Bilateral naevus of Ota with choroidal melanoma and diffuse retinal pigmentation in a dark skinned person

Naevus of Ota (naevus fusoculocorneus ophthalmomaxillaris) was described by the Japanese dermatologist, Ota, in 1939 as a dermal melanocytic hamartoma that presents as bluish hyperpigmentation along the ophthalmic, maxillary, and mandibular branches of the trigeminal nerve. It is bilateral in less than 5% cases, occurring frequently in Orientals (0.2%–1%) and darker races and rarely in white people (0.04%). Open angle glaucomas and choroidal melano-ma are the rare ocular involvements. Ota’s naevus is more common in Asians than white people but uveal melanoma occurs predominantly in white populations. Dark skinned patients represent only 1% of all cases of orbital melanomas. The risk of developing uveal melanoma in a patient with naevus of Ota is one in 400 patients in their lifetime. We report a rare case of bilateral naevus of Ota with a right (RE) choroidal melanoma and left (LE) diffuse pigmentation of retina.

Case report

A 73 year old Anglo-Indian woman was referred with complaints of photopsia. She had black hair and light brown skin. Examination revealed a brownish-black pigmentation of the conjunctiva, episclera, and periorbital skin bilaterally (fig 1). Visual acuity for distance and near was 6/6 and N5, respectively, in each eye. Heterochromia was present, the right iris being a darker brown than the left, which had a sector of light brown colour. Gonioscopy and intraocular pressure were normal. The right fundus revealed a pigmented, large, elevated choroidal mass 10 disc diameter (DD) in size, 4 DD superonasal to the disc. Drusen were overlying it. No subretinal fluid was seen. The left eye showed a patchy dark pigmentation 3 DD in size, at the temporal edge of the macula. A ridge-like pigmented elevation, 3 DD long, was also seen along the superonasal vessels. Both optic discs and maculas were normal. Ultrasound in the right eye showed a 10 mm tumour, 4.2 mm high. Fluorescein angiography confirmed its independent circulation. A systemic examination found no signs of metastasis. A diagnosis of bilateral naevus of Ota with low grade, choroidal melanoma in the right eye (fig 2) and retinal pigmentation in the left eye was made. The patient was reluctant to accept the option of enucleation in view of the right vision. A 125I radioactive plaque was applied (COMS study). A follow up examination 3 years postoperatively showed a flattener, yellow 4 DD x 1.5 DD scarred tumour with mottled pigmentation. The left melanoma remained unchanged. The vision was 6/6 in both eyes 6 years after 125I treatment and cataract surgery.

Comment

Ota’s naevus is commonly seen unilaterally (90%). Bilateral involvement is rare. It represents melanocytes that have not migrated completely from the neural crest to the epidermis during the embryonic stage. Orientals and pigmented races have a high frequency of Ota’s naevus. The naevus of Ota is a highly distinctive lesion and may involve oral mucosa, tympanic membrane, intranasal mucosa, leptomeninges and ocular structures such as the sclera, retinal, ciliary body in black patients. Bilateral naevus of Ota with a right (RE) choroidal melanoma and diffuse retinal pigmentation in the left eye was made. The patient was reluctant to accept the option of enucleation in view of the right vision. A 125I radioactive plaque was applied (COMS study). A follow up examination 3 years postoperatively showed a flattener, yellow 4 DD x 1.5 DD scarred tumour with mottled pigmentation. The left melanoma remained unchanged. The vision was 6/6 in both eyes 6 years after 125I treatment and cataract surgery.

References


Treatment of neurotrophic keratopathy with nasal dilator strips

Neurotrophic keratopathy, characterised by poorly healing corneal epithelium, occurs in eyes with decreased corneal sensory innervation. Clinical findings include chronic epithelial defects and corneal ulceration. Numerous conditions predispose to neurotrophic keratopathy including diabetes mellitus, accidental and surgical trauma, herpes simplex and zoster keratitis, leprosy, and topical anaesthetic abuse.

Management of neurotrophic keratopathy includes ocular lubrication, pressure patching, autologous serum eye drops, fitting of a bandage contact lens, amniotic membrane grafting, and surgical tarsorrhaphy. Surgical tarsorrhaphy can be very successful in resolving neurotrophic corneal ulceration, but many patients find this option cosmetically unacceptable.

We describe a novel method of non-surgical tarsorrhaphy using over the counter adhesive, non-medicated, nasal dilator strips (NDS) (Breathe Right Nasal Strips, Whitpany, NJ, USA) applied vertically across the eyelids (fig 1). The adhesive strip consists of parallel bands of plastic imbedded in a pad, and is available in different sizes.

The nasal strips were originally developed to treat patients with snoring problems, or to improve nasal congestion. In rhinological applications, the strip is typically used to improve nasal airflowobilization.
neurotrophic corneal ulceration and describe two representative cases.

Case reports
A 60 year old woman developed a neurotrophic corneal ulcer following a complicated retinal detachment repair. After a year of standard medical therapies including lubrication and frequent conventional patching, she continued to have a 4 mm x 4 mm chronic non-healing epithelial defect. Treatment with reversible NDS tarsorrhaphy was initiated with instructions to apply the strips at bedtime and as much as possible during the day. Nine weeks later the corneal epithelial defect had healed completely. Over the next year she gradually decreased the wearing time of the strips and is currently stable without their use.

A 48 year old woman with a 6 mm x 2 mm neurotrophic corneal ulcer was referred for management after failing numerous medical and surgical therapies including lubrication, autologous serum eye drops, patching, and an amniotic membrane graft. The patient was instructed to use NDS tarsorrhaphy according to the schedule described in the previous case. Within 2 weeks the corneal epithelial defect healed completely. The patient continues to apply the tarsorrhaphy but with decreasing frequency.

The novel use of nasal dilator strips to perform a temporary tarsorrhaphy has aided us greatly in our management of neurotrophic corneal ulceration. We believe it is an attractive, cost effective, efficient alternative to patching for any ocular condition. In addition, nasal strip tarsorrhaphy allows for immediate reversibility that facilitates patient acceptance.

References

Confocal microscopy of the cornea in nephropathic cystinosis
Cystinosis is an autosomal recessive inherited disorder of amino acid metabolism characterised by the deposition of cystine crystals in the eye, kidney, reticuloendothelial system, and various other tissues.1 Childhood or nephropathic cystinosis can present as an infantile or a juvenile variant.2 The infantile variant tends to have a more devastating course and is associated with growth retardation, rickets, and eventual renal failure which requires transplantation within the first decade.3 The juvenile variant has later onset and milder nephropathy.

In nephropathic cystinosis, crystal deposits usually appear in the peripheral, anterior cornea within the first year of life and progress centrally and posteriorly until the entire cornea is involved.4 The diagnosis can be confirmed histopathologically by demonstration of characteristic crystals by electron microscopy in a conjunctival biopsy.5-7 Stromal deposition of crystal deposits has been demonstrated by confocal microscopy.5,7 We provide the first demonstration, to the best of our knowledge, of cystine crystals in the corneal epithelium using in vivo confocal microscopy.

