A rare case of bilateral optic neuritis and Guillain-Barré Syndrome post- Mycoplasma pneumoniae infection

Journal: Neuro-Ophthalmology

Manuscript ID: NOPH-2016-0036.R1

Manuscript Type: Case Report

Date Submitted by the Author: n/a

Complete List of Authors: Ross Russell, Amy; Darent Valley Hospital, Neurology
Baheerathan, Aravindhan; National Hospital for Neurology and Neurosurgery
Farmer, Simon; National Hospital for Neurology and Neurosurgery, Neurology

Keywords: Mycoplasma pneumoniae, Optic neuritis, Radiculopathy

URL: http://mc.manuscriptcentral.com/noph
Title: A rare case of bilateral optic neuritis and Guillain–Barré Syndrome post-Mycoplasma Pneumoniae infection

Short title: Mycoplasma optic neuropathy

Authors:

Aravindhan Baheerathan¹*
Core Medical Trainee

Amy Ross Russell²*
Neurology Specialist Registrar

Simon F Farmer¹
Consultant Neurologist

*Aravindhan Baheerathan and Amy Ross Russell contributed equally to this manuscript and are joint first co-authors

Affiliations:

1) Department Neurology
   National Hospital for Neurology & Neurosurgery
   Queen Square London
   WC1N 3BG

2) Department of Neurology
   Darent Valley Hospital
   Dartford & Gravesham NHS Trust
   Dartford
   DA2 8DA

Corresponding Author: Amy Ross Russell
Darent Valley Hospital
Dartford & Gravesham NHS Trust
Dartford
DA2 8DA
Email: amyrossrussell@nhs.net

Acknowledgements
SFF acknowledges funding support from the UCLH Biomedical Research Centre

URL: http://mc.manuscriptcentral.com/noph
Conflict of interest

The authors declared no potential conflicts of interests with respect to the authorship and/or publication of this article.

Financial disclosure/funding

The authors received no financial support for the research and/or authorship of this article.

Ethical approval

Not applicable.
A rare case of bilateral optic neuritis and Guillain–Barré syndrome post-Mycoplasma pneumoniae infection

Abstract

Neurological complications are the most commonly encountered extra-pulmonary manifestation of infection with Mycoplasma pneumoniae. Here we report the case of a 39-year-old female who was admitted with acute onset, bilateral visual loss coinciding with ascending numbness. Clinical examination, neurological imaging and nerve conduction studies revealed a syndrome of bilateral optic neuritis and acute inflammatory demyelinating polyneuropathy. Serological testing confirmed recent exposure to Mycoplasma pneumoniae. The patient did not experience any clinical benefit with pulsed intravenous methylprednisolone but demonstrated marked clinical and radiological improvement following five days of plasma exchange. This report will explore the diagnostic and therapeutic approach to patients with neuro-ophthalmological and neurological complications of Mycoplasma pneumoniae infection in addition to discussing previously encountered cases.

Case report

A 39-year-old Afro-Caribbean female was admitted urgently to our neurological department from the local ophthalmic hospital casualty department, having presented with acute-onset bilateral visual loss. Ten days preceding her admission, she had noted a frontal headache, followed by bilateral eye pain and gradual reduction in visual clarity over the subsequent five days. Upon initial assessment visual acuity (VA) was nil perception of light (NPL) in either eye. Pupillary reflexes were absent. She had bilateral swelling of the optic discs with splinter haemorrhages (figure 1a). There was bilateral globe tenderness but no pain on eye movements. Assessment of her visual fields demonstrated large central scotomas bilaterally (figure 1b). The remainder of cranial nerve examination was normal.

She also noted sensory disturbance in her fingers and toes. Examination revealed reduction in both light-touch and pin-prick in a length dependent fashion in both the upper and lower limbs. Reflexes were symmetrical and present bilaterally, although were later lost in the lower limbs.

MRI of the brain and orbits on admission showed bilateral enhancement and enlargement of the intra-orbital portion of the optic nerves (figure 3a). The remainder of the brain parenchyma were normal. PET-CT of the whole body did not show any pathological uptake.

Electrophysiological investigation demonstrated a motor predominant acquired distal demyelinating polyneuropathy.

