weighted images and high signal on the spin echo T1 weighted images and with enhancement following the intravenous administration of Gd-DTPA (fig 2A, B). These appearances are attributed to the paramagnetic effect by stable radicals in melanin. Widespread metastases were detected including in the brain. Chemotherapy and later radiotherapy were unsuccessful and the patient died 7 months after the onset of these visual symptoms. No autopsy was performed.

Comment

Bilateral uveal and conjunctival melanocytic tumours without a previous history of cutaneous melanoma and without visible sign of a primary cutaneous tumour are extremely rare.

Multiple ocular melanocytic tumours in the absence of a primary melanoma give rise to an interesting differential diagnosis, which included (a) multiple primary uveal and conjunctival melanomas, (b) bilateral diffuse uveal melanocytic proliferation (BDUMP), and (c) metastases from an occult primary melanoma.

Eyes with ocular melanocytosis can develop more than one uveal melanoma, but melanocytosis was absent in our patient. Only isolated cases of bilateral primary uveal melanoma have been reported and the simultaneous bilateral occurrence of uveal melanoma is even more exceptional.[1] BDUMP is a rare paraneoplastic condition associated with visual loss.[2 3] On the basis of the absence of red patches and diffuse early hyperfluorescence in the posterior poles and on the presence of conjunctival melanomas, BDUMP can be considered unlikely in our patient.

Uveal metastasis from cutaneous melanoma is rare and bilateral ocular involvement is even more exceptional.[4–6] We believe that in our patient the metastatic disease arose either from an undetected primary visceral or cutaneous melanoma or from a primary tumour that regressed spontaneously. Both of these occurrences have been well documented in patients with metastatic cutaneous melanoma without apparent ocular involvement.[7 8]

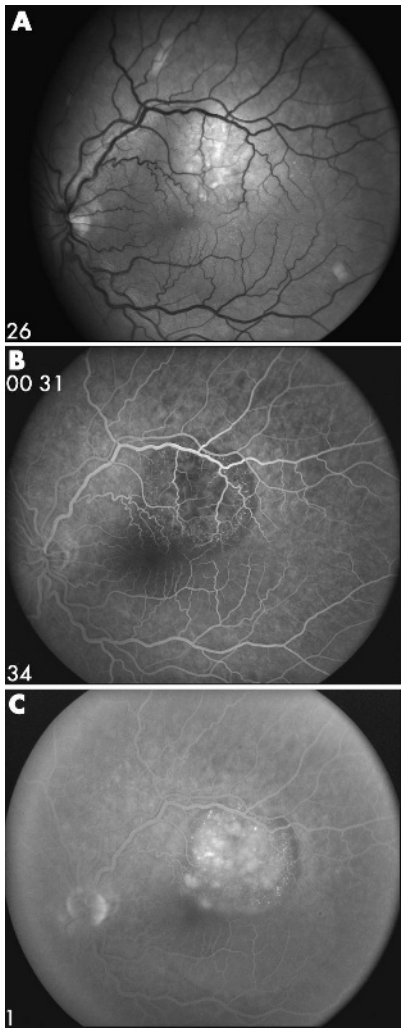

Figure 1 Red free (A), early (B), and late (C) fluorescence angiographic images of the left eye showing the supramacular mass with early central masking, pinpoint lesions at the borders and leakage over the surface of the mass and under the neurosensory detachment.

