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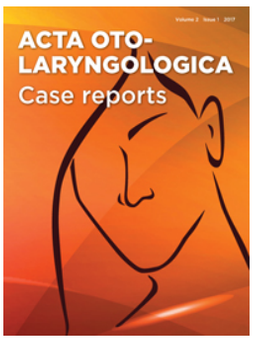

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CASE REPORT

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Meningoencephalitis and otitis media in a child with *Mycoplasma pneumoniae* infection*

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ABSTRACT

We report on a previously healthy 11-year-old male presenting with meningoencephalitis and otitis media. Computed tomography demonstrated opacification of the right middle ear and mastoid ear cells, but no destructive changes. Anti-*Mycoplasma pneumoniae* IgG and IgM were positive in serum and at high concentrations in cerebrospinal fluid (CSF), and its nucleic acid was detected in the middle ear fluid and in a throat swab, but not in CSF. EEG showed generalized slowing and right temporal sharp waves. Brain MRI imaging remained normal. After a 3-week treatment with doxycycline and a tympanostomy tube, the patient recovered, and no long-term neurological sequelae have appeared. Diagnostics and pathogenetic mechanisms in meningoencephalitis caused by *M. pneumoniae* are discussed.

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KEYWORDS
Meningoencephalitis; otitis media; child; *Mycoplasma pneumoniae*

Introduction

Mycoplasma pneumoniae (Mp) causes common respiratory tract infections. Neurological symptoms are seen in about 1–12% of the patients hospitalized for *Mp* infection.[1,2] In children, encephalitis is the most frequent extrapulmonary manifestation. About 10–17% of acute childhood encephalitis in Europe and North America are caused by *Mp*.[3,4] Other less frequent neurological manifestations include acute disseminated encephalomyelitis, transverse myelitis, polyradiculitis, cerebellar ataxia, meningitis and stroke.[1,2]

In the northern hemisphere *Mp* infections have increasingly been reported in outbreaks.[5–7] A central nervous system (CNS) invasion by *Mp* is diagnosed based on serology, culture or polymerase chain reaction (PCR) from the cerebrospinal fluid (CSF), and after excluding other causes.[8,9] Up to one-third of patients with *Mp* infection may have ear infection, but PCR has been positive from middle ear fluid in rare cases.[5,10,11] The CNS manifestations of *Mp* infections are known to arise from different pathogenetic pathways with and without direct invasion of the pathogen into the CSF.[1,2,9]

Case report

An 11-year-old boy had a history of atopic eczema and allergic rhinitis. Due to secretory otitis media, ventilation tubes were installed in both tympanic membranes in November 2010, after which his ears healed and hearing recovered. He had no history of neurological or cognitive concerns, except for mild difficulties in mathematics at school. The boy was referred to our hospital on 29 September 2014 due to 11 days of cough, headache and a fever of up to 39.4 °C. He had had a 5-day course of oral cefalexin with no relief of his symptoms. The main symptoms, clinical findings, laboratory and imaging results and therapeutic interventions are summarized in Table 1.

Discussion

Our patient presented with respiratory symptoms, otitis media, and meningoencephalitis caused by *Mp*. A respiratory tract infection with *Mp* was confirmed by positive PCR from a throat swab as well as from the middle ear fluid and positive serology. The diagnosis of *Mp* meningoencephalitis was based on the clinical picture, CSF findings, EEG, and antibody detection in the

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*The research was conducted at the Helsinki University Hospital.

Table 1. Clinical history and outcome of the patient in chronological order.

	Symptoms	Clinical findings	Test results	Therapy
On admission	Fever Cough Headache	Prostrated, pale Pulmonary crepitations Opaque tympanic membranes	CRP normal ESR 84 mm/h B-leuk 14.8 × 109/L Neutrophils 78% Chest X-ray normal Mucosal inflammation in the ethmoid sinuses (sinus x-ray)	Hospitalized IV-fluids Oral cefalexin continued From day 3 oral doxycycline (suspicion of Mp infection based on the clinical picture)
Days 4–10	Short spells of disorientation Tired, bedridden	Neck stiffness Unsteady walking Hyperactive deep-tendon reflexes Right ear lobe erythematous Temporarily local pain over right mastoid area	CSF: CSF-leuk 87 × 106/L All mononuclear CSF-protein 805 mg/L CSF-glucose normal Bacterial staining and culture negative Viral, borrelia and Mp PCR assays negative CSF-Mp IgG/IgM antibodies >400/+ EEG: general slowing, sharp waves in the right temporal area Head MRI: normal, except for mucosal edema and fluid in the right middle ear and mastoid air cells Ear CT: opacification of the right middle ear and the temporal bone air cell system (Figure 1)	Doxycycline changed to iv form IV acyclovir (until negative viral results) IV ceftriaxone (suspicion of acute mastoiditis)
Day 11	Head tilted to the right side Walking still unsteady and skewed to the right	ORL consultation: Frenzel's glasses: no nystagmus Nasoendoscopy: enlarged adenoid gland, and secretion in the right tubal orifice Mp PCR + in the middle ear secretion and the throat swap	ORL consultation: Audiometry: conductive hearing loss of the right ear	Myringotomy; purulent secretion suctioned from the right middle ear Tympanostomy tube inserted
Days 12–16	Afebrile Neck rigidity and headache resolved		Serum Mp IgG/IgM antibodies 318/+ (day 1) and 343/+ (day 15)	Discharged on day 16 Oral doxycycline to complete a 21-day course
Follow-up visits after 4 and 6 weeks	Fatigue	Physical and neurological examinations normal	EEG normal	
Follow-up visit after 6 months		Neuropsychological testing revealed mild difficulties in visuospatial perception but otherwise age-appropriate cognitive performance		

CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; B-leuk: blood leucocytes; X-ray: radiograph; IV: intravenous; *Mp: Mycoplasma pneumonia*; CSF: cerebrospinal fluid; PCR: polymerase chain reaction; IgG/IgM: immunoglobulin G/M; EEG: electroencephalogram; MRI: magnetic resonance imaging; CT: computed tomography; ORL: otorhinolaryngological.

