with the setting of the ventriculoperitoneal shunt. **Conclusion.** Intracranial complications of acute *otitis media* in children are extremely rare and they require a multidisciplinary treatment. Surgical treatment of the ear should not be postponed and the choice of the type of otosurgical intervention should be individually adapted. Audiological and neurological complications of the disease are frequent and they further prolong and impair the treatment.

### Key words:

**otitis media, suppurative; meningoencephalitis; hydrocephalus; surgery, operative; antibiotics.**

### Apstrakt

**Uvod.** Intrakranijalne komplikacije zapaljenja srednjeg uva još uvek se javljaju, uprkos velikom napretku u lečenju svih oblika zapaljenja. Predstavljaju ozbiljna stanja koja i dan danas ugrožavaju život bolesnika i zahtevaju brzu i preciznu dijagnostiku i adekvatno lečenje. Prikazujemo ilustrativan slučaj akutne, pneumokokne, supurativne upale srednjeg uva fudroajantnog toka sa širenjem infekcije u endokranijum i razvojem meningoencefalitisa i hidrocefalusa. **Prikaz bolesnika.** Šestogodišnja devojčica hospitalizovana je na Univerzitetnoj dečjoj klinici u Beogradu, Srbija, zbog visoke febrilnosti, glavobolje, povraćanja i pogoršanja stanja svesti. Kompjuterizovana tomografija endokranijuma i temporalne kosti pokazala je edem mozga i hipodenzni sadržaj u celulama levog mastoida i kavuma timpani. Postavljena je

dijagnoza akutnog zapaljenja srednjeg uva sa meningoencefalitisom i započeta je intenzivna antibiotska terapija i mehanička ventilacija na odeljenju intenzivne nege. Lumbalna punkcija i hemokultura pokazale su pneumokoknu infekciju. Zbog neadekvatnog odgovora na konzervativni tretman i pogoršanja opšteg stanja, devojčica je operisana i načinjena je implantacija aeracione cevčice sa mastoidektomijom levo. Nakon toga došlo je do inicijalnog poboljšanja opšteg stanja, da bi od desetog postoperativnog dana stanje ponovo počelo da se pogoršava. Zbog toga je odlučeno da se načini radikalna timpanomastoidektomija levo koja je i urađena četrnaestog postoperativnog dana. Dvadeset drugog dana nakon druge operacije urađena je magnetna rezonanca endokranijuma i dijagnostikovana je otički hidrocefalus koji je neurohirurški zbrinut istog dana postavljanjem ventrikuloperitonealnog šanta. **Zaključak.** Intrakranijalne komplikaci

je akutnog zapaljenja srednjeg uva kod dece ekstremno su retke. Lečenje dece sa ovim komplikacijama je multidisciplinarno. Hirurško lečenje uva ne treba odlagati, a izbor tipa otolirurške intervencije treba se individualno prilagoditi. Audiološke i neurološke komplikacije bolesti su česte i do-

datno produžavaju i otežavaju lečenje.

**Ključne reči:**  
**otitis medija, supurativni; meningoencefalitis; hidrocefalus; hirurgija, operativna; antibiotici.**

## Introduction

Acute *otitis media* (AOM) is one of the most common infectious diseases in the world. More than 80% of children experience the AOM at least once before the age of 3, and 40% of children in the world experience six or more recurrences by the age of seven<sup>1</sup>. The most common causes of the AOM are *Streptococcus pneumoniae* and *Haemophilus influenzae*<sup>2</sup>.

Despite great progress in the treatment of all forms of infectious *otitis media* (OM), complications still occur. The frequency of complications significantly decreased in the antibiotic era, as well as the need for the surgical treatment. Intracranial complications (ICC), particularly meningitis, intracranial abscesses, lateral sinus thrombosis and hydrocephalus, are still life-threatening conditions and require a fast and accurate diagnosis and an adequate and aggressive treatment. These complications are mainly caused by the chronic OM (about 80% of cases), but they are significantly less frequently caused by the AOM<sup>2,3</sup>. The incidence of ICC in patients with AOM is under 1%, while the incidence of meningitis, which is the most common ICC, is between 0.002% and 0.3%. In the pre-antibiotic era, ICC incidence was up to 6%<sup>4,5</sup>. The common symptoms of the ICC are: fever, headache, nausea and vomiting, and a disorder of consciousness may also occur<sup>2,3</sup>. A particular problem in early diagnosis of the ICC of AOM is the fact that local otoscopic finding is not always typical, especially in small children. A quarter of children with otogenic meningitis experience headache and high temperature as the most common symptoms with an unconvincing otoscopic finding for acute inflammation<sup>6</sup>.