Case report
A 9 year old boy presented to the King Khaled Eye Specialist Hospital in Riyadh, Saudi Arabia, with a complaint of recurrent foreign body sensation, associated with severe photophobia and blepharospasm. He had been diagnosed with infantile nephropathic cystinosis at age of 9 months and had been treated with systemic cysteamine. On examination, the visual acuity was 20/20 in the right eye and 20/25 in the left eye. The intraocular pressure was 12 mm Hg in both eyes. Slit lamp examination showed crystal deposits of 2.5 in Gahl density score2 in both corneas, predominantly involving the anterior stroma and with limbus to limbus distribution (fig 1). Dilated fundus examination was normal with no maculopathy or peripheral retinal pigment abnormalities. Topical treatment with cysteamine 0.5% drops resulted in symptomatic relief.

Confocal microscopy (Confoscan 3, Nidek Technologies, Vigonza, Italy) demonstrated crystalline deposits in the corneal epithelium (fig 2A, B) and stroma (fig 2C, D). Crystal deposits in the corneal epithelium were needle shaped and fusiform shaped and oriented parallel to the plane of the epithelial cells (fig 2A, B). In the basal cell layer, the crystals were associated with dendritic cells (fig 2B). The highest crystal density was in the mid-stroma, where fusiform shaped crystals were more predominant than needle shaped crystals (fig 2C). The lowest crystal density was in the posterior stroma, where most of the deposits were needle shaped (fig 2E). Within the stroma the crystals were oriented parallel to the plane of the stromal lamella. The needle shaped crystals were highly variable in length with some as long as 100 µm. The endothelial cell layer was normal.

Comment
The current case clearly documents that crystalline deposits may be found in the epithelium of patients with nephropathic cystinosis, unlike previous electron microscopic6 and confocal microscopic7 studies that suggest these deposits are localised to the stroma. In addition, we found maximum crystal density in the mid-stroma and minimum density in the posterior stroma, in contrast with a previous report in which maximum crystal density was just anterior to Descemet’s membrane.7

We hypothesise the presence of these abnormal deposits in the corneal epithelium may contribute, in part, to the foreign body sensation and photophobia that is invariably associated with this disorder, as well as the predisposition to recurrent epithelial erosions. Chronic low grade inflammation of the epithelium and epithelial basement membrane zone associated with recurrent epithelial erosions is the probable explanation for the presence of dendritic cells in the basal epithelium of the central cornea. Successful reduction in the density of corneal crystals and symptomatic relief was obtained with the use of topical cysteamine 0.5% drops, as in previous reports.6,7
Figure 2 Crystal deposits in the corneal epithelium and stroma. A mixture of needle shaped and fusiform shaped crystals are present in (A) the superficial epithelial cell layer and (B) the wing cell layer. (C) Dendritic cells are present in the basal cell layer. (D) The greatest density of crystals is in the mid-stroma, where fusiform shaped crystals are the predominant morphology. (E) The least density of crystals is in the posterior stroma, where needle shaped crystals are the predominant morphology.

A H Alsuhaibani, M D Wagoner
Anterior Segment Division, Department of Ophthalmology, King Khaled Eye Specialist Hospital, Riyadh, Kingdom of Saudi Arabia

A O Khan
Pediatric Ophthalmology and Strabismus Division, Department of Ophthalmology, King Khaled Eye Specialist Hospital, Riyadh, Kingdom of Saudi Arabia

Correspondence to: Michael D Wagoner, MD, King Khaled Eye Specialist Hospital, PO Box 7191, Riyadh 11422, Kingdom of Saudi Arabia

mwagoner@kkesh.med.sa

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References


Total parenteral nutrition, vitamin E, and reversible macular dysfunction morphologically mimicking age related macular degeneration

A variety of nutrient deficiencies may predispose to the development of age related macular degeneration (AMD). Patients receiving parenteral nutrition (TPN) may be at particular risk of early onset AMD, because of inadequate or excess nutritional supplementation. Studies including the Eye Disease Case-Control Study and Beaver Dam Eye Study have evaluated the relation between antioxidant and micronutrient levels, and the risk of AMD. A protective effect of high plasma vitamin E levels was convincingly demonstrated. We describe a patient treated with parenteral fluid support who developed visual symptoms and signs of AMD, in conjunction with longstanding vitamin E deficiency. Isolated cases of visual disturbance in patients undergoing TPN have been reported in the literature; however, to our knowledge, no case of visual disturbance attributed to vitamin E deficiency has been reported in this context.

Case report

A 57 year old man received parenteral fluid five times a week at home because of short bowel syndrome secondary to Crohn’s disease. It was thought he had undergone bowel adaptation to meet macronutrient and micronutrient needs in the 13 years since his surgery. He presented with subacute visual disturbance. He described altered colour perception in situations analogous to macular stress testing (moving from dark adapted situations to bright lights) and enlarging central scotoma. Visual acuity was 6/6 in the right eye, 6/12 in the left. Visual fields, intraocular pressures, and neuro-ophthalmic examination were normal. Funduscopy revealed macular soft drusen, and extensive subretinal basal laminar deposits in the macular region, more marked in the right than left eye (fig 1). Electroretinogram was normal.

The patient was receiving electrolyte support 6 days a week at time of presentation. Measured haematological parameters and urea and electrolyte levels revealed a low haemoglobin level (11.0 g/dl), and a mild degree of macrocytosis (102.3 fl). Because hypervitaminosis and/or deficiency in trace minerals were suspected, serum values of vitamins A, E, B1, B2, B6, plasma zinc, copper, selenium, manganese, caeruloplasmin, and red cell GSH activity were measured. Results revealed vitamin E deficiency (12 mg/l), normal range 60-220 mg/l. A retrospective survey of previous serum vitamin E levels suggested longstanding deficiency, with levels of 10 µmol/l, and 13 µmol/l, 6 months and 1 year respectively, before onset of symptoms. Treatment with vitamin supplementation lead to complete resolution of symptoms in 3 weeks. Vitamin E levels returned to normal; however, fudal appearances remained unchanged.

Comment

The presence of bilateral hard and soft drusen and pigmentary abnormalities in the macula are the clinical hallmarks of AMD. The early onset of morphological changes at Bruch’s membrane/retinal pigment epithelium (RPE) interface may relate to vitamin or micronutrient deficiency, associated with parenteral nutrition. Cumulative oxidative damage may have an important role in the pathogenesis of AMD, since accumulation of lipofuscin pigments may arise as a consequence of antioxidant deficiency, or under pro-oxidant conditions. Evidence exists for an association between atrophic AMD and excessive lipofuscin accumulation. Compromised RPE in this context is believed to be due to the amphiphilic structure and photoreactivity of the di-retinal conjugate A2E, the major constituent of lipofuscin. Antioxidant vitamins have been shown to aid in the defence against AMD. Vitamins E and C suppress A2E epoxidation, suggesting one mechanism by which these vitamins may protect the ageing macula.