Cerebrospinal fluid showed protein of 0.21g/L, white cell count of 4, negative culture and cytology. Routine blood tests were normal. HIV, aquaporin-4; anti-neuronal antibodies and other auto-antibodies were negative. Mycoplasma pneumoniae serology showed a titre of...
1:20480, highly suspicious of acute infection. Subsequent convalescent sera confirmed that this was a recent exposure and on further questioning the patient recalled a mild upper respiratory tract infection two weeks earlier in the community characterised by a dry cough and headache. Mycoplasma was not isolated from the CSF, and CSF Mycoplasma PCR was negative.

A diagnosis of bilateral optic neuritis and acute inflammatory demyelinating polyneuropathy secondary to Mycoplasma pneumoniae infection was made.

The mycoplasma infection was treated on admission with an oral course of clarithromycin (seven days). The patient was treated on admission with six doses of 1g intravenous methylprednisolone on consecutive days without clinical improvement. We then proceeded immediately to plasma exchange, completing five courses over five days. This produced rapid clinical improvement of visual acuity and gradual improvement of her sensory symptoms. Upon discharge of the patient, the VA in the right eye was 6/18 and the VA in the left eye was 6/9. She was discharged on an oral taper of prednisolone over 1 month starting at 1 mg/kg.

Repeat imaging two weeks after completion of plasma exchange demonstrated radiological resolution of the bilateral optic neuritis (figure 3b) and repeat nerve conduction studies showed marked improvement of the polyneuropathy. Fundal photography eight weeks post-treatment demonstrated bilateral optic disc pallor (figure 2a).

Eight months later, upon review in the outpatient clinic, the patient had a VA of 6/5 in the left eye and a VA of 6/12 in the right eye. Despite improvement in the diameter of the scotomas, there were persisting visual field deficits in the right & left eyes (figure 2b). She has not had any relapse of her optic neuritis following complete tapering of oral steroid therapy. She had no remaining symptoms of her previous polyneuropathy.

**Discussion**

Mycoplasma pneumoniae is a commonly encountered pathogen that is often associated with infection of the respiratory system and produces a highly variable clinical phenotype, ranging from a mild upper respiratory tract infection to a severe pneumonia\(^1\). In addition to its respiratory manifestations it can also give rise to numerous extra-pulmonary manifestations, particularly neurological\(^1\).

Neurological complications have been reported to occur in between 0.1-7% of patients infected with Mycoplasma pneumoniae, typically occurring between 2 and 14 days after initial respiratory symptoms\(^2\). These have been widely reported in the paediatric population\(^1\-^3\). Central nervous system (CNS) manifestations include: encephalitis, meningoencephalitis, aseptic meningitis, transverse myelitis, cerebellar ataxia, choreoathetosis, ischaemic stroke and syndrome of inappropriate anti-diuretic hormone. Peripheral nervous system manifestations are less commonly described but include: optic neuritis, cranial nerve palsies, Guillain–Barré Syndrome, polyradiculitis and peripheral neuropathy (box 1)\(^1\-^5\).
The pathogenesis of the neurological complications of Mycoplasma infection is poorly understood and is a source of debate\(^1,6\). It has been postulated that there may be two distinct mechanisms of mycoplasma-induced neurological disease: first, the direct result of mycoplasma invasion into the CSF\(^7\) and second, a systemic immune-mediated response to infection, with CNS sequelae. The latter mechanism fits best with the clinical presentation of our patient.

The diagnosis of Mycoplasma pneumoniae can prove challenging. Historically, cold agglutinins were used to aid the diagnosis of Mycoplasma pneumoniae infection. Cold agglutinins are produced 1-2 weeks after infection in 50% of patients and may persist for several weeks but due to their poor sensitivity and specificity they are now considered obsolete in making a diagnosis. Microbial culture is technically demanding, and seldom successful in routine medical practice. Diagnosis of Mycoplasma infection is primarily achieved through a consistent clinical presentation that coincides with positive serological testing, such as passive agglutination, complement fixation and ELISA. Serological tests for anti-Mycoplasma antibody represent the most common method for retrospective diagnosis of Mycoplasma infections but they depend on convalescent sera for confirmation and false positive results from cross reactivity are a problem\(^1,2\). Seroconversion is defined as a four-fold increase in titre between acute and convalescent sera, or a single high anti-Mycoplasma complement fixation antibody titre of >1:128\(^1\). These criteria were both met in our patient. A combination of PCR and serology is recommended for accurate diagnosis especially for patients with neurological and other extra-pulmonary manifestations\(^1,2\).