Modern radiographic methods – computed tomography (CT) and magnetic resonance imaging (MRI) have made the diagnosis of complications faster and more precise. The sensitivity of CT with contrast in the detection of the ICC is 92.75%<sup>7</sup>.

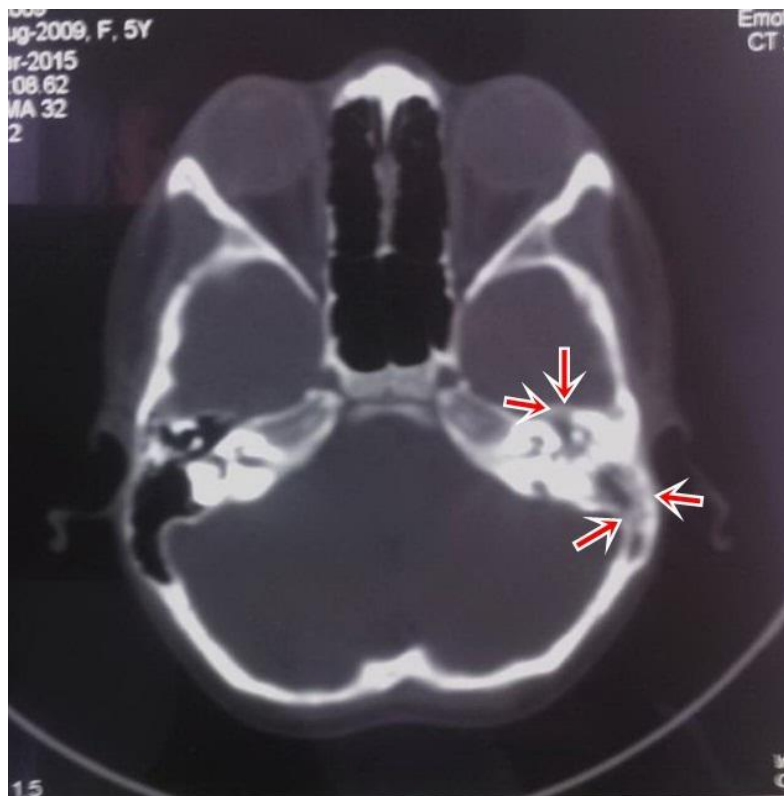
The ICC treatment is complex and involves a combination of an intensive antibiotic therapy and a surgical treatment. The intravenous use of third generation cephalosporins and glycopeptides is recommended for the conservative treatment of otogenic meningitis. Carbapenem involvement can also be considered<sup>8</sup>. Systemic antiedematous and anti-inflammatory corticosteroid therapy is still controversial. Patients receiving corticosteroids have 50% fewer neurological sequelae, but it has been found that corticosteroids do not affect the reduction in the incidence of deafness<sup>9</sup>. Despite all the measures taken in the treatment, the prognosis is sometimes uncertain<sup>10</sup>.

A case of an acute, pneumococcal, suppurative OM with foudroyant course of the disease is presented with infec-

tion spreading into endocranium and the development of meningoencephalitis and hydrocephalus, as well as bilateral deafness as sequelae of the disease in the six-year-old girl.

