Ocular melanomas in xeroderma pigmentosum

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Xeroderma pigmentosum is a hereditary condition with an incidence of 1:250,000 live births.\(^1\) Inheritance is autosomal recessive and consanguinity of parents is common.\(^2\) Cells exhibit defective repair of ultraviolet induced or chemical damage to DNA and this has been demonstrated for cultured conjunctival cells.\(^3\)

Case reports

**CASE 1**

A 22-year-old woman presented with a pigmented right limbal lesion. She had progressive sensorineural deafness from childhood. Parental consanguinity could not be established. Multiple, pigmented, irregular freckles were evident on the exposed skin of her face, arms, and legs. Ophthalmic examination revealed a raised pigmented lesion of the right limbus associated with an area of conjunctival melanosis. Histology of the biopsy specimen showed a mass of pleomorphic cells with hyperchromatic nuclei and a high mitotic count. Dark brown pigment deposits proved to be melanin supporting the diagnosis of malignant melanoma of the conjunctiva. Two years later she presented with a pigmented mass on the inferior bulbar conjunctiva of the right eye. Histology showed spindle shaped cells with nuclear pleomorphism and frequent mitotic figures. The diagnosis of malignant melanoma was supported by immunocytochemical studies which showed expression of the S-100 protein and HMB-45 antigen by the tumour cells.

**CASE 2**

This patient, 2 years younger than her sister (case 1), presented aged 22 years. A vascularised limbal lesion of the left eye encroached onto the lateral cornea (Fig 1) requiring penetrating keratoplasty. The corneal graft specimen showed extensive pannus formation and irregularity of Bowman's membrane. Pleomorphic cells unconnected to the overlying epithelium were scattered throughout the stroma and at the time of the biopsy report were considered to be reactive in nature. Retrospective immunocytochemical examination did not show expression of the S-100 or HMB-45 antigen.

Seven years after her initial presentation a B scan ultrasound showed a ciliary body mass and the left eye was enucleated. The enucleated left eye contained a choroidal melanoma arising near the ciliary body and invading the iris (Figs 2A and 2B). The pleomorphic multinucleated spindle cells contained melanin pigment and the mitotic count was high with abnormal tripolar forms. Immunocytochemical studies showed no expression of S-100 or HMB-45.

Comment

Giller and Kaufmann\(^4\) considered that only 30% of patients with xeroderma pigmentosum had ocular involvement, but of the 46 cases reported by El-Hafrawi and Mortada,\(^5\) 91% presented with photophobia and conjunctivitis. Tumours affecting the eyelids include basal cell carcinomas, squamous cell carcinomas, and melanocytic lesions. Bellows et al\(^6\) reported an angiosarcoma affecting the cornea of one of three siblings with xeroderma pigmentosum. Squamous carcinoma of the limbus is the most common malignant tumour (occurring in up to 13% of patients).\(^7\)\(^8\) El Hafrawi and Mortada\(^9\) reported four cases with melanocytic lesions affecting the eye, two of which they considered were malignant. One was a conjunctival melanoma. The second was an advanced melanoma affecting the whole orbit and base of skull.

Ocular melanomas occurred in both sisters reported here. Case 1 had two separate melanomas of the conjunctiva both arising from areas of melanosis. A choroidal melanoma developed in case 2 which showed malignant cytological features, but did not label with antibodies to S-100 or HMB-45 by immunocytochemical

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**Figure 1** Left eye of case 2. An opaque lesion encroaches onto the lateral cornea.
methods. These antibodies label a majority of malignant melanomas. However, Nakajima et al. found three S-100 negative tumours in a series of malignant melanomas from many sites. All three were pigmented primary choroidal melanomas. It is possible that the original limbal lesion from case 2 represents a neoplastic process similar in nature to the intraocular melanoma rather than a reactive process, but this cannot be resolved.

Intraocular pathology in xeroderma pigmentosum is very rare due to attenuation of ultraviolet light as it passes through the cornea and lens. Johnson et al. describe a patient with malignant melanoma of the iris and refer to only two other reports of uveal (choroidal) melanoma from 830 reported cases of xeroderma pigmentosum. This represents a rate of occurrence 23 times greater than expected in the normal population.

The heterogeneity of the genetic defect in xeroderma pigmentosum has been demonstrated by De-Weerd-Kastelein et al. using somatic cell hybridisation techniques. Nine 'complementation' groups have been found with correlation between complementation groups and clinical presentation. Both cases reported here developed ocular melanomas, a rare occurrence even in xeroderma pigmentosum, and perhaps reflecting a shared genetic abnormality. Similar clinical manifestations of xeroderma pigmentosum in siblings have been reported previously by Hertle et al. who described two brothers who developed squamous cell carcinomas of conjunctiva.

Figure 2  Case 2. (A) A malignant melanoma encases a degenerate lens which shows dystrophic calcification. The tumour invades the adjacent iris (haematoxylin and eosin, × 20). (B) Higher magnification shows a pleomorphic spindle cell melanoma with an abnormal mitosis (haematoxylin and eosin, × 120).