CASE REPORTS

Ocular melanomas in xeroderma pigmentosum

A J Vivian, D W Ellison, J I McGill

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 unrelated 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 immunocytological 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 Kaufmann⁴ considered that only 30% of patients with xeroderma pigmentosum had ocular involvement, but of the 46 cases reported by El-Hafrawi and Mortada,² 91% presented with photophobia and conjunctivitis. Tumours affecting the eyelids include basal cell carcinomas, squamous cell carcinomas, and melanocytic lesions. Bellows *et al*³ 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).^{2,3,6} El Hafrawi and Mortada² 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

Hospital for Sick
Children, Great Ormond
St, London WC1N 3JH
Anthony J Vivian

Southampton General
Hospital, Southampton
SO9 4XY
David W Ellison

Southampton Eye
Hospital, Southampton
SO9 4XW
James I McGill

Correspondence to:
Mr Anthony J Vivian.

Accepted for publication
19 March 1993

Figure 1 Left eye of case 2. An opaque lesion encroaches onto the lateral cornea.

Fig 2A

Fig 2B

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, $\times 20$). (B) Higher magnification shows a pleomorphic spindle cell melanoma with an abnormal mitosis (haematoxylin and eosin, $\times 120$).

methods. These antibodies label a majority of malignant melanomas. However, Nakajima *et al*⁷ 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*⁸ 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 DeWeerd-Kastelein *et al*⁹ 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*¹⁰ who described two brothers who developed squamous cell carcinomas of conjunctiva.

- 1 Robbins JH, Kraemer KH, Lutzner MA, Festoff BW, Coon HP. Xeroderma pigmentosum. An inherited disease with sun sensitivity, multiple cutaneous neoplasms and abnormal DNA repair. *Ann Intern Med* 1974; **80**: 221-48.
- 2 El-Hafrawi H, Mortada A. Ocular manifestations of xeroderma pigmentosum. *Br J Dermatol* 1965; **77**: 261-76.
- 3 Newsome DA, Kraemer KH, Robbins JH. Repair of DNA in xeroderma pigmentosum conjunctiva. *Arch Ophthalmol* 1975; **93**: 660-2.
- 4 Giller H, Kaufmann WC. Ocular lesions in xeroderma pigmentosum. A case report of carcinoma of the cornea. *Arch Ophthalmol* 1959; **62**: 158-61.
- 5 Bellows RA, Lahav M, Lepreau FJ, Albert DM. Ocular manifestations of xeroderma pigmentosum in a black family. *Arch Ophthalmol* 1974; **92**: 113-7.
- 6 Reese AB, Wilber IE. The eye manifestations of xeroderma pigmentosum. *Am J Ophthalmol* 1943; **26**: 901-11.
- 7 Nakajima T, Watanabe S, Sato Y, Kameya T, Shinosato Y, Ishihara K. Immunohistochemical demonstration of S-100 protein in malignant melanoma and pigmented naevus and its diagnostic application. *Cancer* 1982; **50**: 912-8.
- 8 Johnson M, Skuta G, Kinkaid M, Nelson C, Wolter J. Malignant melanoma of the iris in xeroderma pigmentosum. *Arch Ophthalmol* 1989; **107**: 402-7.
- 9 DeWeerd-Kastelein EA, Keijzer W, Bootsma D. Genetic heterogeneity of xeroderma pigmentosum demonstrated by somatic cell hybridization. *Nature* 1972; **238**: 80-3.
- 10 Hertle RW, Durso F, Metzler JP, Varsa EW. Epibulbar squamous cell carcinomas in brothers with xeroderma pigmentosa. *J Paediatr Ophthalmol Strabismus* 1991; **28**: 350-3.