## Case report

A girl, aged 5 years and 7 months, was admitted to the University Children's Clinic (UCC) in Belgrade, Serbia, because of fever, headache and vomiting that lasted for two days before admission and a disorder of consciousness on the day of admission. The score on the Glasgow Coma Scale (GCS) was 8/15, body temperature (BT) was 39.9°C and the level of C-reactive protein (CRP) was 446 mg/L. Immediately after the admission, lumbar puncture was performed: cerebrospinal fluid was turbid, protein level 170 mg/dL, glucose level 10 mg/dL, white cell count 11,000/mm<sup>3</sup> with 97% of polymorphonuclear cells. The diagnosis of meningitis was made. Initial medical treatment started with the third generation cephalosporin (ceftriaxone 100 mg/kg *iv/day*), glycopeptide antibiotic (vancomycin 60 mg/kg *iv/day*), osmotic diuretic and systemic corticosteroids. CT scan of endocranium and temporal bone was performed in the next few hours and was shown brain edema and hypodense content in the left mastoid and tympanic cavity (Figure 1). On the next day, the state of consciousness deteriorated (GCS 5/15), and mechanical ventilation started. Barbiturates and benzodiazepines were introduced into the therapy due to the appearance of convulsions. Analysis of blood and cerebrospinal fluid showed that *Streptococcus pneumoniae* type 3 sensitive to ceftriaxone and vancomycin was the cause of the infection. An otorhinolaryngologist was consulted on the third day after the admission and the diagnosis of meningoencephalitis with AOM was made. An emergency otosurgical intervention was performed. The implantation of a ventilation tube with simple mastoidectomy was done. During the surgery, a purulent secretion was obtained after paracentesis (the swab was sterile). Intraoperatively, it was found that the *antrum mucosae* was edematous and that there was no pathological finding in the mastoid cells. The state of consciousness and the general state began to improve after the surgery. On the fifth postoperative day, the GCS was 12, body temperature (BT) was 36.5°C, the CRP level was 22 mg/L, the girl was extubated and spontaneous breathing was established. After three days, a control CT scan of endocranium and temporal bone was made and it showed that there was hypodensity in trepanated mastoid cavity, with the empty tympanic cavity and a tube in position. In the following days, the general condition began to deteriorate, the girl became febrile again and an increase in laboratory parameters of inflammation was registered.



**Fig. 1 – Computed tomography (CT) scan of endocranium and temporal bone reveals brain edema and hypodense content in the left mastoid and tympanic cavity.**

It was decided to perform a radical otosurgical intervention: a modified radical tympanomastoidectomy, which was performed on the fourteenth postoperative day. During the operation, it was found that the mucosa of the mastoid cavity, perisigmoid and peridural mucosa, as well as mucosa in the mastoid antrum and attic was inflamed and thickened. The antibiotic therapy was changed, in addition to vancomycin (60 mg/kg *iv/day*) and barbiturate, carbapenem (meropenem 120 mg/kg *iv/day*) was administered postoperatively. Clindamycin 40 mg/kg *iv/day* was introduced into therapy too, in order to cover a possible concomitant anaerobic infection of temporal bone. The general condition began to improve again, the laboratory parameters of inflammation returned to the limits of reference values on the tenth day after the second operation, and BT was up to 38°C, which was interpreted as a central disorder of thermoregulation.

On the 22nd day after the second operation, MRI of the endocranium was performed and it showed the enlargement of the chamber system with encephalitic changes in the brain. It was decided to perform a neurosurgical operation on the same day and the external ventricular drain and convert with ventriculoperitoneal shunt was done due to otic hydrocephalus. A pediatric immunologist was consulted and after the immunological analysis, he concluded that it had been an "infection in an immunocompetent child". After three days, a control CT scan (Figure 2) was carried out and it showed a satisfying finding.



**Fig. 2 – Computed tomography (CT) scan of endocranium and temporal bone reveals satisfying finding in the left mastoid and tympanic cavity.**

The girl was discharged on the 49th day after the admission in the UCC in a good general condition, with aphasia and the inability to walk alone. Otomicroscopic finding of the left ear showed that the ventilation tube was in position, passable and without drainage, and that the mastoid cavity is dry, in the process of epithelialization. Auditory evoked potential test was performed and showed bilateral prolonged interpeak latencies and delayed absolute latencies of waves I, III, V. After the release from hospital, the patient continued with intensive physical rehabilitation with audiological control within a month.