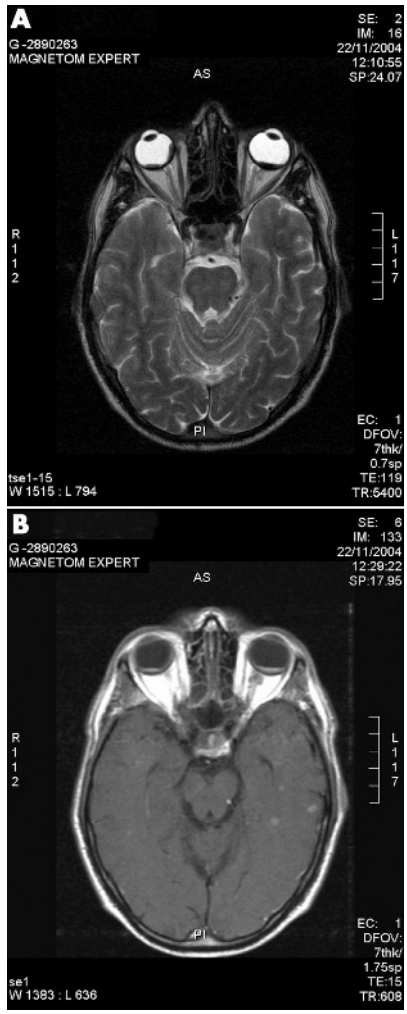

Figure 2 Axial T2 weighted (A) and gadolinium enhanced T1 weighted spin echo image (B) demonstrate the uveal masses on both sides. Note the characteristic signal of the melanin containing lesions.

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Thiopurine methyltransferase screening before azathioprine therapy

Azathioprine is used to treat various inflammatory eye conditions such as uveitis and dysthyroid orbitopathy. Despite good overall clinical response rates, particularly when used as steroid sparing agent, adverse effects such as severe myelosuppression can lead to early withdrawal in approximately a quarter of patients.[1 2]

Thiopurine methyltransferase (TPMT) is a cytosolic enzyme that metabolises azathioprine in vivo. The risk of azathioprine induced myelosuppression may be predicted by detecting patients with intermediate or low TPMT activity. The human TPMT gene exhibits genetic polymorphism that is evident in all populations studied to date.[3] Population studies have shown 89% of white people have high TPMT activity, 11% have intermediate, and 0.3% have low TPMT activity.[2 4] People heterozygous for TPMT mutations have intermediate activity while those homozygous for the mutation have low activity and are therefore at a higher risk of thiopurine induced myelosuppression. Conversely, individuals with very high levels of TPMT activity are known to have the homozygous wild type phenotype, in which the clinical response to thiopurines is less likely.[3] This in turn suggests that pretreatment TPMT levels may be used to titrate the starting dose of azathioprine.

Some debate still exists regarding the best method of monitoring TPMT activity—namely genotyping or assay assessment. At present, there is no conclusive evidence suggesting that either alone is predictive of the myelosupressive effects without regular blood monitoring. Genotyping can predict the one in 220 individuals who is TPMT deficient,[5] including those with intermediate activity. However, this method cannot yet predict those individuals with high TPMT activity.[2] There are also uncertainties regarding the interpretation of allelic polymorphisms in different racial groups.[6] Phenotype testing is able to quantify the biological enzyme activity and is hence thought to be a more reliable reflection of in vivo events.[6] Sies *et al*[7] have established the normal range of TPMT to be 9.3–17.6 units/ml red blood cells. However, these results can have considerable inconsistencies as a result of factors such as recent blood transfusions, certain medications, alcohol, and interlaboratory variation.[8] Oh *et al*[8] report that polymerase chain reaction genotyping of the TPMT polymorphism produces a rapid result and is accepted to have a 95% concordance with blood enzyme activity. Hence, performing both, genotype and phenotype TPMT tests is likely to be a more reliable predictor of the myelosuppressive effects of azathioprine. It must, however, be emphasised that these tests do not obviate the need for regular haematological monitoring during azathioprine therapy.

The direct cost of hospital treatment in the United Kingdom of an azathioprine related myelotoxicity episode was estimated at £3200 in 1997.[9] Studies have since shown the cost effectiveness of pretreatment TPMT screening.[8 10]

To the best of our knowledge, TPMT screening has not been considered in the ophthalmic literature to date. We would like to raise awareness in the ophthalmic community that screening for the TPMT enzyme, genotypically or phenotypically, may help titrate the starting dosage of azathioprine and help prevent potentially fatal side effects. We suggest that ophthalmologists should consider the incorporation of TPMT testing in the routine investigations performed before starting immunomodulatory therapy with thiopurines.

