CASE REPORT

Chronic meningitis with intracranial hypertension and bilateral neuroretinitis following *Mycoplasma pneumoniae* infection

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SUMMARY

A previously well 12-year-old boy presented with a 2-week history of headache, nausea, vomiting and left-sided weakness. He subsequently developed meningism, right abducens nerve palsy, persistent papilloedema and reduced visual acuity in association with a bilateral macular star, consistent with neuroretinitis. Cerebrospinal fluid (CSF) examination indicated chronic meningitis and serological testing confirmed recent *Mycoplasma pneumoniae* infection, although PCR in CSF was negative. He was treated for aseptic meningitis with ceftriaxone, aciclovir, azithromycin and acetazolamide for intracranial hypertension, with gradual improvement in clinical condition and visual acuity over several weeks. This is the first report of *M. pneumoniae* chronic meningitis further complicated with bilateral neuroretinitis and intracranial hypertension. Evidence of central nervous system inflammation in the absence of direct infection suggests an immune-mediated pathophysiology. Although the use of macrolides with antibiotic and immunomodulatory activity might be beneficial, it was not possible to ascertain whether it influenced clinical recovery in this case.

BACKGROUND

Mycoplasma pneumoniae is a ubiquitous pathogen that predominantly causes respiratory disease in children; however, extrapulmonary complications, including neurological and ocular manifestations, can occur. We report an unusual case of chronic aseptic meningitis associated with intracranial hypertension and bilateral neuroretinitis. We believe this case is of interest because both of these manifestations of *Mycoplasma* infection are rare and their coexistence may imply a common pathogenic mechanism, which we speculate on in this manuscript. There is a paucity of evidence to guide the management of extrapulmonary manifestations of *Mycoplasma* infection and for describing the spectrum of severe disease that can be caused by this pathogen; this highlights the need for further evidence on how best to manage children with central nervous system (CNS) complications.

CASE PRESENTATION

A previously well 12-year-old boy presented to his local hospital with 14 days of headache, nausea and vomiting, complicated by sudden onset of left-sided weakness. He was fully vaccinated, with no recent history of foreign travel or animal contact.

On admission, he had a low-grade fever; his vital signs and conscious level were normal.

Cerebrospinal fluid (CSF) examination revealed 74 leucocytes/mm³ (85% lymphocytes), protein 610 mg/L and glucose 3.9 mmol/L, with plasma glucose of 5.7 mmol/L (table 1). No organisms were seen in CSF microscopy. Cranial CT showed a left-sided maxillary cyst consistent with previous sinusitis, but no evidence of an intracranial lesion. MRI and angiography of the brain showed non-specific signal change in the right periventricular area. He was treated with acyclovir, ceftriaxone and azithromycin, and was discharged after 7 days.

He was re-presented after 3 days with worsening frontal headache, photophobia, phonophobia, diplopia and ataxia. Funduscopy revealed bilateral papilloedema. Repeat CSF examination, 3 weeks of illness, showed an opening pressure of 40 cm water, leucocyte count 40 cells/mm³ (100% lymphocytes), protein 500 mg/L and glucose 3.1 mmol/L. CSF of 40 mL was removed and he was started on acetazolamide for suspected idiopathic intracranial hypertension. His headache improved and he was discharged after 5 days without antimicrobial treatment.

Two weeks later he presented to our hospital with persistent headache, vomiting and diplopia. On admission, he was afebrile, with normal vital signs and conscious level. He had meningism, mild ataxia, right-sided laterocollis and right abducens nerve palsy. He had bilateral optic disc swelling and reduced visual acuity (6/38) in the right eye. Repeat CSF examination (6 weeks after his symptoms began) showed a persistent elevated opening pressure of 35 cm water, 33 leukocytes/mm³ (70% lymphocytes), protein 530 mg/L and glucose 3.8 mmol/L, with plasma glucose of 6.9 mmol/L. Repeat MRI of the brain and spine showed no evidence of inflammatory enhancement or clinically relevant findings. The T2 signal change around the right occipital horn, noticed in the initial scan, was indicative of localised mature gliosis. A small focal cystic area posterior to the second thoracic vertebral body was suggestive of a developmental cyst. He was diagnosed with chronic meningitis complicated by secondary intracranial hypertension. Follow-up funduscopy examination demonstrated persistent bilateral optic disc swelling with a macular star figure, consistent with a diagnosis of bilateral neuroretinitis together with papilloedema from intracranial hypertension (figure 1).