Vitamin E deficiency was present consistently over the 12 month period preceding symptom onset, reinforcing the likelihood that the clinical presentation had been caused by vitamin E deficiency. Vitamin E deficiency results in retinal degeneration, excessive RPE lipofuscin, and decrease in the polyunsaturated fatty acid content of rod outer segments and the RPE. Furthermore, vitamin E deficiency may cause mild macrocyclic anaemia and accumulation of ceroid lipofuscin in nerves, affecting function of central and peripheral nervous systems. Patients with sufficient gut length for protein calorie nutrition receiving parenteral fluids may run the risk of micronutrient deficiency despite a normal diet, and may present to the ophthalmology department. We recommend formal micronutrient screening in patients with extensive small bowel resection.
Spontaneous involution of autologous lenses and phacoanaphylaxis reaction in Stickler syndrome

Stickler syndrome is a “hereditary progressive arthro-ophthalmopathy” caused in the majority of cases by mutations of the COL2A1 gene encoding for type II collagen.1 The disease is transmitted as an autosomal dominant trait with high penetrance but variable expressivity.1 Most common ocular manifestations of the disease are myopia, vitreous vells and degeneration, early cataract, retinal peripheral breaks and retinal detachment.1, 4

Case report

This patient had typical ocular and extraskeletal clinical manifestations of Stickler syndrome. She was fitted with contact lenses (~17.00 dioptres) at the age of 1 month. Despite the relatively poor vision, hearing impairment and skeletal problems, she developed well mentally and attended regular school. With glasses (~15.00) the visual acuity (VA) was stable, around 6/21 (20/75) for distance and J2 for near in both eyes. A mild central opacity of the posterior lens capsule was initially observed in both eyes when she was 7 years old (fig 1A). The IOP was 12 mm Hg, the corneas clear, anterior chambers deep and devoid of any inflammatory signs. Fundus examination disclosed no changes from previous examinations (fig 1B). Refraction and VA in both eyes remained unchanged.

References


Figure 1 (A) Mild opacity of the lens posterior capsule of the right eye initially observed at the age of 7 years. (B) Appearance of the fundus demonstrating the retinal pigmentary changes in the periphery and retinal degenerative changes within the posterior pole. (C) Marked opacification and fusion of the lens capsules in the right eye observed at 9 years of age. (D) Mild capsule opacities are still observed 2 years later, at 11 years of age. The refractive error at this stage is +1.25 and the visual acuity for distance is 6/12 (20/40).

Figure 2 (A) Large cortical remnants are seen within the capsular bag remnant in the left eye with an intense flare and many inflammatory cells. The cornea is still mildly hazy 2 weeks after the phacoanaphylactic reaction. (B) The vitreous of the left eye is hazy with many cortical lens remnants observed with transillumination at the slit lamp. (C) Right eye is quiet, the refractive error is +1.25, and the uncorrected visual acuity 6/12 (20/40) despite the presence of mild lens capsule opacities. (D) Left eye is also quiet showing the same characteristics as the right eye.
On 23 June 2002, at the age of 9 years, she complained of blurred vision in the right eye. Without glasses, VA for distance was 6/60 (20/200) and for near less than 1/16. Involution of the lens material with marked opacity of the fused capsule was detected (fig 1C). Accurate retinoscopy was not possible. No intraocular inflammatory signs were observed.

On 23 May 2004, the right eye lens opacities reabsorbed. Mild posterior capsule opacity remains (fig 1D). VA without correction was 6/12 (20/40) and J10 in both eyes. With (figs 2C and 2D). The left eye VA and myopia remained unchanged.

Six weeks later sudden pain, redness, and loss of vision in the left eye occurred. A high IOP of 60 mm Hg, hazy cornea, mutton fat keratic precipitates with flare +3 and cells +4 were observed in the left eye anterior chamber. She was treated with corticosteroids and antiglaucoma drops. Two weeks later, a central tear of the posterior capsule with remnants was present in the capsular bag (fig 2A) and a multitude of floating lens remnants with a granulomatous inflammatory reaction were observed in the vitreous (fig 2B). Following complete arrest of the inflammatory processes and a return to normal of the IOP, medical treatment was discontinued 5 weeks after its initiation.

At her last visit on 21 November 2004, both eyes were quiet. Only mild scattered lens capsule opacities were detected in both eyes (figs 2C and 2D). The VA without correction was 6/12 (20/40) and J10 in both eyes. With correction (+1.25) for distance and near addition (+3.00), the VA in both eyes was 6/9 (20/30) and J1 respectively. Multifocal glasses were prescribed.

Comment

A quiet and uneventful involution of the autologous lens occurred in the right eye when the child was 9 years old. The mechanism of this phenomenon is unclear and may be associated with abnormalities of the lens collagen and/or crystallines. The lens involvement in the right eye was not associated with any noticeable symptom but for a drop in vision. Progressive clearing of the lens opacity was followed by emmetropisation of the initial refractive error and visual improvement in the left eye. Two years later, spontaneous involution of the lens in the other eye was associated with a marked intraocular granulomatous inflammatory reaction (“granulomatous uveitis”) reminiscent of a phacoanaphylaxis reaction. This acute reaction was, most probably, associated with the “escape” of immune tolerance towards the autologous lens antigens.

We are not aware of previous reports in the literature describing similar ocular phenomena.

I Habi, E Cohen, I Karshai, D Ben-Ezra
Pediatric Ophthalmology Unit, Hadassah Hebrew University, Jerusalem, Israel

F Behar-Cohen
Rothschild Ophthalmic Foundation, Paris, France

D Ben-Ezra, F Behar-Cohen
USP51, INSERM, Paris, France

Correspondence to: David Ben-Ezra, MD, PhD, Hadassah Hebrew University Hospital, POB 12000 Jerusalem, Israel; benezra@md.huji.ac.il
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References


Temporal pterygium: benign or not?

A true pterygium is a degenerative and hyperplastic process in which the cornea is invaded by a triangular fold of bulbar conjunctiva. Duke-Elder states that the pterygium when single is almost invariably found on the nasal side. The literature on pterygium is abundant and almost from the beginning the emphasis has been placed on its location on the nasal side.

Squamous cell neoplasia of the conjunctiva is relatively uncommon and can masquerade as common, but less significant, ocular surface conditions including pterygium or chronic blepharoconjunctivitis. We present a case of intraepithelial neoplasia, initially diagnosed as inflamed pterygium.

Case report

A 77 year old man, who had worked on the railways, presented with a 3 week history of redness on the outer aspect of the left eye. No history of associated pain, discharge, or watering was elicited.

His medical history included hypertension and hypercholesterolaemia under treatment. His ocular history included squamous cell carcinoma and 17 carcinoma in situ arising in 100 pterygia found that it can be difficult to distinguish a “reactive pterygium” from carcinoma in situ and malignant change should be considered in a pterygium if there is unusual evidence of invasion, extension, or if the lesion becomes particularly vascular. To our knowledge, the last reported case of temporal pterygium was in the 1970s. We present this case to refresh the memory and to highlight the importance of keeping an index of suspicion for squamous cell neoplasia in any atypical presentation of the more
A 39 year old patient showing proptosis and ptosis in the right eye. (B) Gadolinium enhanced coronal T1 fat saturated image through the orbits demonstrates an intraosseous mass in the right orbital roof, with intraorbital and intracranial extension. The intracranial portion was completely extra-axial, with associated dural involvement, as indicated by the thickened and enhancing dura adjacent to the dominant intracranial component. (C) Contrast enhanced coronal computed tomography (CT) image through the orbits demonstrates an intraosseous mass in the right orbital roof, with intraorbital and intracranial extension. Its heterogeneous appearance is the result, in part, of scattered calcifications throughout the mass. Mass effect upon the superior extraocular muscle group is evident.