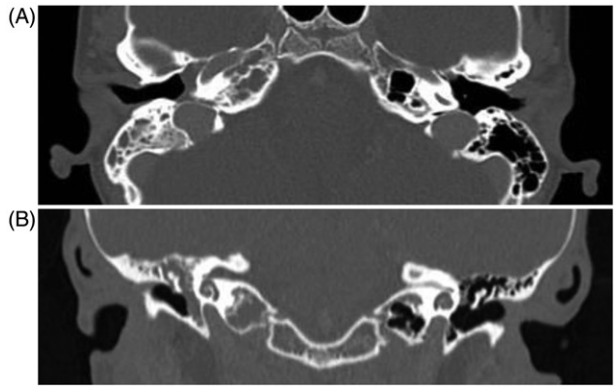

Figure 1. Computed tomography. (a). Horizontal section. (b). Coronal section. Opacification of the right middle ear and the temporal bone air cell system, including the mastoid and pars petrosal, but no destruction of the bony septa.

CSF and serum. CSF contained a higher IgG titer than serum, and CSF IgM was also positive, a finding indicative of endogenous intrathecal antibody production.

Acute childhood encephalitis is a potentially fatal disease,[9] but a Californian study found that *Mp*-associated encephalitis, compared to other etiologies, caused less-severe hospital courses.[12] Other studies, however, have reported long-term neurologic sequelae in about half of the patients.[1,3] The absence of any brain MRI abnormalities and seizures during the disease course may have been indicators for better prognosis in case of our patient.

The CSF findings of our patient were similar to those described in the literature: mild-to-moderate pleocytosis with a predominance of lymphocytes, slightly elevated protein concentrations, and normal glucose levels.[3,9,12] Like our patient, more than half of the patients reportedly had an elevated erythrocyte sedimentation rate.[3] The diagnosis is challenging and should not rely on a single test. *Mp* infections are common, and diagnostic methods have their limitations.[4,5,12] Serologic testing can yield positive results several months after an infection, or even false negative results.[3,5,12] Cultures lack sensitivity. PCR is the most sensitive test, especially in the early stage of the disease, but different assays perform variably.[3,9,12] Recent studies have also shown that asymptomatic carriage of *Mp* in the upper respiratory tract is common in children.[5,13]

EEG is often abnormal with diffuse slowing, as in our patient; focal abnormalities are less common.[3,12] Brain MRI shows abnormalities in about half of the patients, mainly focal ischaemia or edema, or increased signal intensities.[1,3,12]

In previous reports, only about half of the children with *Mp* encephalitis experienced respiratory symptoms.[3,12] In our patient, *Mp* was detected in a pharyngeal swab and in middle ear fluid. To our knowledge, rare cases of otitis have shown *Mp* in the middle ear fluid,[10,11] but no case with concomitant meningoencephalitis has been described before. Italian researchers did, however, publish a case report on a child with meningitis following acute otitis media and positive *Mp* serology 25 years ago.[14] In most cases, the respiratory tract is considered the likely entry point.[3,12] Our patient's meningoencephalitis could have been otogenic. However, the long prodrome of respiratory signs and fever before the neurological symptoms suggests the possibility of an immunologically mediated pathogenetic mechanism.

A recent study of neurological complications of PCR-proven *Mp* infections in children observed two distinct patterns of encephalitis: (1) no or short (<7 days) prodrome, less frequent respiratory manifestations and detection of *Mp* by PCR in the CSF (in 75%) but not in respiratory tract, and (2) a prolonged prodrome (>7 days), respiratory manifestations, and detection of *Mp* in the respiratory tract but not in CSF. They speculated the presence of an immunologically mediated disease mechanism in the latter group, and direct invasion of CNS by the bacteria in the former.[1]

Treatment targets the mechanism of the disease. Intravenous immunoglobulin and steroids have been administered on suspicion of autoimmune mechanisms in *Mp* encephalitis.[3,5,12] No controlled clinical trials on antimicrobial therapy in *Mp* encephalitis exist, but antibiotic therapy has in some cases – including ours – temporally associated with improvement.[3] An antibiotic such as azithromycin, doxycycline, or a fluoroquinolone should be used, because of their antimycoplasmal activity and their ability to traverse the blood–brain barrier.[3,9,12] Fluoroquinolones can be used in children to treat severe infections. Doxycycline can be used in children over 8 years of age. An oral permission to publish this case report was obtained from the parents.

Disclosure statement

None of the authors has conflicts of interest. The authors alone are responsible for the content and writing of this article.

Notes on contributor

Participated in patient treatment (TP, AS, TR, STS, JJ), participated in preparing the manuscript (TP, AS, TR, STS, JJ).

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