Recurrent malignant melanoma of the corneal stroma: a case of 'black cornea'

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Abstract
A 39-year-old Caucasian woman with a history of recurrent conjunctival melanoma of her right eye developed an intrastromal heavily pigmented malignant melanoma, which involved the whole corneal diameter. The patient was treated by corneoscleral lamellar keratoplasty and there has been no evidence of recurrent neoplasm during 4 years of follow-up. This apparently unique presentation of malignant melanoma of the cornea is illustrated and the differential diagnosis of corneal pigmentation is discussed.

Malignant melanoma of the cornea is very uncommon. Though primary corneal melanoma has been reported[1-5] this neoplasm is usually seen in association with an adjacent limbal or conjunctival melanocytic lesion. We describe a patient with a history of recurrent conjunctival melanoma who presented with a black cornea due to extensive malignant melanocytic invasion into corneal stroma.

Case report
In February 1987 a 39-year-old Caucasian woman was referred to Moorfields Eye Hospital with a 9-year history of recurrent malignant melanoma of her right conjunctiva. The diagnosis had been established by excision biopsies of temporal perilimbal pigmented tumours in 1983 and 1985, which showed that the melanoma originated from an area of primary acquired melanosis with atypia. No additional cryotherapy or β irradiation had been given.

She complained of having had right photophobia and blurred vision for several months. On examination there was extensive and dense pigmentation of the entire cornea, interfering with the central visual axis (Fig 1A). Slit-lamp examination showed involvement of superficial corneal stroma. There was evidence of melanosis of the temporal limbus but no nodular disease was noted. No further areas of conjunctival pigmentation were seen. The right visual acuity was 6/18 with pinhole and 6/36 unaided. The left unaided visual acuity was 6/6. The intraocular pressure was 10 mm Hg in both eyes. The left eye showed no abnormalities.

In June 1987 a corneoscleral lamellar keratoplasty was performed. More than two thirds of the thickness of the whole cornea were excised en bloc with a scleral component in the inferotemporal quadrant, which resulted in a keyhole shaped defect with a diameter of 15 mm by 24 mm (Fig 2). In addition diagnostic biopsies were taken from nasal conjunctiva, Tenon's capsule, and inferior fornix. A donor corneal graft was then sutured to the edges of the corneal host defect using interrupted 10/0 Nylon. The conjunctiva was closed over the bare scleral component of the donor corneal graft, so that the graft was covered to the level of the host limbus.

Postoperatively, there was a mild corneal stromal haze and the epithelial defect of the donor graft healed within 2 weeks. Some pigment and interface irregularity was noted at the graft host interface at 10 o'clock and both superficial and deep neovascularisation were seen at 6 o'clock. One year after the surgery, the cosmetic result was very satisfactory (Fig 1B) and no noticeable changes of the pigmentation and vascularisation were observed, except for a small area of flat pigmentation of the corneal edge at the 10-11 o'clock position. The best corrected visual acuity was 6/9 (20/30) with −5 D. Because of anisekonia the patient was fitted with a daily wear soft contact lens, which was well tolerated. Topical steroid therapy has been continued in gradually decreasing dosage (currently prednisolone drops, 3% twice daily).

On her last visit in May 1991, 4 years after removal of the corneal malignant melanoma, the visual acuity was 6/9 and there was no evidence of recurrence of frank malignancy.

HISTOPATHOLOGY
Histopathological examination of sections of the cornea and adjacent sclera showed a small focus of residual or recurrent malignant melanoma at the periphery of the cornea within the superficial stroma (Figs 3 and 4). Heavily pigmented cells were observed between stromal lamellae across the entire corneal diameter, almost reaching the resection margin on the opposite side. The corneal epithelium was atrophic but otherwise normal and there was no appreciable stromal vascularisation. Some infiltration of the adjacent bulbar conjunctiva by neoplastic cells was also seen together with mild inflammation in the underlying stroma. Within the conjunctiva the tumour was intraepithelial. Separate specimens from the vicinity of the lateral rectus muscle, the inferior Tenon's capsule, and from the nasal conjunctiva showed no abnormality.

Discussion
Pigmentation of the cornea is grossly or biomicroscopically visible and is of several origins including ocular inflammation, conjunctival melanocytic lesions, anterior segment trauma, the pigment dispersion syndrome,[6] and drugs.[7,8] Depositions of metals, blood pigments, lipids, and lipofuscin[9] may mimic the gold-brown to black melanin pigmentation.

