activity. Valsalva retinopathy produces retinal and vitreous haemorrhage in the macular area.[2] In the absence of other symptoms and signs subarachnoid haemorrhage was felt to be extremely unlikely.

Clinical progression showed the diagnosis to be Terson's syndrome, vitreous haemorrhage occurring secondary to subarachnoid haemorrhage.This occurs in 3–5% of cases of subarachnoid haemorrhage[3] and usually comes to the attention of an ophthalmologist during recovery when the patient regains consciousness. It has been retrospectively reported as being associated with a worse prognosis after subarachnoid haemorrhage; the mortality is twice as high in patients with intraocular haemorrhage.[4] Seizure, as probably happened in this case, is an uncommon presentation of subarachnoid haemorrhage.[5]

It is extremely rare for a patient with Terson's syndrome to present with no residual headache or neurological symptoms, walking into the eye casualty after a subarachnoid haemorrhage less than 1 day previously. The importance of recognising this at an early stage is clear. Any patient presenting with retinal or vitreal haemorrhage and a recent history of neurological symptoms such as altered consciousness, nausea or headache should be investigated urgently for the presence of intracranial haemorrhage or aneurysm. These patients with vitreous haemorrhage have a good visual outcome. If spontaneous recovery does not occur vitrectomy offers good results.[6,7]

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Sir,

Bilateral Spontaneously Regressed Retinoblastoma with Preservation of Vision

Retinoblastoma is an intraocular tumour occurring almost exclusively in children in hereditary and sporadic forms. There is a higher incidence of spontaneous regression in these tumours than in other malignancies; however, it is rare. Incidence rates of 1–2% have been reported.[1] Bilateral cases are even rarer, with 10 reported cases in the English literature.[2] Only one case of bilateral regressed retinoblastoma with preservation of vision has been reported to our knowledge.[3] The diagnosis is made on the basis of characteristic clinical findings in the presence of either a positive family history or histologically proven retinoblastoma in the fellow eye.

We present a case of bilateral spontaneously regressed retinoblastoma with preservation of visual acuity in a patient with a positive family history, and discuss clinical and genetic aspects of the management of this family.

Case Report

A 32-year-old Libyan man presented to the ophthalmic department with longstanding reduced visual acuity in the right eye which could not be improved with spectacles. The family history revealed that the patient had a 4-year-old son with Down's syndrome whose right eye had been enucleated at the age of 7 months for a histologically proven retinoblastoma.

On examination of the patient, corrected visual acuities were 6/18 right, 6/5 left. Retinoscopy showed myopic astigmatism of the right eye but the left eye was emmetropic. He had a good degree of stereopsis (60 seconds of arc). There was no relative afferent pupillary defect. The ocular media were clear and the intraocular pressures were normal.

Examination of the fundi revealed multiple, well-circumscribed, elevated lesions which had the appearance of irregular calcific collections within areas of pigment hyperplasia (Fig. 1). The discs and maculae were healthy. The fundal appearances were unusual but the family history gave rise to a suspicion of spontaneously regressed retinoblastoma. Investigations including FBC, U&E, LFT and ESR were normal. *Toxoplasma* and *Toxocara* titres and a VDRL were negative. A cranial CT scan showed calcific plaques in the right orbit but was otherwise normal.

A literature search showed photographs of similar lesions and therefore the diagnosis of spontaneously regressed retinoblastoma was made on the basis of the clinical appearance, the presence of calcification and the positive family history. The patient's other son, aged 3 years, was examined and found to have normal eyes. The patient's wife had recently suffered