At present, the TPMT test most readily available in the United Kingdom is the phenotypic enzyme assay which is offered by laboratories at Guy's Hospital, London; The John Radcliffe Hospital, Oxford; and City Hospital, Birmingham.

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Use of an autologous lamellar scleral graft to repair a corneal perforation

We present the use of a novel technique, an autologous partial thickness scleral patch graft, to reform the integrity of an eye with corneal perforation. Despite being first described early in the last century, and offering significant advantages over traditional surgical approaches, there have been no recent reports of its use.

Case report

A 42 year old man was referred with a traumatic peripheral corneal perforation, 1.5 mm in diameter. Attempts to seal the hole with cyanoacrylate glue failed and a definitive surgical procedure was required.

The patient was a lorry driver and could not return to work until vision in this eye had returned to at least 6/12. Traditional approaches of penetrating or lamellar keratoplasty were unsuitable as they would have resulted in a prolonged period of reduced vision.

We therefore used a partial thickness autologous scleral patch graft.

A fornix based flap of superior conjunctiva was formed in the same eye and a 3 mm trephine used to harvest a sliver of sclera. The same trephine was used to cut an indent around the perforation and a superficial keratectomy performed within this region. Donor sclera was sutured using interrupted 10-0 nylon and covered with a therapeutic contact lens.

The next day intraocular pressure was 14 mm Hg with no evidence of a leak. Sutures were removed at 1 month and thereafter acuity remained at 6/5 unaided with normal intraocular pressure. There was remarkable clearing of the scleral patch leaving just a faint opacity at 1 year (fig 1).

Comment

Transplantation of sclera into cornea was first studied in rabbits by Thomas[1] and in human eyes by Larsson.[2] Larsson used a 2.5 mm autologous disc of sclera to repair a corneal perforation secondary to exposure. Several authors have since reported clearing of sclera transplanted into cornea.[3–6]

Maurice and Singh[7] used electron microscopy to examine the ultrastructural changes. His observations substantiated Winkelman's[4]

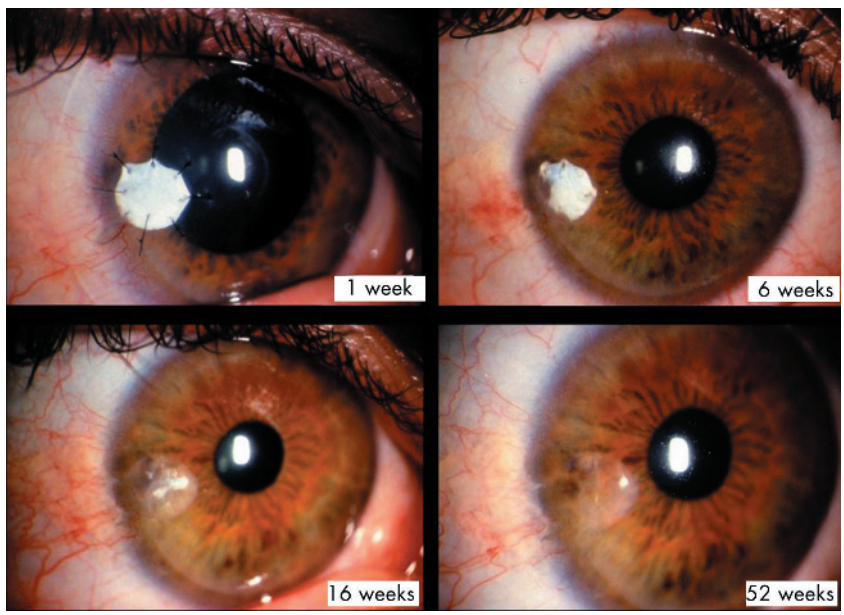

Figure 1 Sequential photographs showing partial thickness autologous scleral patch graft used to repair corneal perforation with progressive increase in transparency over a period of 1 year after the procedure.