Small cell carcinoma presenting as ocular paraneoplastic syndrome due to CRMP-5

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ABSTRACT

We report the case of a lady who presented with 3 weeks of visual floaters and optic disc swelling. Subsequent investigations revealed deep white matter changes on brain imaging, and enlarged mediastinal nodes. The presence of anti-CRMP-5 antibodies finally led to the diagnosis of a paraneoplastic syndrome, and mediastinal lymph node biopsy confirmed the diagnosis of small-cell lung cancer. The learning points from this case include that optic neuritis can be the only presenting feature of a paraneoplastic neurological syndrome, and the usefulness of anti-neuronal antibody measurement as a diagnostic marker of an underlying paraneoplastic disease process. The great challenge is to recognise these tumour-associated autoimmune system presentations early, as they often appear long before the primary cancer is evident. Prompt treatment leads to an earlier reduction in circulating auto-antibody possibly due to reduction in tumour size, and thus less likelihood of permanent neuronal damage.
to significant improvement. The swelling of her optic nerves significantly reduced as did the vitreous haze. Her vision had improved in her right eye to 6/24 and her vision in her left eye improved to 6/9.

**Diagnostic assessment.** The MRI of head (Figure 1) with contrast showed no evidence of venous thrombosis, no meningeal enhancement or space occupying lesion, but the radiologist questioned whether the white matter lesions that had been noted initially were due to ischaemia. They were not typical of neurosarcoid but lumbar puncture was arranged. Serum ACE was not possible as she already took an ACE inhibitor for hypertension.

**Lumbar puncture.** This showed an opening pressure of 4cm, and a CSF lymphocyte count of 7. There were unmatched oligoclonal bands, and normal cytology. The CT scan of thorax, abdomen and pelvis: no evidence of malignancy.

**BLOODS.** normal CRP, ESR and FBC. Protein electrophoresis- normal.

Her blood was also sent for antineuronal antibody serology, and showed that CRMP-5 and SOX-1 paraneoplastic antibodies were positive. Therefore, PET scan was arranged which showed mediastinal and left hilar lymphadenopathy (Figure 2) that the radiologist felt was not typical of lymphoma.

**Therapeutic intervention.** Her case was discussed with the respiratory and thoracic teams and lymph node sampling by endobronchial ultrasound was organised, and the mediastinal nodes confirmed small cell lung cancer (TXN2M0) as the diagnosis.

**Follow up and outcomes.** She commenced Etoposide and Carboplatin chemotherapy. Her oral steroids were steadily reduced, and vision improved after chemotherapy began, with her right cataract to be dealt with later. She remains in clinical remission.

**Discussion.** Collapsin response-mediator protein, in particular CRMP-5, is a neuronal cytoplasmic antigen. Onconeural antibodies against this antigen are seen in tumour cells of small cell lung cancer and thymoma, and lead to cross reacting immune-mediated autoimmunity. Other auto-antibodies are possibly involved also, and in this case anti-Sox-1 was detected.

![Figure 1 - MRI head showing bilateral white matter changes.](image1)

![Figure 2 - Left hilar and mediastinal lymphadenopathy.](image2)
A wide variety of neurological syndromes have been associated with CRMP-5 antibodies and associated ophthalmic findings described, for example disc swelling and with associated uveitis.\textsuperscript{4,5} Cross et al\textsuperscript{6} described the triad of vitreous cells, retinal vessel leakage and optic neuritis linked to anti-CRMP-5 antibodies, and that positive serology could avoid the need for vitreous biopsy.

The great challenge is to recognise these tumour-associated immune system presentations, as they often appear long before the primary cancer is evident.\textsuperscript{7} It has been shown that early treatment sometimes results in rapid resolution of the ocular symptoms, and prompt treatment leads to an earlier reduction in circulating auto-antibody\textsuperscript{8} possibly due to reduction in tumour size,\textsuperscript{9} and thus less likelihood of permanent neuronal damage.

In conclusion, when confronted by patients like this, for example smokers with visual changes and swollen optic discs, then a high index of suspicion might lead to improved prognosis due to earlier diagnosis. Paraneoplastic syndromes should certainly be considered as part of the differential diagnosis and anti-CRMP-5 levels should be measured.

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