ocular colobomata and would seem plausible in sporadic cases. Thalidomide 'A' is a well-documented environmental cause of coloboma with or without phocomelia.[4] The use of anticonvulsants in pregnancy,[5] as well as alcohol,[6] has also been implicated in the formation of coloboma and other multiple systemic malformations.

The finding of a coloboma should alert the physician to the possibility of chromosomal aberration and the need for a complete systemic evaluation. Accurate refraction is fundamental since there is a wide range of refractive errors in eyes with coloboma. Cycloplegic refraction was performed in our patient and was within the normal limits for this age group. Essential in the treatment of children with colobomata is the determination of visual prognosis. Measurements of corneal diameter and axial length are useful parameters in assessing the visual potential in infants with coloboma. Hornby *et al*[7] have shown that microphthalmos with cyst had the worst prognosis, coloboma with microcornea and microphtalmos had a poor prognosis, coloboma with microcornea had an intermediate prognosis, and simple coloboma had the best prognosis. Our patient had corneal diameters of 10.1 and 10.2 mm and axial lengths of 22.05 and 22.38 mm in the right and the left eye, respectively. However, the coloboma extended posteriorly to involve the optic nerve and therefore associated with a poor visual prognosis.

Genetic evaluation is becoming increasingly more important in the understanding of molecular disorders and is warranted in all cases of ocular colobomata associated with other malformations. Recent reports have shown that there are over 20 reported cases of interstitial deletion in 2q, the most common single deletion being del 2(q31q33) with 14 cases in the literature.[8] Nixon *et al* reported on a 9-year-old boy with *de novo* deletion of chromosome 2q, including bands 2q24.3 and 2q31.[8] The clinical findings included growth failure, minor facial anomalies, craniosynostosis, heart defects, coloboma of the iris, retina and optic nerve and limb abnormalities. Boles *et al*[9] have drawn attention to the emerging association between del 2q31.1 and limb defects. Deletion of chromosome 22q11 has been well documented and is a major cause of DiGeorge syndrome.[10] Digilio *et al*[11] reported on a neonate with del 22q11 presenting with facial dysmorphism, congenital heart defect, urogenital malformation, ocular coloboma, and unilateral radial aplasia. We believe that there may be other genes responsible for producing ocular coloboma and other systematic malformations. Further delineation of genes involved in these disorders may help in understanding the molecular defects causing ocular colobomata.

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Sir,

Interferon-associated retinopathy

Eye (2002) **17,** 534–536. doi:10.1038/sj.eye.6700391

Interferon (INF) alpha is known to have antiviral, antifibroblastic and antitumour effects.[1,2] It has been tried in the treatment of ocular disorders such as dendritic keratitis, subretinal neovascularisation in age-related macular degeneration,[3] glaucoma filtering surgery, and

ocular cicatricial pemphigoid.[3,4] However, ocular side effects of INF-alpha are also being increasingly reported.[3] We describe a case with severe proliferative retinopathy while on low-dose INF-alpha therapy.

Case report

A 69-year-old woman presented to the eye clinic with photophobia and reduced vision of gradual onset, via her optometrist. She was diagnosed to have chronic myeloid leukaemia 18 months ago. She had been treated with hydroxyurea with a good response and later (2 months from diagnosis) agreed to participate in a randomised clinical trial to assess the merits of low/high-dose INF treatment for chronic myeloid leukaemia. She was randomised to receive low INF, INF Alpha-N1 3 million IU, 5 days a week. She had not received any systemic steroid treatment. She was also hypertensive on atenolol. At the time of ophthalmic presentation, she was in haematological remission and had received 16 months of INF-alpha treatment. She had two transient ischaemic attacks (transient total loss of vision in the right eye lasting for 5 min) in the following few months, for which she received aspirin 150 mg daily.

Visual acuities on presentation were 6/12 in the right eye and 6/18 in the left eye. Anterior segment examination showed 1+ cells and flare in the anterior chamber of left eye, and bilateral early cortical lens opacities. Fundoscopy revealed bilateral optic disc neovascularisation, multiple cotton wool spots, venous dilatation and tortuosity, and peripheral retinal neovascularisation in the left eye (Figure 1). The different possibilities were retinal ischaemia secondary to leukaemia, ocular ischaemia, and INF-associated retinopathy. Leukaemia was considered less likely as the patient had normal blood counts on treatment before and during the course of INF therapy. Investigations performed for diabetes mellitus, carotid ischaemia, collagen vascular diseases, and sarcoidosis did not reveal any abnormalities. Carotid Doppler ultrasound showed bilateral atheromas but no significant stenosis. Fluorescein angiography documented the ischaemic retinopathy and retinal neovascularisation.

Argon laser panretinal photocoagulation was carried out in multiple sessions with fill-in laser undertaken on subsequent visits over the few months causing regression of proliferative retinopathy. INF treatment was stopped. The proliferative retinopathy gradually regressed; however, the left eye developed fibrous proliferation over the temporal arcades with macular tractional retinal detachment. Visual acuities by then had reduced to 6/24 in the right and 6/36 in the left eye. She subsequently underwent left vitrectomy and her visual acuity has stabilised to 6/24 in the left eye.