Upon the discharge, the girl was vaccinated with a pneumococcal conjugate vaccine (PCV) 13 and evaluated audiotically. A profound bilateral sensorineural hearing loss with aphasia was identified as a consequence of encephalitis. Before the disease, the girl was a bilingual speaking child. CT scan of the temporal bone was performed nine months after the hospitalization, since the preoperative procedure for cochlear implantation (CI) showed that bilateral cochlear ossification had started. A CI was placed firstly in the right, untreated ear (10 months after the onset of the disease), and six months after that, another CI was placed in the left ear. Intensive hearing and speech rehabilitation started in the native language. Two years after the illness, the girl was completely rehabilitated and she began to attend an elementary school.

### Discussion

Intracranial complications of AOM are extremely rare. The infection most commonly spreads from the middle ear directly into the endocranium through the bone weakened by osteomyelitis. Much less frequently, the infection also may be spread in the endocranium along preformed pathways, such as the oval and round windows. Intraoperative finding in the first operation showed that there was no pathological content in the mastoid cells, which indicates possible hematogenic spread of the infection from the middle ear to the endocranium, with the occurrence of a severe form of meningoencephalitis. Literature data also show that meningitis is often caused by hematogenic spread of the infection from the middle ear, and that the mastoid is not inflamed<sup>11</sup>. Some authors showed the possible role of silent OM in the development of meningitis in children. They showed considerable histopathological tissue changes of acute OM and inflammatory cells in the round window membrane and within the perilymph, the modiolus, and the cochlear aqueduct, suggesting the latter as likely portals from the inner ear to the meninges. This would be a silent route of infection from the middle ear to the endocranium<sup>12</sup>.

The treatment of ICC should start as soon as the diagnosis is made, with high doses of antibiotics. When it comes to surgical engagement in the treatment, the recommendations are consistent – otosurgical treatment is postponed until the patient is neurologically and systemically stabilized. If there is a deterioration of the patient's clinical condition and the progression of infection despite the use of high doses of antibiotics, it is necessary to perform an ear operation as soon as possible in order to evacuate the primary infectious focus<sup>2</sup>. The state of consciousness and general condition of our patient was deteriorated despite an intensive antibiotic therapy, and therefore it was decided to perform an emergency otosurgical intervention. There was a dilemma about which surgical method is the right choice in this case. Gower and McGuirt<sup>13</sup> have conducted a survey that included 100 patients with ICC that occurred as a result of OM. The most common ICC by far has been meningitis that developed in 76 patients. There were five patients with hydrocephalus. They agree that ICC needs to be treated with paracentesis, but only

if there is no improvement in patient's condition after the use of antibiotics<sup>14</sup>. In contrast, Singh and Maharaj<sup>14</sup> suggest that all ICCs should be treated with cortical mastoidectomy, except for chronic OM with cholesteatoma which should be treated with radical mastoidectomy<sup>14</sup>. Felisati et al.<sup>15</sup> have administered an intensive antibiotic therapy that has been ineffective in three adult patients with otogenic meningitis, making a surgical treatment necessary. They recommend wall up mastoidectomy for patients with otogenic meningitis. Samuel and Fernandes<sup>16</sup> suggest an urgent otosurgical treatment, cortical mastoidectomy and myringotomy (with the implantation of ventilation tubes if necessary). In our case, the implantation of the ventilation tube and simple mastoidectomy led to a short-term initial improvement of the state of consciousness and general condition of the girl. A few days following the surgery, the condition began to deteriorate again, and there was a dilemma about whether to change antibiotics or, in addition, to make a more radical surgical intervention. In a retrospective eighteen-year study, Barry et al.<sup>17</sup> had 79 patients with otogenic ICC. Thirteen patients had meningitis, and AOM was diagnosed in 32 patients. They believe that the pre-antibiotic practice of performing mastoidectomy in the first 24 hours is inappropriate, although some authors still recommend this. They agree with Gower and McGuirt<sup>13</sup> that the urgent otosurgical intervention is indicated in patients with coalescent mastoiditis, as well as in patients who have a deterioration of clinical condition and the progression of infection during the first 48 hours of intensive antibiotic therapy. They suggest that paracentesis should be done first and if there is no improvement in the patient's condition, a mastoidectomy is indicated<sup>17</sup>, which is also recommended by Slovik et al.<sup>18</sup>. Our patient has experienced an improvement in the condition after a more radical otosurgical intervention. Consequently, it raises the question of whether it has been necessary to perform an instant radical surgery intervention. Dudvarski et al.<sup>10</sup> had similar experience. They described a case of meningoencephalitis as a complication of AOM in an 11-year-old child, which is the first paper in Serbian literature that describes the case of AOM with ICC. The authors state that they first performed a mastoidectomy with the implantation of the ventilation tube, followed by a radical tympanomastoidectomy because there was no clinical improvement<sup>19</sup>.