The patient underwent right sided frontal craniotomy and orbital osteotomy with piece wise gross total resection of the right orbital roof, the involved adjacent periorbita, dura and bone.

Grossly, pathological samples including dura (fig 2A) were soft and reddish-light tan coloured in appearance. Microscopic examination (fig 2B) revealed a cellular capillary haemangioma of bone, with peri orbital and dural involvement (fig 2D), consisting of thin walled blood vessels with some osteohlastic activity and new bone formation. Tumour immunohistochemistry stains for CD34 (fig 2C), CD31, vimentin, and O13 were positive, confirming a vascular origin.

Comment
Intraosseous haemangiomas are benign tumours arising from the intrinsic blood vessels of bone and are two to three times more common in females than males. They are slow growing, accounting for only 0.7–1% of bone tumours, with the most common site being the vertebrae and skull (frontal and parietal). They are typically seen in the adult population, with a peak in the fourth decade, although any age can be affected. Haemangiomas are histopathologically classified as either cavernous (common in the skull and orbit) or capillary (found mainly in vertebrae). The pathogenesis of these tumours is unknown.

The clinical presentation of orbital intraosseous haemangioma is usually a progressive asymptomatic mass which may lead to proptosis, diplopia, optic neuropathy, and ptosis. To date, the largest series contained 21 cases, of which four were of the capillary type. Though intracranial extension has been noted in the past, intradural lesion is reported only once with calvarial capillary haemangioma (sphenoid) but never with orbital invasion.

Plain films typically show bony erosion with scalloped bone giving a “sunburst” appearance. Cavernous and capillary haemangiomas usually have similar imaging findings with differentiation made on histopathological analysis.

The differential diagnosis for a localised lytic bone lesion with calcifications is wide, including primary bone tumours such as osteosarcoma, chondrosarcoma, meningioma, haemangioma, brown tumour, or infection. Reactive lesions, such as xanthoma of bone, aneurysmal bone cyst, and reparative granuloma are also in the differential. Careful radiological evaluation in combination with clinical history and findings usually allows for differentiation among these different lesions.

With respect to our case, the characteristic high signal intensity on T1 imaging usually seen in vertebral haemangiomas was absent, probably the result of a relatively low fat content.
In our case, atypical dural enhancement on imaging was noted with associated erosion of overlying frontal bone. Preferred treatment for symptomatic haemangiomas is surgical resection of the entire lesion, with preoperative embolisation. Radiation has been advocated for large and/or unresectable lesions.

Two novel mutations of connexin genes in Chinese families with autosomal dominant congenital nuclear cataract

Congenital or childhood cataract is a clinically and genetically highly heterogeneous lens disorder, with autosomal dominant inheritance being most common. Non-syndromic congenital cataracts have an estimated frequency of 1–6 per 10,000 live births, with one third of cases familial. Underlying mutations have identified 14 genes involved in the pathogenesis of isolated inherited cataract, including seven genes coding for crystallins (CRYAA, CRYAB, CRYBA1/A3, CRYBB1, CRYBB2, CRYGC, CRYGD), two for gap junctional channel protein (GJA3 and GJA8), two for lens membrane protein (LIM2 and MIP), one for beaded filament structural protein 2 (BFSP2), and one for glucosaminyl (N-acetyl) transferase 2 (GCNT2), one for heat shock transcription factor (HSF4). Here we report two novel heterozygous mutations in the GJA8 and GJA3 genes, in two Chinese families affected by autosomal dominant congenital nuclear cataracts.

Table 2 Two point LOD scores for linkage between the cataract locus and 13q markers in family B

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Table 1 Two point LOD scores for linkage between the cataract locus and 1q markers in family A

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References


Pedigree and haplotype construction were undertaken using Cyrillic v.2.1 software (figs 1A and 2A).

Competing interests: none declared
**Case report**

We studied two Chinese three generation nuclear cataract families with a dominant pattern of inheritance. Clinical information and blood specimens were obtained from 16 members of family A (seven affected and nine unaffected), and 13 members of family B (nine affected and four unaffected). All participants had a full ocular assessment to document the phenotype. The phenotype of two families was characterised by bilateral nuclear cataract that was present at birth or developed during infancy. There was no evidence of other systemic or ocular defects.

After obtaining informed consent, we used a panel of 46 microsatellite markers to study 13 loci for known candidate genes of autosomal dominant congenital cataract susceptibility. The markers’ order and position were obtained from the Marshfield Genetic Database (www.marshfield.org/genetics/maps). Genotyping and data collection were conducted by ABI Prism GeneMapper v 3.0 software. We carried out two point linkage analysis using the MLINK program from the Linkage v.5.10 software package. It suggested positive linkage on chromosome 1q21.1 (lod score was 2.44 for marker D1S1167) in family A and chromosome 13q11–12 (lod score was 1.63 for marker D13S1326) in family B (tables 1 and 2).

There are two strong candidate genes in these regions, GJA8 encoding connexin 50 (Cx50) and GJA3 encoding connexin 46 (Cx46). We screened the mutation of candidate genes by bidirectional sequencing polymerase chain reaction products (300–700 bp). Sequence analysis of the entire coding region and immediate flanking regions detected a heterozygous 191 T→G (AP217524) transition in exon 2 of GJA8, resulting in a Val→Gly substitution at codon 64 (fig 1B).

Sequence analysis of GJA3 detected a heterozygous 134 G→C (AF075290) transition, resulting in a Thr→Ser (TGG→SG) substitution at codon 45 (fig 2B). We examined all unaffected members of two families and 200 unrelated normal controls for GJA3 and GJA8 gene mutations but failed to detect these sequence variations.

**Comment**

Three connexins are expressed in the lens: connexin 43, connexin 46, and connexin 50. Gap junction intercellular communication is an essential part of the cell-cell communication system, which facilitates the exchange of ions, metabolites, signalling molecules, and other molecules with a molecular weight up to 1 kDa.

Each gap junction channel is composed of two hemi-channels, or connexons, which dock in the extracellular space between adjacent cells, and each connexon comprised six integral transmembrane protein subunits known as connexins. All connexins have four transmembrane domains and two extracellular loops with cytoplasmic N and C termini.

To date, four heterozygous missense Cx50 mutations (P88S, E48K, R237T, and I247M) have been described, causing a nuclear or zonular nuclear pulverulent cataract.** Six mutations of Cx46 have been associated with ADCC, including five missense mutations (F32L, P59L, N65S, P187L, and N188T) and one insertion mutation (1137 insC), which resulted in a frame shift at codon 380 (S380fs).**

Currently, two mutations occurred: Cx50 (G22R and D47A) results in cataracts in the mouse, but no dominant spontaneous or mutagen induced cataracts have been associated with the murine gene for GJA3 (Gja3). V64G and W45S substitutions in two Chinese families occurred within evolutionarily conserved residues across species for Cx50 and Cx46 (figs 1E and 2E). These two mutant amino acid residue locate at the phylogenetically conserved extracellular loop 1 (E1). The two extracellular loops mediate docking between connexons and the E1 loop has also been shown to be important for determinant of the transjunctional voltage required for closure of gap junction pores.** The mutant proteins may disrupt normal interactions between the two connexons, which may reduce resistance of the intercellular channel to the leakage of small ions.

