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A cranial nerve palsy associated with *Mycoplasma pneumoniae* infection

Polymerase chain reaction evidence against an infectious mechanism

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Mycoplasma pneumoniae is primarily a pathogen of the respiratory tract but is associated with a spectrum of non-respiratory disease. Individual cases provide some insight into the pathological processes.

Case report

A 4-year-old Caucasian female presented complaining of double vision of sudden onset. Eight days earlier the patient had a severe respiratory tract infection without lymphadenopathy, which was treated with amoxycillin, following which she developed a macular rash over the trunk and limbs for 5 days. Medication was changed to erythromycin.

Ophthalmic examination showed a right partial third nerve palsy affecting the levator palpebrae superioris, superior rectus, and inferior oblique muscle, but sparing the medial rectus, inferior rectus, and parasympathetic fibres to the pupillary sphincter and ciliary muscles. Double vision was present on attempted upgaze but absent in the primary position. Bell's phenomenon was equivocal on first visit and normal subsequently. The patient's visual acuity was 6/5 unaided in both eyes. There was no evidence of intraocular pathology. Orbital or sinus pathology was excluded. A computed tomogram was normal and a lumbar puncture was not clinically justified.

The rash and chest infection resolved 8 days after first presentation. Blood was taken for an antibody screen with a follow up blood sample 10 days later.

There was no further progression of the third nerve palsy after presentation. A recovery of

function over 4 months was evident with a slower resolution of residual deficit over 9 months when the patient finally lost a respiratory wheeze that had developed with the upper respiratory tract infection (URTI). The paired sera showed no evidence of Epstein-Barr virus infection (glandular fever) but gave a constant and significant level of *Mycoplasma* antigen agglutination (1/320) (Serodia-Myco-II kit, Fujirebio, Japan). In the complement fixation test (antigen; Behringwerke AG, Marburg, Germany) both sera gave the same significant titre of 1/512. A u-capture enzyme linked immunosorbent assay for IgM specific to *M. pneumoniae* (Diatech Diagnostica Ltd, Israel) showed a rising IgM in the sera confirmed with another *M. pneumoniae* IgM detection system.¹ A polymerase chain reaction (PCR) amplification of the DNA from both sera using *M. pneumoniae* specific primers² gave no evidence of organisms in the serum.

Comment

M. pneumoniae infection causes intermittent infection in the community between 4 year infection peaks in the United Kingdom. In the respiratory tract it causes illnesses ranging from mild URTI to severe pneumonia and occasional unexpected death in young people.^{3,4,5} It has been recorded as the cause of non-respiratory disease in children and adults including central nervous system lesions, haemolytic anaemia,⁶ and maculopapular rash or erythema multiforme.⁷ The pathological processes in *Mycoplasma* non-respiratory manifestations are believed to involve an exaggerated immune response possibly with induction of autoantibodies,⁸ changes of the proteins on the red cell

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membrane,^{9 10} and lymphocyte infiltration around blood vessels.¹¹ The mechanisms in respiratory disease are also ill understood.¹² There is a dilemma about the therapeutic advantage in antibiotic treatment of non-respiratory manifestations, as these may not involve organisms.

In this case a differential diagnosis included viral causes of cranial nerve palsies,^{13 14} but the serological results and a well recognised¹⁵ clinical sequence of an emerging central nervous system lesion after a respiratory infection confirmed *M pneumoniae* infection. Often the serological response will be late, making a laboratory diagnosis difficult and of limited clinical value. A new exquisitely sensitive PCR detection method specific for *M pneumoniae* DNA² applied to this child's sera failed to detect any evidence of *Mycoplasma* DNA.

Partial third nerve palsies, particularly those which are pupil sparing, are well documented in microvascular disease especially diabetes mellitus. The lesion site in this case is likely to be the superior division of the third nerve as complete recovery eventually occurred. The inferior oblique is known to be unable to elevate the globe above the primary position in the presence of a paretic superior rectus. Other observers¹⁶ looked at seven patients with an acquired monocular elevation paresis. Their patients showed impairment of Bell's phenomenon but no ptosis and no significant recovery and they postulated that a microvascular lesion in the pretectal area close to the oculomotor nucleus was responsible.

If *M pneumoniae* organisms were associated directly with any microvascular occlusion in our case, it is very likely that the PCR system would have detected *M pneumoniae* DNA in the serum, with detection levels of one copy of DNA per sample which is at least a thousand times more sensitive than any culture or antigen detection system for *M pneumoniae*.² These findings suggest that the pathology resulted from host immune activity without organisms being directly involved. The antibiotic given to this patient may shorten the time that organisms are present in the host but would not destroy

specific DNA recognised by PCR until later degradation by host enzyme activity. A lumbar puncture was not justified in this case, but studies (Fink CG, Read SR, Butler L, Pike M. *Mycoplasma pneumoniae* and CNS lesions. PCR evidence that the pathology is immune mediated, in preparation) have shown no evidence of organisms in the cerebrospinal fluid in central nervous system lesions associated with *Mycoplasma* infection.

These findings support the observation that *Mycoplasma* associated central nervous system lesions are an exaggerated immune response.

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Topical chemotherapy for conjunctival melanoma

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Surgical excision, cryotherapy, and radiotherapy have been used for treatment of conjunctival tumours.¹⁻³ When treating conjunctival melanoma surgical margins include areas of visible pigmentation and 2 mm pigment-free margins. Since pathological evaluations of excised specimens commonly display patches of

amelanotic melanoma extending beyond hyperpigmented areas, the visually pigmented margin offers a poor definition of the tumour's 'edge'.

Topical chemotherapy of conjunctival tumours offers a non-surgical treatment with less dependence on surgical margins, should treat tumour extension onto the corneal epithelium,

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