The leading cause of postnatal deafness in children is bacterial meningitis. Infection spreads from meninges to the cochlea, which leads to its fibrosis and ossification in up to 34% of children with bacterial meningitis. CI is challenging due to frequent cochlear ossification<sup>19</sup>. Cochlear ossification presents a surgical problem. There are solutions that can lead to a satisfactory outcome nowadays, but it is still desirable to perform CI at the earliest stage, before the cochlear ossification starts, in order to optimize the outcome of the treatment<sup>20</sup>.

The AOM clinical course in this immunocompetent girl was fulminant although the infection had been caused by a low-invasive *Streptococcus pneumoniae* type 3. There are more than 90 immunologically distinct serotypes of *Streptococcus pneumoniae*. According to their invasive potential, they have been classified into serotypes with a high (sero-

types 1,5 and 7), intermediate (serotypes 4, 9, 14 and 18) and low invasive potential (serotypes 3, 6, 8, 15, 19, 23 and 33). Ahl et al.<sup>21</sup> have established that the septic shock is more frequently caused by *pneumococcus* type 3 rather than by *pneumococcus* type 14 that has an intermediate invasive potential. The results of their research have shown that serotypes with high invasive potential mostly cause the diseases in younger patients, unlike serotypes with a medium and low invasive potential that most frequently cause the diseases in the elderly patients with comorbidities<sup>22</sup>, which was not the case with the girl. It is possible that the foudroyant course of AOM was caused by the fact that the girl had not been vaccinated with pneumococcal vaccine (PCV). The first PCV, which contains the antigens of 7 different pneumococcal serotypes (PCV7) was licensed and introduced into the Immunization Schedule in the United States in 2000. PCV7 was included in the national immunization programs, or was recommended for routine vaccination, in a number of European countries, between 2006 and 2008<sup>23</sup>. This vaccine was replaced by a vaccine containing antigens of 6 additional pneumococcal serotypes (PCV13) between 2009 and 2011<sup>24</sup>. Since March 1, 2018, this vaccine has been included in the mandatory immunization calendar in Serbia.

The application of PCV7 has significantly reduced the percentage of nasopharynx colonization with PCV7 serotypes and also the frequency of AOM (in Finland by 6%, Israel by 17%, the UK by 19.8% and Sweden by 26%), as well as the frequency of repeated AOMs to 23%. By introducing PCV13, the incidence of AOM in Israel has been reduced by an additional 43% compared to the period when PCV7 was

used (resulting in a total of 60% reduction in regard to pre-PCV period)<sup>25, 26</sup>. The application of PCV has also reduced the resistance of pneumococcus to antibiotics (vaccine serotypes), as well as the reduction of AOM complications. The incidence of pneumococcal acute mastoiditis in Australia has significantly reduced since PCV 7 has been introduced, and the incidence of total mastoiditis has significantly decreased, too, as well as the ICC incidence<sup>25</sup>. In Denmark, after the application of PCV7 and PCV13, the incidence of severe AOM forms decreased by almost 10%, while the incidence of AOM complications decreased by about 20%<sup>26</sup>.

### Conclusion

Meningoencephalitis is a very rare and unusual complication of AOM. Foudroyant course of the disease requires rapid diagnostics and a multidisciplinary treatment. It is necessary that a neurologist, radiologist, neurosurgeon, infectologist, clinical pharmacologist and psychiatrist also have an active participation in the treatment, in addition to the pediatrician in intensive care and otorhinolaryngologist. Antibiotic therapy is the basis of the treatment, but otosurgical treatment is still indicated when there is no improvement in the patient's clinical condition after the administration of antibiotics. After a complete evaluation of patient's condition, it is necessary to correctly evaluate the time of the surgical treatment of the ear. The choice of otosurgical method should be adapted to each patient individually. Audiological and neurological complications are frequent and they further prolong and impair the treatment.

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