In conclusion, two novel heterozygous mutations, V64G in Cx50 and W45S in Cx46, were identified in two Chinese families. These further expand the genetic and phenotypic heterogeneity of cataract.

**References**

**Pneumosinus dilatans in a 13 year old female**

**Case report**

A 13 year old female presented with gradual painless decrease of vision in both eyes for 1.5 years. Over this period her visual acuity dropped from 20/30 (RE) and 20/160 (LE) to 1/200. Her visual acuity was 20/1200 in both eyes.

Significant expansion of paranasal sinuses including maxillary, frontal, ethmoidal, and sphenoid sinus was visible on magnetic resonance images (MRI) of the patient as shown in figure 1. Based on the MRI of the patient, the diagnosis of PSD would be appropriate.

Bilateral consecutive frontal craniotomy was performed in order to unroof the optic canal with the hope to release stretching of the optic nerve which we thought was the reason for her visual deterioration. Figure 1 (bottom) is an image of the surgical procedure. It is clear that the optic nerves have been entrapped in the bony canal and probably suffered from severe stretching and/or compressive effects. Six months after the procedure her visual acuity was 20/1200 in both eyes.

**Comment**

Pneumosinus dilatans is an abnormal dilatation of one or more of the paranasal sinuses. It has diverse manifestations including progressive visual loss if the sphenoid sinus is involved and/or if it is associated with optic nerve meningioma. If the ethmoidal sinus is involved it may present with proptosis. Although a valve mechanism raising the pressure inside the sinus is thought to be responsible for this condition, the exact etiology is unknown. In case of optic nerve damage the nerve is usually compressed in long bony tubes. Pneumosinus dilatans has been associated with meningioma of the intracranial optic nerve and anterior chiasmal angle, middle cranial fossa arachnoid cyst, cerebral hemiatrophy, and prolonged cerebrospinal fluid shunting.

To our knowledge this is the first case of PSD associated with sickle cell trait. PSD has not been associated previously with haematological disorders. Considering the fact that sickle cell trait is generally an asymptomatic condition and the patient's mother was also an asymptomatic carrier, an aetiological relation is unproved. On the other hand, both conditions are rare in our population, therefore the probability of coincidence by chance would seem to be extremely low. The question remains whether our patient had an unusual form of sickle cell trait associated with gross bony involvement and deformity.

Different treatments have been proposed for PSD. These include subtotal resection of the medial wall of the maxillary sinus by an endoscopic approach, osteotomy of the deformed fronto-orbital bossing, and obliteration of the sinus with fat. Because of global and massive expansion of the sinuses and severe optic nerve dysfunction in this case, we preferred to decompress the optic nerve by removing the roof of bony canal which surrounded the intracranial optic nerve. This resulted in mild visual improvement.

M S Sanjari, M Modarreszadeh, K Tarassoly
Ophthalmology Department Eye Research Center, Rasool Akram Hospital, Tehran, Iran

Correspondence to: Kia Tarassoly, MD, Ophthalmology Department, Eye Research Center, Rasool Akram Hospital, Tehran, Iran; kitarassoly@hotmail.com

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Accepted for publication 1 March 2005
Pellucid marginal degeneration coexistent with cornea plana in one member of a family exhibiting a novel KERA mutation

Characterised by flattening of the normally convex corneal surface, small corneas, high hyperopia, and arcus senilis, autosomal recessive cornea plana is secondary to KERA mutation.\(^1\)\(^3\) KERA encodes keratocan, an evolutionary conserved small leucine rich proteoglycan. Keratocan, highly and uniquely expressed in the cornea, is composed of core proteins consisting mostly of leucine rich repeats (LRRs).\(^1\)\(^2\) All patients documented to be homozygous for one of the four previously reported KERA mutations have disruption of LRR architecture and demonstrate similar cornea plana phenotypes.\(^1\)\(^2\) In contrast, corneal pellucid marginal degeneration (PMD) is an idiopathic progressive ectatic corneal disorder that is clinically diagnosed by characteristic thinning, resultant “against the rule” astigmatism, and absence of opacity.\(^3\) We report a case of superior PMD coexistent with cornea plana in a family exhibiting a novel KERA mutation and document the ophthalmic findings of the family.

**Case series**

Twelve individuals from a Saudi nuclear family were studied after institutional review board approval and family informed consent had been obtained from the family. Clinical findings and diagnoses are summarised in figures 1 and 2, and table 1. Only one family member (patient 4) had a history of progressive visual difficulty over the last several years, and this was due to an increasing astigmatic refractive error. Axial lengths and keratometry readings were recorded using the Zeiss IOL-Master (2001 model), and corneal topography was performed using the Bausch & Lomb Orbiscan ZZ (2002 model).

All family members underwent KERA DNA sequencing using methods previously described.\(^1\) A novel mutation was detected.
Table 1: Pertinent biometric and clinical characteristics of the family are summarised

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<th>6</th>
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<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
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</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>50</td>
<td>43</td>
<td>26</td>
<td>24</td>
<td>23</td>
<td>19</td>
<td>18</td>
<td>17</td>
<td>12</td>
<td>10</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>Keratometry RE</td>
<td>43.32</td>
<td>40.61</td>
<td>26.49</td>
<td>45.79</td>
<td>52.73</td>
<td>8085</td>
<td>32.23</td>
<td>8138</td>
<td>38.66</td>
<td>41.11</td>
<td>26.66</td>
<td>43.44</td>
</tr>
<tr>
<td>Keratometry LE</td>
<td>43.95</td>
<td>41.06</td>
<td>8017</td>
<td>28.60</td>
<td>8060</td>
<td>38.66</td>
<td>41.11</td>
<td>26.66</td>
<td>43.95</td>
<td>41.06</td>
<td>26.66</td>
<td>43.95</td>
</tr>
<tr>
<td>Horizontal corneal diameter (RE, LE in mm)</td>
<td>10,11</td>
<td>11</td>
<td>11</td>
<td>8,8</td>
<td>8,8</td>
<td>8,8</td>
<td>8,8</td>
<td>8,8</td>
<td>8,8</td>
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<td>8,8</td>
</tr>
</tbody>
</table>

References


Correspondence to: Arif O Khan, MD, Division of Pediatric Ophthalmology, King Khaled Eye Specialist Hospital, PO Box 7191, Riyadh 11462, Saudi Arabia. arif.khan@mssm.edu

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All four previously reported KERA mutations disrupt keratocan LER function and are associated with similar clinical phenotypes in consanguineous families, including corneal thinning and astigmatism. The current family was homozygous in the siblings. The mutation was not found in the parents, who were carriers. The mutation was also found in the sister with clinical findings of keratitis and cornea plana (No 4). All other family members (Nos 1, 2, 6, 8, 9, 10) were heterozygous for the mutation and clinically unaffected.
### Case report

A 57-year-old woman was referred to Kaohsiung Medical University Hospital with the complaint of a periodic visual fluctuation of a “good day” and a “bad day” alternately for about 6 months. She had diplopia on bad days. She did not have diabetes or hypertension. There was no history of strabismus, amblyopia, patching therapy, ocular trauma, or oculomotor palsy. She had received trials of Mestinon treatment by two neurologists. She had experienced constant strabismus without oculomotor palsy. The visual acuity was unchanged. Brain and orbit magnetic resonance imaging studies were unremarkable except for a suspected small arachnoid cyst on the right side of the falx.