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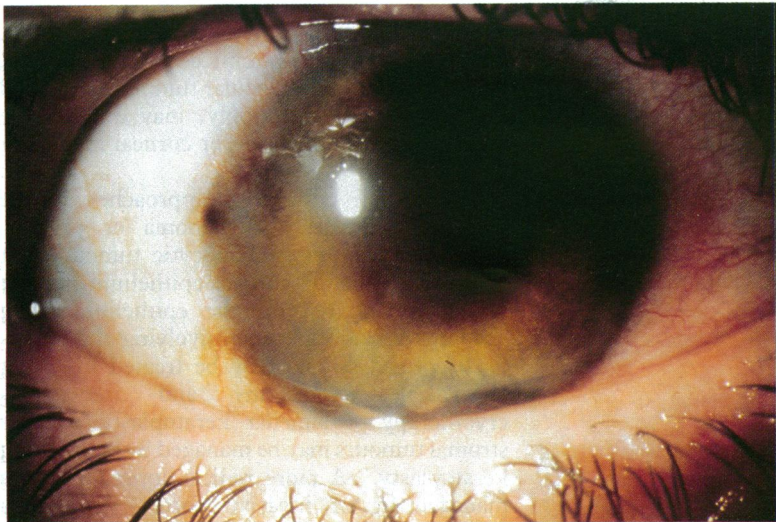Department of Pathology,
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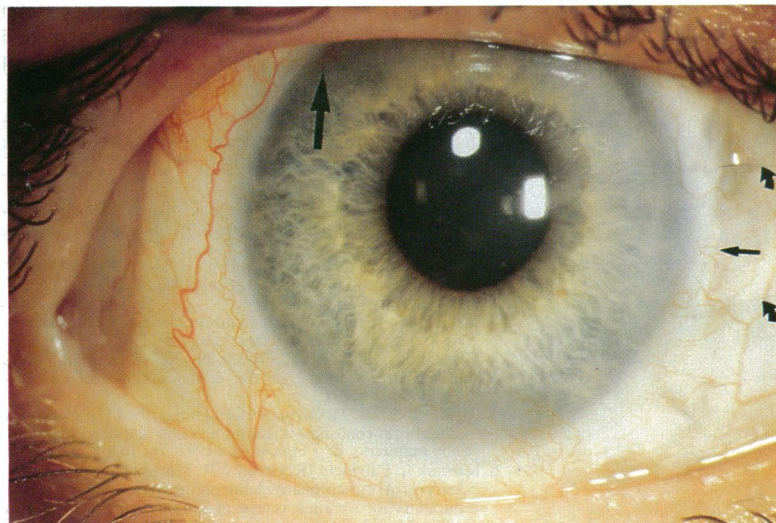London EC1V 9AT.

Fig 1A

Fig 1B

Figure 1 (A) 'Black cornea': extensive and dense pigmentation of the entire right cornea of a 39-year-old woman with a 9-year history of recurrent conjunctival malignant melanoma of her right eye. (B) One year after lamellar keratoplasty, the cosmetic result is very satisfactory. Except for a small area of flat corneal pigmentation (big arrow) between the 10 and 11 o'clock meridian, no pigmentary changes are noted. The edge of the lamellar graft (small arrow) and some stitches (curved arrows) can be identified.
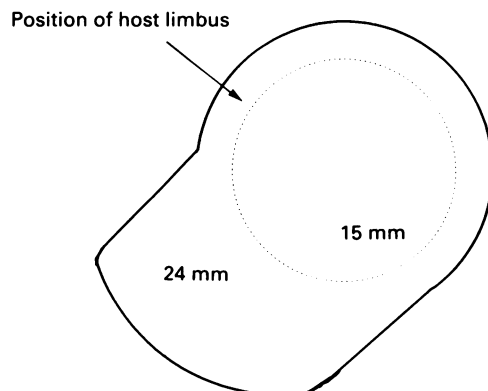

Figure 2 A donor graft was used to cover the keyhole shaped defect with a diameter of 15 mm by 24 mm, which was the result of en bloc excision of more than two thirds of thickness of the entire cornea with a scleral component in the inferotemporal quadrant.
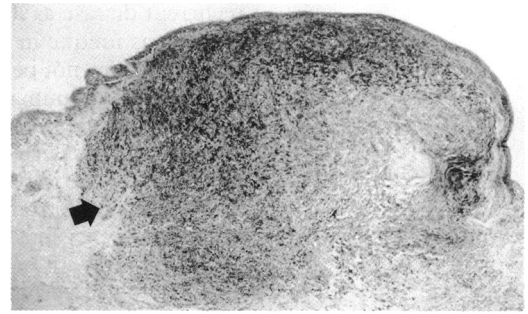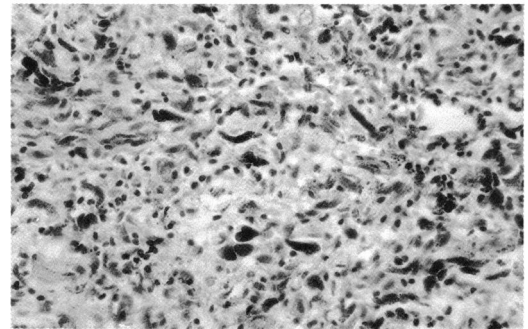

Fig 3A

Fig 3B

Figure 3 (A) Histological examination of biopsy specimens of the right temporal limbus and conjunctiva shows conjunctival malignant melanoma (arrow) originating from areas of primary acquired melanosis with atypia (haematoxylin and eosin, ×20). The maximal thickness of this nodule is 1·8 mm. (B) Higher power examination shows heavily pigmented, large pleomorphic cells and spindle cells (haematoxylin and eosin, ×200).

