

Sir,
New ocular phenotype associated with a mutation in the PAX2 gene

Renal-coloboma syndrome (RCS) is an autosomal dominant disorder caused by *PAX2* gene mutations and defined by the association of optic nerve coloboma and renal hypoplasia.^{1–3} We report a previously unknown phenotypic presentation of RCS in which calcified keratopathy and posterior lens luxation were associated with optic nerve defect.

Case description

A 10-year-old girl was referred to our hospital because of progressive loss of visual acuity in the right eye. Several years before, the child had been diagnosed as having RCS on the basis of renal hypoplasia associated with optic nerve colobomas. Genetic studies had confirmed the presence of a heterozygous *PAX2* gene mutation: 619insG. The child had additional anomalies such as mental retardation, epilepsy, vesicoureteral reflux, and joint laxity. There was no history of ocular trauma, and no family history of renal or ocular disorder was identified. Examination under anaesthesia revealed severe calcified keratopathy of the right cornea (Figure 1). The lens did not seem to be present through the pupil of the right eye and fundus was hardly accessible because of corneal opacity, so that a B-scan ultrasonography was performed and showed posterior lens luxation (Figure 1). As expected, the left eye fundus revealed an optic disc coloboma.

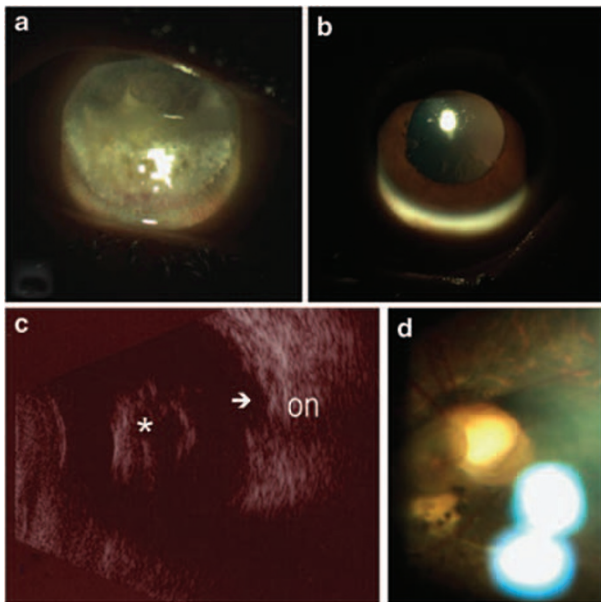


Figure 1 Unusual ocular phenotype associated with RCS and *PAX2* mutation (a–d). Operating room photographs of right eye (a) and left eye (b). The right anterior segment presented with severe calcified keratopathy (a) whereas the left anterior segment appeared normal (b). (c) B-scan ultrasonography of the right eye showing lens dislocation (asterisk) in the vitreous and optic nerve colobomas (white arrow). on: optic nerve. (d) Photograph of left eye fundus showing optic disc coloboma.

Comment

In this case report, the extra-ocular phenotype is characteristic of RCS. Conversely, the phenotype exhibited on the right eye has not been previously reported. Calcified keratopathy, which represents the first corneal defect ever documented in RCS, is probably consecutive to chronic renal failure with calcium phosphate disturbances.⁴ The second intriguing ocular abnormality was the presence of spontaneous lens luxation. Interestingly, investigators have previously reported that patients with RCS may have joint abnormalities such as joint laxity.^{2,5} In this case, the child also suffered from joint laxity and had been operated on for bilateral hip dislocation. Therefore, we suggest the possibility that lens luxation could be part of a general disorder involving the connective tissue or elastic fibres of different types and locations. This original description stresses the importance of investigating potential cornea or lens damage in patients presenting with such a syndrome.

Conflict of interest

The authors declare no conflict of interest.

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Sir,
Conjunctival lymphoma following treatment with cyclophosphamide

Conjunctival lymphomas typically result from a monoclonal B-cell proliferation and represent either localized disease or a systemic malignancy.¹ Most patients are over 60 years of age or are immunosuppressed.¹ Patients typically present with insidious onset of an asymptomatic, salmon-coloured, well-demarcated mass. Uncommonly, lymphoma may occur following treatment with immunosuppressive medications.² We present a case of conjunctival lymphoma that presented 4 years after treatment with cyclophosphamide. Although the association may be coincidental, our case emphasizes that physicians should be alert to the possibility of secondary malignancy occurring in the eye following systemic immunosuppression.

Case report

A 68-year-old man, with a history of sympathetic ophthalmia that occurred 6 years earlier, noticed a painless red mass in his right eye. Therapy for sympathetic ophthalmia included prednisone and a 6-month course of cyclophosphamide 50 mg/day. His past ocular history was otherwise notable for multiple intraocular surgeries in the right eye for cataract and open-angle glaucoma. On presentation, his visual acuity was 20/25 OU. Examination of the right conjunctiva revealed a salmon-coloured, vascularized mass from 1 o'clock to 3 o'clock (Figure 1). Fundus examination revealed a sunset glow appearance and chorioretinal scars bilaterally.

Biopsy revealed a diffuse lymphocytic stromal infiltrate (Figure 1b). Most lymphocytes were enlarged, with variable cytoplasm, irregular nuclei, and intranuclear inclusions (Dutcher bodies). Immunophenotyping revealed strong CD20 and kappa light chain positivity. The histopathological diagnosis was a low-grade B-cell lymphoma that was mostly consistent with marginal zone lymphoma. This type of lymphoma is often referred to as mucosa-associated lymphoid tissue lymphoma. Treatment involves evaluation for systemic disease. Localized conjunctival lymphoma may be treated with radiotherapy, although some cases may be cured by local excision.

Comment

Long-term studies of patients treated with cyclophosphamide showed an increased risk for malignancy, including lymphomas.^{2–4} Hoffman *et al*² observed a 2.4-fold overall increase in the incidence of malignancies, and an 11-fold greater incidence of systemic lymphomas in the general population. The risk appears to be dose-dependent, particularly with cumulative doses > 50 g, but is also reported with lower doses, and may

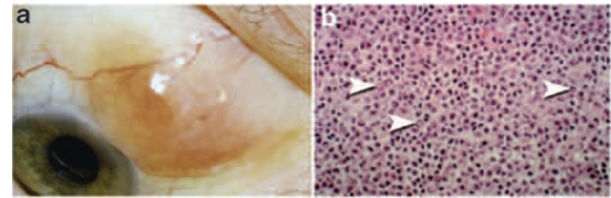


Figure 1 (a) Salmon-coloured, vascularized conjunctival mass of the right eye, extending from approximately 1 o'clock to 3 o'clock. Note the intact overlying conjunctiva and lack of feeder vessels. (b) Biopsy of the conjunctival mass, showing a nodular and diffuse lymphocytic infiltrate in the conjunctival stroma. Note the enlarged lymphocytes with variable cytoplasm and somewhat irregular nuclei. Higher magnification revealed intranuclear inclusions (Dutcher bodies, indicated by arrowheads). Most of the cells stained positively for CD20 and kappa light chains.

develop for up to 10 years.⁵ Our patient received a total of 9 g. Potential mechanisms of malignancy include induced chromosomal alterations, altered immune-mediated anti-tumour surveillance, and increased susceptibility to oncogenic agents.³ Although the possibility remains that the association was spurious, our report of conjunctival lymphoma following treatment with systemic cyclophosphamide is the first report of such a secondary ocular malignancy, and illustrates that physicians should be alert to the possibility of secondary malignancy occurring in the eye following systemic immunosuppression.

Conflict of interest

The authors declare no conflict of interest.

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