She received 2.5 U botulinum toxin (Botox) injection in her right medial rectus muscle (MR). The alignment was orthotropia 1 week after the injection. She was asymptomatic for about 2 months, but the cyclic pattern returned with a 96-hour cycle by patient history. A repeated 2.5 U Botox injection in right MR, which was given 3 months after the first, produced another asymptomatic period of 2 months. Two months after the second injection, she experienced constant strabismus without cyclic pattern, which persisted for about 1 year. She received right MR recession by 4 mm and right lateral rectus muscle resection by 5 mm for constant esotropia of 25 prism diopters. After the surgery, the alignment was orthotropic and no recurrent of the cyclic pattern during 1 month of follow up. The stereopsis was 200 seconds of arc by Titmus test.

### Table 1

<table>
<thead>
<tr>
<th>Case No</th>
<th>Age of onset (years)</th>
<th>Sex</th>
<th>Cyclic pattern</th>
<th>Duration of cycles</th>
<th>Angle (Δ)</th>
<th>Related diseases or coexisting conditions</th>
<th>Outcome</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>34</td>
<td>Male</td>
<td>4 days</td>
<td>3 years</td>
<td>ET 35</td>
<td>Optic atrophy both eyes, alcohol abuse</td>
<td>No treatment</td>
<td>Frenkel⁸</td>
</tr>
<tr>
<td>2</td>
<td>32</td>
<td>Female*</td>
<td>2 days</td>
<td>NA</td>
<td>ET 35</td>
<td>NA</td>
<td>No treatment</td>
<td>HELVESTON⁷</td>
</tr>
<tr>
<td>3</td>
<td>53</td>
<td>Female</td>
<td>2 days</td>
<td>NA</td>
<td>XT 15, RHT 30</td>
<td>Graves’ disease</td>
<td>OT after muscle surgery</td>
<td>KNAPP⁴</td>
</tr>
<tr>
<td>4</td>
<td>55</td>
<td>Female</td>
<td>2 days</td>
<td>NA</td>
<td>RHT 25</td>
<td>Graves’ disease, RD RE, 360° encircling scleral buckling procedure RE, cyclic mydriasis, ptosis</td>
<td>OT after muscle surgery</td>
<td>KNAPP⁴</td>
</tr>
<tr>
<td>5</td>
<td>67</td>
<td>Female</td>
<td>2 days</td>
<td>5 years</td>
<td>ET 25, RHT B</td>
<td>Craniofacial surgery for fronto-orbital fibrous dysplasia, left side</td>
<td>No treatment</td>
<td>TRossal⁴</td>
</tr>
<tr>
<td>6</td>
<td>34</td>
<td>Female</td>
<td>2 days</td>
<td>9 weeks</td>
<td>LHT 20, XT 10</td>
<td>ECCE RE, high myopia RE, retinal detachment</td>
<td>No treatment</td>
<td>Metz⁷</td>
</tr>
<tr>
<td>7</td>
<td>46</td>
<td>Female</td>
<td>2 days</td>
<td>1 year</td>
<td>ET 12 to 45</td>
<td>Retinal detachment, RD RE, vitreoretinopathy and silicone oil exchange RE, ECCE RE, RD and PVR RE, PVT</td>
<td>No treatment</td>
<td>RIODAN-EVA⁷</td>
</tr>
<tr>
<td>8</td>
<td>21</td>
<td>Female</td>
<td>5 days?</td>
<td>2 years</td>
<td>ET 25</td>
<td>RD RE, vitreoretinopathy and silicone oil exchange RE, ECCE RE, RD and PVR RE, PVT</td>
<td>No treatment</td>
<td>RIODAN-EVA⁷</td>
</tr>
<tr>
<td>9</td>
<td>49</td>
<td>Female</td>
<td>2 days</td>
<td>7 years</td>
<td>RHT 15, ET 25</td>
<td>Retinal detachment, RD RE, vitreoretinopathy and silicone oil exchange RE, ECCE LE, prophyphacty encircling band surgery LE</td>
<td>No treatment</td>
<td>BAGHIERI⁷</td>
</tr>
<tr>
<td>10</td>
<td>57</td>
<td>Female</td>
<td>2 days</td>
<td>1 year</td>
<td>ET 30</td>
<td>Recurrent pterygia in both eyes</td>
<td>Recurrent pterygia in both eyes</td>
<td>Present report</td>
</tr>
</tbody>
</table>

*Information provided by Dr. Eugene HELVESTON (personal communication). NA, not available; CPP, cyclic pattern persisted; Δ, prism dioptr; ET, esotropia; XT, exotropia; RHT, right hypertropia; LHT, left hypertropia; OT, orthotropia; RD, retinal detachment; PVR, proliferative vitreoretinopathy; ECCE, extracapsular cataract extraction; PVT, posterior vitrectomy.

**Comment**

Adult onset cyclic strabismus is rare and, to the best of our knowledge, only 10 patients have been reported. The reported cases of adult onset cyclic strabismus are summarised in table 1. The patients had various ages of onset between 21 and 67 years. Most reported cases demonstrated 48-hour cyclic patterns. The persistence of the cycles, if not interrupted by surgery, was as long as 7 years. It is interesting that adult onset cyclic strabismus occurs predominantly in females and is frequently related to ocular or orbital diseases, trauma, or surgery. Botox injection has been used as treatment of cyclic strabismus. However, no change of the cyclic pattern was mentioned. We noted that the cyclic pattern in our patient changed 3 months after the first Botox injection, and the cycles were eliminated 2 months after the second injection.

The characteristics of cyclic strabismus in children are an average age of onset between 3 and 4 years, moderate hyperopia, and moderate angle. However, a female preponderance was not noted in childhood onset cyclic esotropia. No pertinent explanation for cyclic strabismus has been reported. Although Botox only has a temporary effect, both Botox injection and eye muscle surgery produce good ocular alignment. More evidence and further investigation are required to elucidate the mystery.

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**Acknowledgements**

The authors thank Professor William F Hoyt and Professor Craig S Hoyt for their review and criticism of this letter.

Y-H Lai

Department of Ophthalmology, Kaohsiung Medical University-Hsiao-Kang Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan

D R Fredrick

Department of Ophthalmology, University of California, San Francisco, San Francisco, CA, USA
Hand hygiene in routine glaucoma clinics

Nosocomial infection occurs via the hands of healthcare workers (HCWs). Hand hygiene reduces hospital infection rates; however, HCWs seldom comply with this.

We determined how often ophthalmologists and allied professionals cleaned their hands and whether intervention was effective.

Participants, methods, and results

We conducted the study in the daily glaucoma clinics of Moorfields Eye Hospital where policy states that all HCWs must clean their hands between patients.

Potential hand cleaning opportunities were monitored covertly by two observers. After manipulation of procedures, and after glove removal. Manipulative procedures were defined as 5-fluorouracil subconjunctival injection, taking an eye swab, suture, or supramid removal, and bleb needling or massage.

Without revealing how the study was conducted, preliminary results were presented and also distributed by memo. Two weeks after this intervention, hand hygiene was re-monitored for 1 week.