The concomitant occurrence of bilateral optic neuritis and Guillain–Barré Syndrome post-Mycoplasma infection has been reported on four previous occasions in the published literature; however, in three of the four cases the onset of an acute inflammatory demyelinating polyneuropathy (AIDP) preceded the onset of bilateral optic neuritis\(^9,10\). Ginesta \textit{et al.}\(^8\) described a similar case of bilateral ON preceding AIDP, however, in contrast to our case, their patient demonstrated an AIDP with predominantly motor symptoms. In all four cases, excellent motor recovery and partial visual recovery was achieved with the use of immunotherapy (two cases treated with intravenous immunoglobulins, one with plasma exchange and one with intravenous steroids). Whilst our patient did not improve with the use of intravenous steroid therapy, the use of plasma exchange produced rapid recovery of visual acuity and resolution of the sensory symptoms.

The role of antimicrobials in the treatment of neurological manifestations of Mycoplasma infection remains controversial whilst the mechanism of disease is unclear. If Mycoplasma infection is directly responsible for the pathology, then antibiotic treatment would be recommended. Antibiotic treatment recommendations also need to take in to account CSF bioavailability. If the mechanism is immune-mediated then it is less clear whether antimicrobial therapy is appropriate\(^10,1\), particularly after the acute illness has resolved\(^1\). In practice patients such as ours are treated urgently with antibiotic and immune therapy.
Conclusion

We report a rare case of bilateral optic neuritis in association with acute inflammatory demyelinating polyneuropathy secondary to Mycoplasma pneumoniae with severe neuro-ophthalmological deterioration and a poor initial response to intravenous steroid therapy; thus requiring escalation to plasma exchange with good response.

The most effective treatment protocol is not known, and good clinical response has been seen with steroids and intravenous immunoglobulin therapy. However, given our patient’s dramatic response to plasma exchange in the absence of any improvement with steroid therapy we believe this should be considered early in patients presenting with this clinical syndrome, in order to minimise the potential for long term neurological and neuro-ophthalmic damage.

Key messages

- M. pneumoniae can lead to a diverse range of neurological manifestations and should be considered, particularly in cases with an infectious prodrome
- We report a case of bilateral optic neuritis and acute inflammatory demyelinating polyneuropathy post-M. pneumoniae infection
- The infection can be difficult to diagnose but serological testing and PCR are the most commonly utilised methods
- Early immunotherapy and antibiotic therapy are essential.
References


Acknowledgements. SFF acknowledges funding support from the UCLH Biomedical Research Centre
Box 1: Neurological manifestations of *mycoplasma pneumoniae* infection

**CNS**
- Encephalitis
- Meningoencephalitis
- Aseptic meningitis
- Cerebellar ataxia
- Chorea-hallucinosis
- Transverse myelitis
- Acute psychosis
- Ischaemic stroke

**PNS**
- Optic neuritis
- Cranial nerve palsies
- Guillain Barre syndrome
- Polyradiculitis
- Peripheral neuropathy

210x297mm (200 x 200 DPI)
Figure 1a: Fundal imaging demonstrating bilateral optic disc swelling with splinter haemorrhages in both right and left eyes
Figure 1b: Visual fields obtained via Goldman perimetry on admission demonstrating bilateral central scotomas

210x297mm (200 x 200 DPI)
Figure 2a: Fundal imaging 2 months following initial treatment demonstrating bilateral optic disc pallor
Figure 2b: Visual fields assessed via gold perimetry at 8 months following completion of plasma exchange
demonstrating improvement in the size of the bilateral central scotomas

Figure 2
210x297mm (200 x 200 DPI)
Figure 3a: Bilateral enlargement and post-gadolinium enhancement of the intra-orbital and intra-canalicul
portions of the optic nerve
Figure 3b: Following plasma exchange, marked improvement of the swelling of both optic nerves with
minimal enhancement seen post-gadolinium administration

Figure 3
210x297mm (200 x 200 DPI)