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Table 1 CSF findings and *Mycoplasma pneumoniae* titres according to time after the onset of symptoms

	WCC (cells/mm ³)	Lymphocytes (%)	Protein (mg/L)	Glucose (mmol/L)	Opening pressure (cm water)	<i>M. pneumoniae</i> titres
2 weeks	74	85	610	3.9		1:320
4 weeks	40	100	500	3.1	40	
6 weeks	33	70	530	3.8	35	1:2560
10 weeks	8	100	460	3.5		1:10 240

CSF, cerebrospinal fluid; WCC, white cell count.

INVESTIGATIONS

An extensive work-up was undertaken to investigate autoimmune and infectious causes of chronic meningitis. Notably, serological testing was negative for *Brucella* spp, *Borrelia burgdorferi*, *Rickettsia conorii* and *Toxoplasma gondii*. PCR for Herpesviridae and enteroviruses in plasma and CSF was negative. Serological testing suggested past infection with cytomegalovirus and Epstein-Barr virus. Initial serology for *Bartonella henselae* was equivocal; however, repeat testing was negative for *B. henselae* and *B. quintana*. Serological testing showed evidence of recent *M. pneumoniae* infection, with a progressive rise in particle agglutination titres, from 1:320 at presentation to 1:2560 after 4 weeks and 1:10 240 after 8 weeks (Serodia Myco-II particle agglutination assay that detects both IgG and IgM; table 1). *M. pneumoniae* antibody titres were <1:40 in CSF. *M. pneumoniae* DNA was not detected by PCR in CSF.

TREATMENT

The patient was treated for aseptic meningitis with intravenous ceftriaxone, acyclovir and oral azithromycin, and subsequently with doxycycline and rifampicin until infection with *B. henselae* had been ruled out. Acetazolamide was given for intracranial hypertension; corticosteroids were not administered.

OUTCOME AND FOLLOW-UP

Clinical condition of the patient improved over the following 2 weeks, with gradual resolution of headache and meningism. CSF examination 10 weeks after his initial presentation showed 8 leukocytes/mm³, protein 460 mg/L and glucose 3.5 mmol/L (table 1). Ophthalmic review 16 weeks after initial presentation showed unaided visual acuity of 6/6 in each eye, resolving bilateral neuroretinitis with residual nasal swelling of the optic discs and a persistent macular star in both eyes (figure 2).

Figure 1 Optic disc swelling with a macular star figure, consistent with a diagnosis of neuroretinitis.

DISCUSSION

We describe a case of a 12-year-old boy with chronic meningitis, intracranial hypertension and bilateral neuroretinitis following *M. pneumoniae* infection. Chronic meningitis is a syndrome of meningeal inflammation, based on clinical features and/or CSF findings, persisting for 4 weeks or more. Although rare, the wide range of potential infectious and non-infectious causes makes diagnosis and management challenging.¹ In our case, the only significant positive finding was serological evidence of *M. pneumoniae* infection that lead us to speculate that this was the likely cause of his chronic meningitis.

