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Sir,

Light-near dissociation of pupil reactions as a presenting feature of von Hippel–Lindau disease

Bilateral light-near dissociation of the pupil reactions is typically caused by rostral midbrain lesions, which interrupt the retinotectal input to the Edinger–Westphal nuclei, but not the more ventral accommodative input.[1] We observed light-near dissociation of the pupil reactions as a presenting feature in a patient with a cerebellar haemangioblastoma, and who was subsequently diagnosed with von Hippel–Lindau disease.

A 38-year-old heating engineer presented to us with a 10-week history of blurred distance vision, headaches, impaired balance, vertigo, and fatigue. The deterioration in distance vision was bilateral and not associated with any diplopia.

His corrected acuities were 6/6 in each eye, but he had large dilated pupils, which reacted poorly to light but well to near targets. There was no segmental paralysis or vermiform movements evident on slit-lamp examination. Interestingly, his saccadic and pursuit eye movements were also normal, with no evidence of eyelid retraction or convergence retraction nystagmus on upgaze.

Dilated fundoscopy revealed multiple retinal haemangioblastomas, and a brain MRI demonstrated a large cystic lesion within the cerebellum. This cystic mass contained a superficial nodule which was enhanced following intravenous gadolinium administration, a feature characteristic of haemangioblastomas.[2] The mass was surrounded by oedema and was causing distortion of the IV ventricle, dorsal pons, and midbrain. Further investigations demonstrated a left renal mass and a mutation in the von Hippel–Lindau (VHL) gene.

Von Hippel–Lindau disease is an autosomal dominant disorder caused by mutations in a tumour suppressor gene on chromosome 3. Central nervous system (CNS) and retinal haemangioblastomas are the most frequent features of von Hippel–Lindau disease, with CNS haemangioblastoma being present in up to 80% of patients.[3] CNS haemangioblastomas are slow-growing and can reach large sizes in the cerebellum before becoming apparent clinically; light-near dissociated pupil reactions have not, however, been described previously as a presenting feature. In the months following surgical removal of our patient's cerebellar tumour, the light-near dissocation has been seen to become less apparent. We therefore believe the oedema surrounding the tumour, and associated compression of the dorsal midbrain, was the cause of the abnormal pupil reactions. He is currently under follow-up with repeated imaging.

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Sir,

Reply to Limbal stem cell deficiency: a clinical chamaelon

We read this case report with great interest. The authors described a case of a persistent corneal epithelial defect, stromal changes, and wound leak following a penetrating keratoplasty in an eye which had undergone a pterygium excision and conjunctival autograft.[1] The authors allude the epithelial defect noticed on the first postoperative day to be due to limbal stem cell deficiency. It may be plausible to provide an alternative explanation for the reported finding. The epithelial defect and corneal stromal changes were noticed to a site adjacent to the previous pterygia. Recent studies have shown evidence to suggest that the development of pterygia is linked to matrix metalloproteinases (MMPs) overexpressed by altered limbal epithelial basal cells.[2] MMPs are a family of more than 21 genetically distinct proteases, which are produced in small amounts under normal physiological conditions by fibroblasts and epithelial cells.[3] These MMP's being proteases dissolve and remodel extracellular matrix that includes fibronectins, collagen, and basement membrane.[3] During the development of pterygia, there is overexpression of MMPs that go on to dissolve Bowman's layer, which in turn triggers the fibrovascular pannus formation.[2]

The epithelial and stromal changes observed might have resulted from abnormal activity of MMPs from the previous site of the pterygium. Further, the figure shows the epithelial defect to be involving the donor corneal button as well on day 1. This was a very rapid change and manifestations of limbal stem cell deficiency are generally slow in onset.[4] The epithelial defect in this patient may be due to altered MMP expression resulting in dissolution of Bowman's layer leading to a corneal epithelial defect. The rapid healing of the epithelial defect following limbal stem cell graft may be contributed to the removal of source of the MMPs.

We would be most grateful for the view of the authors

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Sir,

Limbal stem cell deficiency: a clinical chameleon

Zaidi *et al*[1] infer that the corneal donor epithelial defect noted day 1 postkeratoplasty is secondary to limbal stem cell deficiency. How can this be so? A donor epithelial defect day 1 is surely due solely to loss of donor epithelium and has nothing to do with host limbal stem cell function. They have treated the donor epithelial defect with cyclosporin drops and intensive topical preservative-free steroids. This is inappropriate management for both stem cell dysfunction and persistent donor epithelial defect. They have then performed a limbal stem cell graft along with repeat keratoplasty, used the same inappropriate line of clinical management and observed a similar but less severe course of events. Therefore, they have neither demonstrated that limbal stem cell deficiency was the cause of the problem nor shown any convincing benefit from the stem cell graft.