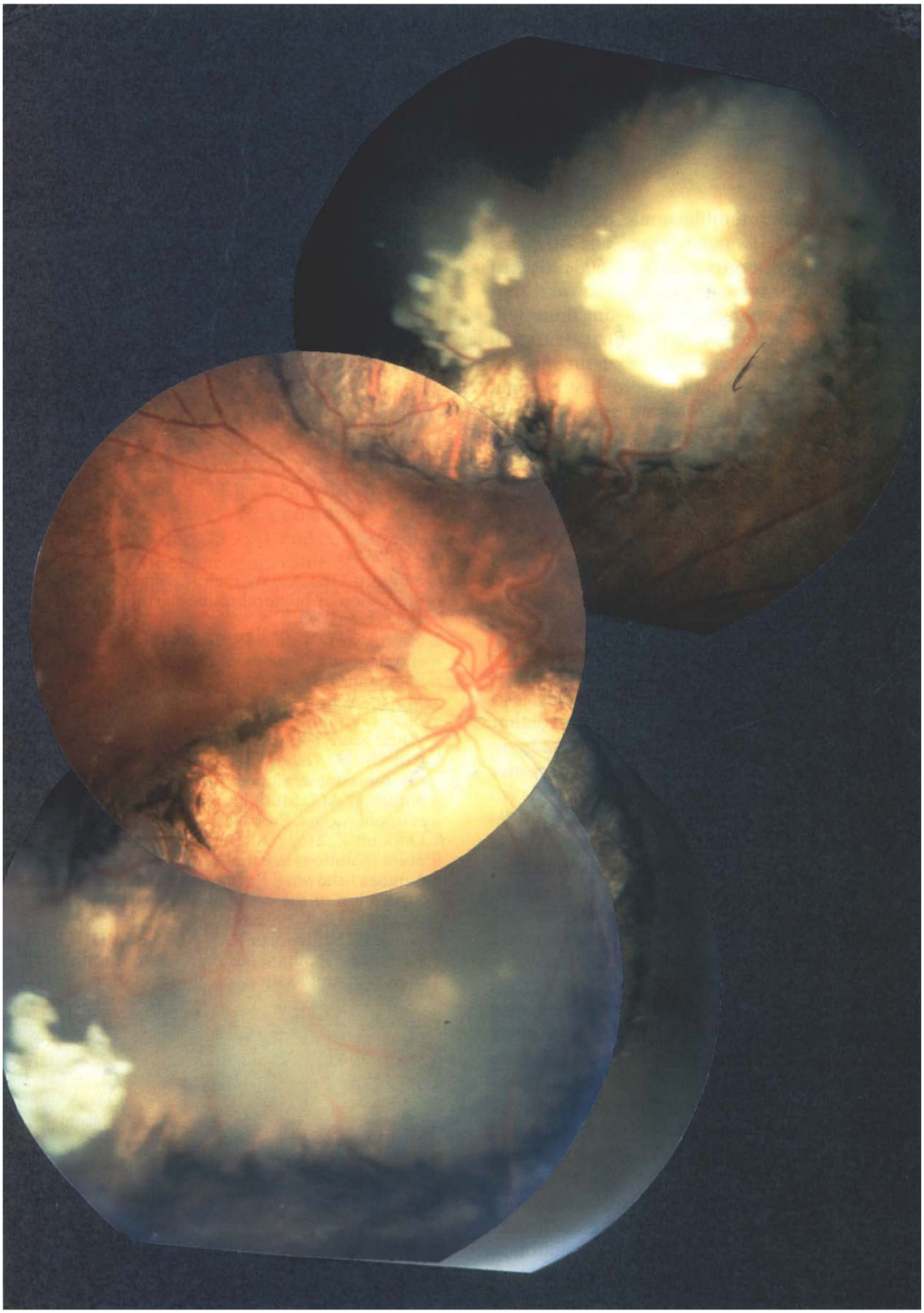

Fig. 1. *Right fundus photography.*

a spontaneous first trimester miscarriage. Chromosomal analysis of his son with Down's syndrome showed a 47XY+21 karyotype, but no evidence of a deletion of 13q14. Chromosome analysis of the patient himself was not performed as the absence of the deletion in his son indicated that he would not be a carrier of the abnormality.

Discussion

The inheritance of retinoblastoma is autosomal dominant with a 90–95% penetrance. The offspring of all gene carriers therefore have a 50% risk of inheriting the mutant gene.[4] Knudson[5] showed that in those individuals carrying a predisposing mutation, a single additional event is sufficient for tumorigenesis. As the chance of this event occurring in the precursor retinal cell population is relatively high, gene carriers usually develop multiple bilateral tumours at an early age. In sporadic cases both mutations are somatic and must occur in homologous genes in the same retinal precursor cell. They are usually unilateral, unifocal and have a later age of onset.

This 'two-hit' hypothesis represents one explanation for the incomplete penetrance observed in familial retinoblastoma. However, incomplete or 'low penetrance', i.e. individuals with unilateral or regressed retinoblastoma, appears to occur more commonly in some families.[6] It has therefore been suggested that the nature of the mutation may also play a role, and a recent series demonstrated that most mutations had altered rather than absent gene function in these families (J. K. Cowell, personal communication).

Spontaneous regression is an uncommon but well-described feature of retinoblastoma. In one study of 1500 cases of retinoblastoma at the Harkness Institute in New York, 1.8% of cases were classified as spontaneously regressed tumours; over half of these were associated with the familial variant.[7] Seventy-eight per cent of patients had visual acuities of 20/40 or better.

This case demonstrates again the importance of ocular fundus examination in first degree relatives of a patient with a unilateral, apparently sporadic case of retinoblastoma, as the finding of spontaneously regressed tumours in a parent substantially alters the risk ratio of tumour development in subsequent family members.[8] This therefore affects the advice given in genetic counselling. Current figures suggest a 1% recurrence risk to siblings of a unilaterally affected child, whereas the offspring of an affected parent have a 45% chance of developing retinoblastoma (1 in 2 chance of inheriting the mutation and 90% penetrance).

Since the retinoblastoma gene (RB1) was cloned, several RFLPs (restriction fragment length polymorphisms) and VNTRs (variable number tandem repeats) have been identified for linkage analysis in familial cases and are informative in about 85–95% of cases.[9] This enables identification and targeted screening of gene carriers, and will reduce the screening load for ophthalmology departments. It also facilitates prenatal diagnosis. Our family was offered linkage analysis to assess the gene carrier status in their unaffected son, but they declined.

In summary, we suggest that all family members of a patient with retinoblastoma should have an ophthalmological examination and the family be offered linkage analysis.

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Sir,

Temperature-Dependent Resistance to Gentamicin in Graft Keratitis by *Stenotrophomonas (Xanthamonas) maltophilia*

A 58-year-old woman with congenital epithelial dyskeratosis was admitted with bacterial keratitis of her right eye. She underwent a penetrating kerato-