The location of corneal pigmentation depends on the underlying cause. Posterior corneal melanin pigmentation has been described in association with congenital melanosis oculi,[10] iris melanocytic proliferation,[11] endothelial phagocytosis of free melanin pigment, and the presence of melanophages or iris pigment epithelial cells.[12] Melanin pigmentation of the anterior cornea has been shown to increase with age and to be related to melanosis of the bulbar conjunctiva.[13] Other causes include the presence of melanin in Langerhans cells, melanophages, neoplastic squamous cells, or in the extracellular space.[14]

Healthy corneal tissue is transparent and does not harbour melanocytes, with the exception of the corneal limbus. Limbal melanocytes may migrate into the corneal epithelium upon exposure to sunlight or chemicals,[15] and both adjacent malignant melanosis and frank melanoma may spread locally to the cornea. When the population of atypical melanocytes is confined to the epithelium the condition is defined as 'corneal primary acquired melanosis with atypia'; when there is invasion of Bowman's layer and stroma of the cornea the lesion is by definition a 'corneal malignant melanoma'. Primary corneal melanoma[1-5] may be unassociated with limbal or conjunctival neoplasia, but is thought to originate from melanocytes, which have migrated from limbus or conjunctiva. A corneal malignant melanoma may vary in its appearance from nodular and amelanotic[15] to flat and pigmented as in our case.

Melanocytic invasion complicating conjunctival melanoma rarely occupies more than one quadrant of the cornea. The presentation of

recurrent disease as described in the above case report was unique in our experience and has in our knowledge not been reported before. Histopathological examination showed absence of atypical melanocytes in the corneal epithelium or between Bowman's layer and the basal membrane. The direct spread of melanocytes into the corneal stroma may have been assisted by previous excisions of limbal melanomas that were removed with an en bloc lamellar dissection of the involved cornea and sclera. The inability

of damaged Bowman's membrane to regenerate results in a defective barrier to cellular invasion. The compact lamellar architecture of the cornea, which limits both intraocular tumour spread and its associated blood supply, may underly the relatively good prognosis for corneal malignant melanomas.

There may be several approaches to the treatment of corneal melanoma or primary acquired melanosis. Melanocytic tumours that are confined to the corneal epithelium may be treated by sliding off the epithelium using absolute alcohol. Lesions involving the superficial corneal stroma may be treated by either superficial keratectomy and freeze-thaw cryotherapy or lamellar keratoplasty. Deeper stromal tumours may be managed by penetrating keratoplasty.[16] A more radical approach in the management of invasive corneal melanoma secondary to primary conjunctival disease is exenteration of the orbit. In our case the relatively young woman, who was treated conservatively, has not only been able to keep her eye, which is cosmetically excellent, but also she has essentially normal visual acuity. Furthermore, in the 4 years of follow-up, no signs of local or distant recurrence of her tumour have been noted.

Fig 4A

Figure 4 (A) A small focus of residual or recurrent malignant melanoma (big arrow) is seen at the periphery of the cornea within the superficial stroma. Tumour cells are present in the corneal stroma (small arrow) but the corneal epithelium (curved arrow) shows no evidence of melanocytic infiltration (haematoxylin and eosin, ×120). (B) Pigmented atypical melanocytes (arrows) have invaded the cornea between the stromal lamellae. The melanocytic invasion involves more than half the corneal thickness and the entire corneal diameter to almost reach the resection margin on the medial side (haematoxylin and eosin, ×320).
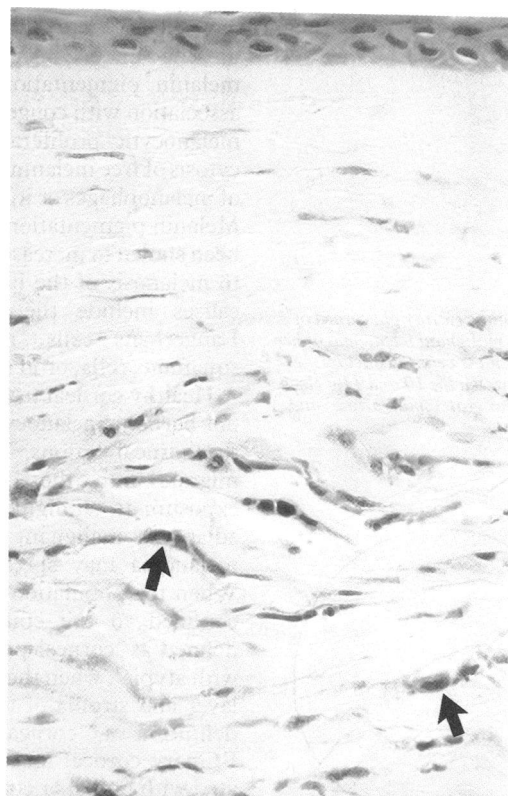

Fig 4B

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