Upper respiratory infection symptoms were not reported and although respiratory symptoms typically precede neurological complications of *M. pneumoniae* infection, they are not universal.^{2,3} The pathogenesis of *Mycoplasma*-associated CNS disease is still incompletely understood; several plausible mechanisms have been proposed. Isolation of *M. pneumoniae* from brain tissue and CSF of patients with CNS complications in some studies supports a hypothesis of direct invasion.³ It is plausible that *Mycoplasma* could invade the CNS following haematogenous dissemination and cause neurological injury by induction of inflammatory cytokines.⁴ Alternative proposed mechanisms include autoantibody production,² neurotoxin-induced disease,³ vasculopathy secondary to immune-complex deposition⁵ and intravascular thrombosis or systemic vasculitis due to hypercoagulability.⁶ In our case, the evidence of systemic and CNS inflammation in the absence of direct infection suggested an immune-mediated pathophysiology. We relied on serology to diagnose recent *M. pneumoniae* infection. Although seroconversion is typically defined as a fourfold rise in titre between acute and convalescent sera, in this case there was a 32-fold rise in titre, indicating unequivocal recent infection with *M. pneumoniae*.

One of the striking features in this case was the combination of chronic meningitis with intracranial hypertension and

Figure 2 Persistent macular exudate 16 weeks after initial presentation.

bilateral neuroretinitis. We feel that the constellation of papilloedema, headache, nausea and vomiting early in the course of his disease was due to intracranial hypertension. Recent reports have described intracranial hypertension in a patient with *Mycoplasma* meningitis and increased CSF production in a child with concomitant *Mycoplasma* meningitis.^{7 8} Given that our patient had chronic symptoms of raised intracranial pressure, we treated him with acetazolamide throughout the course of the disease. Later, our patient was also diagnosed with bilateral neuroretinitis, a form of optic neuritis involving the nerve fibre layer of the retina. *M. pneumoniae* has been associated with various ocular findings, usually occurring several days to weeks after the initial symptoms.⁹ Optic neuropathy is a rare but well-described complication.^{10 11} Neuroretinitis is an inflammatory disorder characterised by optic disc oedema and the subsequent formation of a macular star. The underlying pathophysiology involves inflammation of the optic disc vasculature causing exudation of lipoproteinaceous material into the peripapillary retina.¹² The mechanism of disc vasculitis in neuroretinitis is unclear, but may involve direct nerve invasion or a postinfectious autoimmune response, similar to *Mycoplasma* CNS disease.¹² There does not appear to be a definite role for steroids in treatment of neuroretinitis,¹² although the majority of cases of *Mycoplasma*-associated optic neuropathy respond favourably to systemic steroids and antibiotic treatment with macrolides, tetracyclines or rifampicin.^{9–11}

The role of antibiotics in management of *M. pneumoniae*-associated neurological disease is unclear because of the

uncertain pathogenesis, limited penetration of most macrolide antibiotics into the CSF and absence of randomised trial data. Case series of children with *M. pneumoniae*-associated encephalitis receiving antibiotics report mixed results and complete neurological recovery without antibiotics is described.³ Given the generally benign prognosis of aseptic meningitis caused by *M. pneumoniae*,^{5 6} it is possible that antibiotic therapy does not influence the natural course of the disease, although use of macrolides with antibiotic and immunomodulatory activity might be beneficial.³ Our patient completed a 5-day course of azithromycin during his first hospitalisation and showed resolving CSF pleocytosis after antibiotics were stopped. Re-initiation of macrolide antibiotics did not appear to prevent the development of neuroretinitis and we cannot be certain whether it influenced his clinical recovery.

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Competing interests None.

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Learning points

- *Mycoplasma pneumoniae* can cause extrapulmonary manifestations, such as central nervous system (CNS) and ocular complications even in the absence of respiratory symptoms.
- A combination of chronic meningitis, neuroretinitis and intracranial hypertension is a rare presentation of *M. pneumoniae* infection.
- The pathogenesis of *Mycoplasma*-associated CNS disease is still incompletely understood—direct invasion and immune-mediated mechanisms have been proposed.
- There is a paucity of evidence to guide management of extrapulmonary manifestations of *Mycoplasma* infection, but macrolide antibiotics with antimicrobial and immunomodulatory properties are often used. Better understanding of the pathogenesis may inform future therapeutic approaches.

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