Baseline hand hygiene episodes were 18% but increased significantly to 28% (p = 0.005) following intervention (table 1). Before intervention, two out of seven people performing procedures cleaned their hands, but not for the single episode that 5-fluorouracil was used. However, after intervention six out of seven HCWs cleaned their hands (p = 0.04), including all three episodes in which 5-fluorouracil was handled.

Before intervention, female HCWs cleaned their hands significantly more than males (30% v 9%, p < 0.001). After intervention hand hygiene increased further for females (54%, p < 0.001) with no change for males (11%, p = 0.57).

Nurses had the highest frequency of hand cleaning but with no change after intervention (69% v 58%, p = 0.36). Increased hand hygiene was significant for doctors following intervention (11% v 20%, p = 0.01).

Comment

Recently, nosocomial infection has attracted considerable media interest. While problematic worldwide, the United Kingdom has considerable media interest. While problematic worldwide, the United Kingdom has encountered its fair share. In our study, intervention had its greatest effect on the doctors (p = 0.01). Although numbers are small, intervention had a positive effect on manipulative procedures, especially when using 5-fluorouracil.

Our study demonstrates that hospital policy is not being practised. Getting HCWs to clean their hands has been an ongoing struggle since Semmelweis. It has been suggested that patients should approach the healthcare professional to hand wash. Although controversial, this may help in the eradication of hospital acquired infection.

E Mensah, I E Murdoch, K Binstead, C Rotheram, W Franks
Moorfields Eye Hospital NHS Foundation Trust, City Road, London EC1V 2PD, UK

Accepted for publication 21 May 2005

Table 1 Effect of intervention on hand hygiene compliance

<table>
<thead>
<tr>
<th>Hand hygiene opportunities</th>
<th>Hand hygiene episodes before patient contact</th>
<th>Hand hygiene episodes during patient contact</th>
<th>Total hand hygiene episodes</th>
<th>Hand hygiene episodes for procedures</th>
<th>Sex of healthcare worker</th>
<th>Hand hygiene after intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No (%)</td>
<td>No (%)</td>
<td>44 (18)</td>
<td>2/7 (0/1 for 5-FU)</td>
<td>Female</td>
<td>62/115 (54**))</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Male</td>
<td>20/182 (11**))</td>
</tr>
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<td></td>
<td></td>
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<td></td>
<td>12/133 (9*)</td>
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<td>32/107 (30*)</td>
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<td>12/133 (9*)</td>
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<td>32/107 (30*)</td>
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</table>

* p < 0.001,
** p < 0.001.

Only three out of nine examination bays were observed for 1 hour at a time, in random order, during morning (from 09:30 to 12:30) and afternoon (from 14:00 to 17:00) clinics.

Data were analysed using χ² contingency tests. 5-FU = 5-fluorouracil.
Successful treatment of Wegener’s granulomatosis associated scleritis with rituximab

Rituximab (Rituxan, Genentech, Inc, South San Francisco, CA, USA) is a new anti-CD20 B cell monoclonal antibody that has been used successfully to treat refractory cases of Wegener’s granulomatosis (WG). There has been no published report of its effect in Wegener’s granulomatosis associated scleritis. We describe the successful treatment of Wegener’s associated scleritis with rituximab.

Case report

A 21 year old man with WG, proved on renal biopsy and by anti-neutrophil cytoplasm antibody (ANCA) positivity 6 years earlier, presented with bilateral, painful, red eyes. On examination his visual acuities were 6/4 right eye and 6/5 left eye. Anterior segment examination showed subconjunctival haemorrhage, congested scleral vessels, scleral oedema, peripheral corneal infiltrates, and mild anterior chamber inflammation in each eye. Funduscopy revealed bilateral swollen optic discs with scattered retinal haemorrhages in the right eye. A diagnosis of scleritis was made. Oral prednisolone was increased from 5–40 mg daily and maintenance oral mycophenolate mofetil 2 g daily was continued. Topical prednisolone acetate 1% hourly was commenced to both eyes.

Over the next month the scleritis had not improved and his systemic vasculitis had become more active, causing arthralgia, haemoptysis, and new vasculitic skin lesions. His white cell count (WCC) had risen to 13.9 × 10⁹/μl compared to 9.6 × 10⁹/μl the previous month. His ANCA had become positive by indirect immunofluorescence (titre of 1 in 25), and by proteinase 3 specific ELISA (titre 22 units, normal range <10). A new infiltrate was present in the lower lobe of his right lung on chest x-ray.

Owing to concern over the total cumulative dose of cyclophosphamide he had previously received (>25 g), he was given an intravenous infusion of rituximab 1 g. Intravenous cyclophosphamide (40 mg/kg, adjusted for renal function) was also given with the rituximab infusion. These infusions were repeated after 2 weeks.

This led to an immediate significant systemic improvement accompanied by reduction of WCC to 9.6 × 10⁹ and ANCA became undetectable. The pulmonary infiltrate resolved. The scleritis also resolved promptly, evident from completely white eyes, resolution of active scleral vessels, corneal infiltrates, optic disc swelling, and subjective resolution of ocular pain. At 7 months after the infusion, the patient remained in remission. His systemic treatment was slowly reduced to prednisolone 15 mg daily, mycophenolate mofetil 750 mg twice daily.

Comment

Rituximab is a humanised monoclonal antibody against the CD20 antigen that is expressed on the cell surface during early pre-B cell development and persists through all stages of B cell differentiation. It results in rapid depletion of CD20 positive B lymphocytes from the circulating blood and is well tolerated. The precise role of B cells in the pathogenesis of WG remains elusive at present, but several possibilities exist. B cells can act as antigen presenting cells to T cells or provide additional co-stimulatory signals for their T cells. Another possibility is that self reactive B cells, derived from unusual B cell subsets, may follow a different activation/maturaton process, including the continued expression of CD20 during antibody production.

There has been no report on its effect on WG associated scleritis. Our patient was given rituximab primarily for his generalised vasculitis, but his refractory scleritis also responded promptly. Although he also received cyclophosphamide at the same time, the dose and course were limited to avoid toxicity. Therefore, in this case the prompt improvement was attributed to rituximab, rather than cyclophosphamide.

This is the first case reporting rituximab as an effective treatment for refractory WG associated scleritis.
because of the complex immunological effects of IFNs, including enhanced lymphocyte cytotoxicity, inhibition of T suppressor cell function, increased expression of major histocompatibility complex (MHC) class I antigens, production of proinflammatory cytokines, and differentiation of antigen presenting cell activation of T helper lymphocytes by autoantigens. Some or all of them might contribute to the development of autoimmune disease.  

In this case the patient had no sign of MG or other autoimmune disease before the IFN treatment. His symptom is limited only to extraocular muscles: the condition is relatively mild. That is consistent with the previous report referring to the relation between the severity and the presence of a history of autoimmune disease; but the fact that anti-acetylcholine receptor antibody titre was not elevated is contradictory.  

We could not establish the causality. These days many patients with chronic active hepatitis C virus receive IFN or IFN/ribavirin combined therapy. We usually examine these patients only in terms of retinopathy. Although this case could be a coincidental sporadic autoimmune disorder, we should take MG into consideration. We should recognise the risk of development or worsening of MG and be careful in managing patients undergoing therapy, especially when they already have MG or compatible symptoms. It can be a serious complication although it is very rare.

