Paraneoplastic optic neuropathy associated with papillary renal cell carcinoma

A 54-year-old gentleman presented to our Eye Unit following an optician referral with a 4-month history of gradual visual deterioration. Other significant symptoms included problems with his mobility and balance consistent with an ataxic sensory neuropathy for which he had not sought medical advice. History revealed a significant amount of cigarette smoking and alcohol intake with poor dietary habits. On examination, he had a best-corrected visual acuity of 2/60 in both eyes. Pupil reaction was sluggish, but there was no relative afferent pupil defect and ocular motility and anterior segment examinations were all normal. Due to the severity of visual loss, he was unable to perform formal colour vision tests.

Fundus examination revealed bilateral pale optic discs with atrophy more prominent on the temporal side. A provisional diagnosis of bilateral optic atrophy secondary to nutritional/toxic cause was assumed. The patient then had blood tests, which included serum vitamin levels. Visual field testing revealed peripheral constriction in both eyes. His blood mean corpuscular volume was 110.9 fL (normal=75–95) and ferritin level was 916 μg/L (normal=15–300). The serum folate level was 126 μg/L (normal=160–640). Full blood count, syphilis serology, vitamin B12 levels, liver function tests and urea/electrolyte levels were otherwise normal. Electrodiagnostic testing revealed markedly degraded occipital pattern VEPs while maintaining normal latencies. Pattern ERG macular component was normal, but the N95 components (ganglion cell activity) were degraded. All these were consistent with a marked post-retinal dysfunction and compatible with a diagnosis of toxic (tobacco/alcohol) or nutritional type optic neuropathy. An MRI scan of brain and orbits showed generalised volume loss in the brain as expected for his age and was otherwise normal.

Three months after presentation, his acuity and systemic features had deteriorated clinically. He was now unable to walk and was admitted for further investigation. A full-body CT scan was done at this point which revealed a 4-cm diameter solid mass lesion arising from the upper pole of his left kidney; this was well defined and non-invasive. There was also some fatty infiltration of the liver but no focal lesion. A renal biopsy done confirmed the renal mass as a Papillary cell carcinoma. A full set of anti-neuronal antibodies were requested; anti-Yo, Ri, Hu, Ma1, Ma2, CV2, CRMP5 and amphiphysin were all reported as normal. He then underwent a successful laparoscopic nephrectomy.

QUESTIONS

1. What are the usual ophthalmic manifestations of a paraneoplastic syndrome?
2. What is the pathological mechanism for this condition?
3. How would you manage this case of paraneoplastic optic neuropathy?

See page 438 for answers

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ANSWERS

From the question on page 429

1. Neuro-ophthalmic manifestations in Paraneoplastic syndromes commonly include unilateral/bilateral optic disc oedema, optic neuritis, optic atrophy, etc.[1]
2. The causative mechanism seems to be an immune mediated damage of neuronal tissue by cross-reacting antibodies produced by neoplastic expression of tumour antigens. Positive IgG antibody against neuronal antigens like recoverin (CAR), CV2 and collapsin response-mediated protein (CRMP-5) have been identified in many cases.
3. A high index of suspicion is essential for appropriate diagnosis of these cases. Systemic investigations should take the form of immunological tumour marker screening, full-body CT imaging and a neurology referral. Treatment consists mainly of managing the underlying tumour with a combination of surgery, chemotherapy and/or radiotherapy depending on the extent of the disease. Oral steroids and immunoglobulin therapy in particular may improve visual fields and acuity in some early cases.[1–3]

DISCUSSION

Paraneoplastic optic neuropathy has previously been documented in literature and is reported to be mainly associated with small cell lung carcinoma[4–6] (other reported case associations being with Hodgkins and Non-Hodgkins syndrome, nasopharyngeal carcinoma, bronchial carcinoma and thymoma).[7 1] Clinical recognition and awareness of potential paraneoplastic causes is important to allow appropriate management in these cases with optic neuropathy. Current evidence points to underlying autoimmune-mediated mechanisms presumably triggered by the neoplastic expression of neuronal proteins which cross-react with antigens from the optic nerve. Positive IgG antibody neuronal markers like CAR, CV2 and CRMP-5 have been identified in cases involving small cell lung cancer.[1 8 9] Bataller *et al* have reported associations with other antibody markers like anti-hu, Yo, Ma2, Ri, Tr and voltage-gated calcium channel antibodies.[3] No specific antibody markers have been described in literature for renal cancers.

The autoimmune mechanism for this condition provides the rationale for provision of immunosuppressive therapy in addition to anti-tumour treatment in these cases. With the exception of the paraneoplastic optic neuropathy group presenting with optic neuritis or disc oedema, most patients show little or no response to immunosuppressive therapy.[2 10] However, there are no controlled clinical trials that address the treatment of paraneoplastic optic neuropathy in these cases. There have been no reports of spontaneous visual improvement in these disorders.

In conclusion, we report a novel association of papillary renal cell carcinoma as an underlying cause for optic neuropathy. During the clinical and investigative work up of these cases suspected to be associated with a paraneoplastic syndrome, screening for renal cancers in addition to a full neuronal antibody screen should be considered.

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