A cranial nerve palsy associated with Mycoplasma pneumoniae infection

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 DNA16 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 observers17 looked at seven patients with an acquired monocular elevation paresis. Their patients showed impairment of Bell’s phenomenon but no palsy 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.1 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.1,2 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 hyper-pigmented 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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and could be easily repeated. This approach also allows for high concentrations of chemotherapy to be delivered directly to the tumour.13

Ophthalmologists have experience using 5-fluorouracil (5-FU) and mitomycin C (MMC) to inhibit fibroblast proliferation after glaucoma and pterygium surgery.14,15 While both inhibit DNA synthesis, 5-FU only interacts with S phase cells (those actively synthesising DNA). Dormant cells become able to proliferate when treatment has been discontinued.15 In contrast, MMC affects cells within all phases of the cell cycle inducing scission of tumour DNA even after treatment has been discontinued.16,17 Since melanomas are typically slow growing tumours (with a small subset of S phase cells), and our goal was to sterilise a cancer, we chose to investigate topical MMC chemotherapy.

**Case report**

tA 51-year-old woman underwent primary surgical excision for a conjunctival melanoma on her left eye. Over the next 5 years she received three laser treatments to her temporal limbus to control tumour regrowth.

Upon referral to the Ocular Tumor Service of the New York Eye and Ear Infirmary, ophthalmic examination revealed a visual acuity of 20/25 in both eyes. All conjunctival surfaces were inspected by slit-lamp biomicroscopy. Three hypervascular pigmented lesions were noted to have thickness. Two were located at the corneoscleral limbus at the 3 and 6 o'clock meridians. The third lesion was located on the supero-temporal tarsus. Areas of acquired melanosis covered most of the temporal bulbar conjunctiva and onto the edge of the temporal cornea. A metastatic survey was negative.

Informed consent involved a discussion of the risks and benefits of surgical excision with adjuvant cryotherapy versus topical application of mitomycin C (Bristol Labs, Evansville, Indiana, USA). She was aware that she would be the first patient (to our knowledge) to undergo this form of treatment.

Collagen plugs were placed in her inferior and superior punctae on a weekly basis. The MMC dose regimen was similar to that published for postoperative treatment of pterygium.18,19 One drop of MMC (0.04%) was placed in her superior fornix four times a day. During weekdays she also received an ophthalmic examination and one of her drops in the form of three 15 second applications of MMC-soaked surgical sponges onto the three nodular areas. Treatment was discontinued after 28 consecutive days.

Decreased pigmentation of the acquired melanosis and thinning of the nodal tumours were noted within 1 week of treatment. Areas of pigmentation decreased in size over the next 3 weeks (Fig 1). Residual clumps of pigmentation were noted beneath the conjunctival epithelium. A circular 2 mm corneal abrasion appeared on day 7 and was noted to resolve by day 14. Three weeks after the end of treatment our patient underwent surgical removal of the residual pigmented tissues with adjuvant cryotherapy.

Histopathology revealed no viable tumour in a limbal specimen taken from the 12 to the 9 o'clock meridians. In the tarsal lesion (which had never before been treated by any other means than MMC chemotherapy) the superficial half of this tumour was largely eradicated (Fig 2). Scattered neoplastic cells were present along the tracts of pseudoglands of Henle. These cells were confirmed to be melanomatos by HMB-45 (Dakopatts) immunoperoxidase staining. The deep portion of the tumour persisted and was noted to be associated with reactive lymphoid tissue at its base (Fig 2). The conjunctiva was largely intact, but was thinned and atrophic. There was sclerosis and inflammation (acute and chronic) in the tissues where the neoplasm was eliminated. Frankly necrotic tissue was not seen.

**Comment**

We present a case where topical MMC chemotherapy of conjunctival melanoma induced a partial response characterised by a significant reduction in tumour volume. Though the nodular tumours and subepithelial rests were found to be resistant to chemotherapy, it is important to note that we have investigated only one dosage and duration of treatment. Local

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**Figure 1A** Before topical mitomycin C therapy the nodal lesion had thickened the superior conjunctiva.

**Figure 1B** Three weeks after onset of topical mitomycin C therapy the superficial melanosis had largely resolved leaving a deep nodular nest of melanotic tissue.
cures in subsequent patients may require different dosages and/or durations of treatment, removal of tumour nodules before topical therapy, or a switch to another chemotherapeutic agent (for example, cis-platinum) which may be more effective against malignant melanoma. It was also significant to note that after we treated her residual tumour with excision and extensive cryotherapy no symblepharon formed. This may have been a manifestation of MMC-related long term inhibition of Tenon’s capsule fibroblasts. Prevention of symblepharon after cryotherapy for conjunctival tumours may be an additional use for topical MMC therapy.