**References**


**Case reports**

**Case 1**

A 47 year old woman presented with a gradual decrease in vision over 4 months. Her medical history showed that she has been in excellent health. She smoked one pack of cigarettes per week and had two to three beers daily. She denied any use of any medications in the past few months. She and her husband have been on a diet which contained fewer vegetables than their normal intake, for 4 months. Family history was unremarkable.

Visual acuity was 20/50 right eye and 20/100 left eye. Colour vision using the pseudoisochromatic plates was four of eight in right eye and two of eight in left eye. Intraocular pressure was 12 mm Hg in right eye and two of eight in left eye. She had normal anterior segment in both eyes. Her pupils were sluggish to direct stimulation of light with no afferent defect. Ocular motility was normal. Funduscopy showed anomalous optic nerves with no pallor, and normal maculas. Testing with 24-2 static perimetry revealed an inferior and nasal defect in the right eye; supernasal, inferior, and central defect in the left eye (fig 1A). Humphrey 2-4 static perimetry showed bilateral cecocentral scotomas (fig 1B). Magnetic resonance imaging (MRI) of the brain and orbit with and without contrast was normal. Serology tests for Lyme and antinuclear antibodies (ANA) were negative. Complete blood count, serum vitamin B12, and folate were within normal limits. MERG testing showed severe reduction in amplitude mostly centrally in both eyes (fig 2).

**Case 2**

A 55 year old woman presented with progressive decrease in vision of both eyes over 1 month. She had a history of multiple intracranial aneurysms that were clipped 15 years earlier. She was not using any medications. She smoked one pack of cigarette a day for 25 years and has five to eight drinks per week. Family history was positive for glaucoma in her mother. Visual acuity was counting fingers at 1 foot right eye and at 2 feet left eye. She could not identify any of the pseudoisochromatic colour plates in both eyes. She had normal anterior segment in both eyes. Pupillary reactions were sluggish to light stimulation with no afferent defect. Funduscopy showed mildly swollen optic nerves in both eyes (fig 3). Kinetic perimetry...

A Oishi, K Miyamoto, S Kashii, N Yoshimura

Department of Ophthalmology and Visual Sciences, Kyoto University Graduate School of Medicine, Kyoto, Japan

Correspondence to: Dr Akiko Oishi, Department of Ophthalmology and Visual Sciences, Kyoto University Graduate School of Medicine, Kyoto, Japan; aq_o@yahoo.co.jp

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The clinical findings seen in tobacco-alcohol amblyopia can occur in any disease of anterior visual pathway from the retina to the optic tract and there is little evidence to suggest that the locus of pathology is restricted to the optic nerve. Histopathological studies on animal models of nutritional amblyopia showed lesions in the retina, optic nerve and tract, and the maculopapillary bundle. Electrophysiological abnormalities in animal models of tobacco-alcohol amblyopia showed reduced amplitudes with normal latencies using visual evoked potentials, and increased a-wave and b-wave implicit times and decreased b-wave amplitudes using full field electroretinograms.

The multifocal ERG testing showed decreased amplitudes in both the right eye (A) and the left eye (B) with almost isoelectric responses centrally and improvement towards the periphery.

Comment
We describe two cases of “tobacco-alcohol amblyopia” in patients who had a history of high alcohol intake (cases 1 and 2) and shortly after dietary alteration (case 1). In both cases, MERG testing showed decreased amplitudes in the macula. The condition of the patient in case 2 may have been precipitated by a metabolic injury (tobacco, alcohol) to genetically “compromised” mitochondria. This shows the clinical overlap in conditions of inherited mitochondrial dysfunction and acquired ones such as tobacco-alcohol amblyopia.

The authors have no proprietary interest in any of the instruments used or any other aspect of this study.

References
1 Traquair HM. Toxic amblyopia, including retrobulbar neuritis. Trans Ophthalmol Soc UK 1930;50:35.

TTT: local light absorption and heat convection versus heat conduction
Miura and co-authors have contributed valuable experimental data on transpupillary thermotherapy (TTT) for choroidal neovascularisation (CNV) in a rat model. In their scholarly discussion section, they speculate that the variability in power settings they encountered in heating experimental CNV may be due to a “variation of heat conduction in experimental CNV.” There are more probable explanations for that variability. As reported previously in the authors’ reference 7: “light absorption in pigment clumps from...
prior focal photoocoagulation can cause local hot spots in large TTT treatment fields.

Additionally, local choroidal blood flow may have been altered by vascular remodelling that occurred in the 14 days between the intense focal laser photoocoagulation that the authors used to produce CNV and their subsequent occurrence in the 14 days between the intense TTT exposure at the site. Chorioretinal temperature rise from a lengthy 60 seconds TTT exposure is affected: (1) by pigmentation at the treatment site, which determines how effectively laser radiant energy is converted locally into thermal energy, and (2) to a lesser extent by choroidal blood flow, which transfers thermal energy by heat convection away from the exposure site. It is unlikely that local heat conduction is altered significantly by the initial photoocoagulation or subsequent tissue remodelling because heat conduction in most normal biological tissues is essentially the same as that of water.

M A Mainster
Department of Ophthalmology, University of Kansas Medical School, 3901 Rainbow Boulevard, Kansas City, KS 66160-7379, USA

D H Silney
Laser/Optical Radiation Program, US Army Environmental Hygiene Agency, Aberdeen Proving Ground, MD 21010, USA

Correspondence to: Professor Martin A Mainster, Department of Ophthalmology, M53009, University of Kansas Medical School, 3901 Rainbow Boulevard, Kansas City, KS 66160-7379, USA; mmmainster@kumc.edu
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References

NOTICES

World Ophthalmology Congress 2006 – Brazil
The World Ophthalmology Congress (which is replacing the International Congress of Ophthalmology) is meeting in February 2006 in Brazil.

For further information on the congress and committees, scientific program and coordinators of different areas are available at the congress website www.ophthalmology2006.com.br

Vision 2020
The latest issue of Community Eye Health (No 54) assesses the progress of Vision 2020 at the district level. For further information please contact: Journal of Community Eye Health, International Resource Centre, International Centre for Eye Health, Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK (tel: +44 (0)20 7612 7964; email: Anita.Shah@lshtm.ac.uk; online edition: www.jceh.co.uk). Annual subscription (4 issues) UK £28/US$45. Free to developing country applicants.

CORRECTIONS

doi: 10.1136/bjo.2005.75895corr1

In the paper titled, Patient satisfaction with anaesthesia comparing sun-Tenon’s block and topical anaesthesia (Br J Ophthalmol 2005;89:1228) the second author was omitted. The second author for this letter was R W D Bell, Sunderland Eye Infirmary, Queen Alexandra Road, Sunderland SR2 9HP, UK. The author apologises for this omission.
doi: 10.1136/bjo.2004.58941corr1

In the paper titled, En-face optical coherence tomography (OCT): A new method to analyse structural changes of the optic nerve head in rat glaucoma (Br J Ophthalmol 2005;89:1210–6) one of the author’s names has been spelt incorrectly. The author Podoleanu AG, should be spelt Podoleanu AG. The journal apologises for this error.