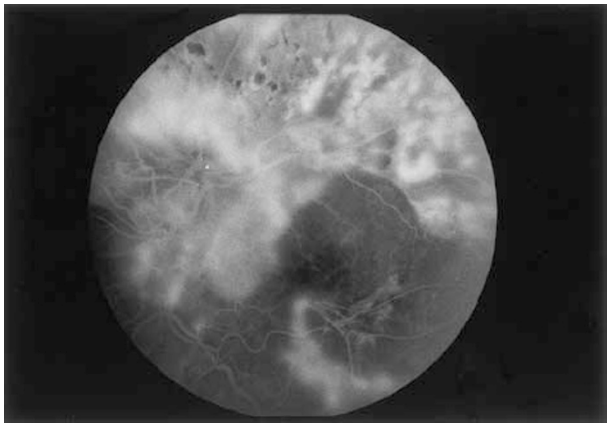

Figure 1 Fundus fluorescein angiogram of the left eye: leakage from new vessels on the disc (NVD) and elsewhere (NVE).

She continues to be in haematological remission of leukaemia.

Comment

INF-alpha therapy has been known to cause a variety of ocular lesions.[1,2] Typical lesions include cottonwool spots and retinal haemorrhages at the posterior fundus, particularly around the optic disc, secondary to retinal ischaemia, which usually appear within 3 months of the onset of therapy.[3,5] The incidence of retinopathy is thought to depend on the initial dose of INF-alpha and patients receiving high dosages such as 9×10^6 IU/day, 6 days per week, are usually at increased risk of retinopathy. Diabetes and systemic hypertension are risk factors.[1,6] The retinopathy may disappear spontaneously during therapy or rapidly after stopping therapy.[3,5] Despite the retinopathy, subjective complaints are uncommon and visual acuity is not always impaired. Most patients with INF-associated retinopathy can continue with the planned course of INF therapy. Pathogenesis of INF-associated retinopathy is unknown, although some investigators have suggested deposition of immune complexes in the retinal vasculature and leucocyte infiltration that cause retinal ischaemia with resultant capillary nonperfusion and nerve fibre layer infarctions.[3]

Our patient was unusual because she developed severe, progressive proliferative retinopathy while on low-dose INF-alpha. Retinopathy needed extensive laser treatment and warranted stoppage of the drug. Retinopathy was first diagnosed on ophthalmic referral made 16 months after the induction of INF-alpha therapy. Mild anterior segment inflammation was an unusual feature. INF-induced retinopathy is not always self-limiting and benign. We recommend ophthalmic

examination of patients pretreatment to look for pre-existing retinopathy and subsequent examinations while on treatment. If severe ocular toxicity occurs, INF therapy should be discontinued.[1]

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Sir,

Intraepithelial sebaceous gland carcinoma with pagetoid spread presenting as marginal keratitis: a case report

Eye (2003) **17,** 536–537. doi:10.1038/sj.eye.6700387

Sebaceous gland carcinoma of the ocular adnexa is a rare lesion arising from the meibomian glands, the glands of Zeis, sebaceous glands in the caruncle, and fine cutaneous pilosebaceous glands of the eyelids. The report incidence ranges from 1 to 5.5% of the malignant eyelid tumours.[1]

We report a case of intraepithelial sebaceous gland carcinoma masquerading as marginal keratitis with extensive intraepithelial involvement of conjunctiva and the skin.

Case report

A 71-year-old man presented with a 2-year history of a chronically irritable left eye. His local doctor had treated him with various topical antibiotics for unilateral blepharitis and recurrent conjunctivitis with little or no improvement. On examination, he was found to have a localized thickening of the left upper lid with surface irregularity and telangiectasia. No cicatrization was noted. The supronasal cornea showed peripheral corneal infiltrates.

The ophthalmic casualty doctor took a punch biopsy of the eyelid lesion and then commenced the patient on Predsol 0.5% four times a day to the left eye for marginal keratitis.The patient was seen 1 week later. At this stage the patient was symptomatically better, but his clinical signs in the cornea did not improve. It was then observed that the supronasal corneal epithelium actually had colonies of abnormal cells associated with superficial vascularization (Figure 1).

The rest of the corneal epithelium was also diffusely abnormal and so also the adjacent conjunctival epithelium. Preauricular and submandibular nodes were not palpable. Multiple corneal biopsies from the suspicious sites were taken. In addition, conjunctival map biopsies from 19 different sites of bulbar, palpebral, and tarsal conjunctiva were also taken. Histology showed intraepithelial sebaceous gland carcinoma with pagetoid spread in the skin, conjunctiva, and the cornea.

The management of the patient included a referral to a multidisciplinary oncology clinic, a magnetic resonance image of brain and orbit, a computerized tomography scan of neck, thorax and abdomen, and also a liver

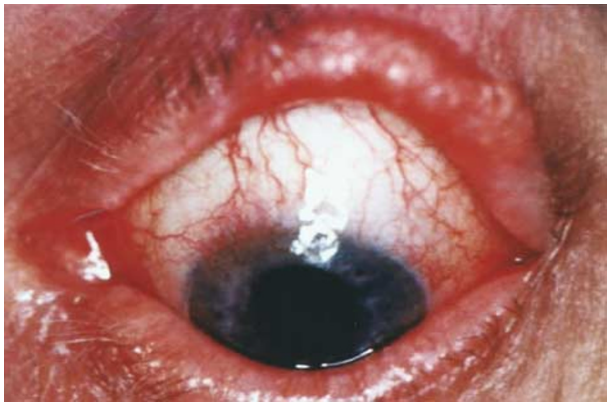

Figure 1 Photograph of the left eye showing thickening of upper lid, superficial corneal vascularization, and peripheral corneal infiltration.