LETTERS TO THE EDITOR

Waardenburg syndrome type 2 in a Turkish family: implications for the importance of the pattern of fundus pigmentation

EDITOR,—Waardenburg syndrome (WS) is a typical auditory pigmentary syndrome with affected individuals showing varying combinations of sensorineural hearing loss, patchy abnormal pigmentation of the eyes, hair and skin, and various defects of neural crest derived tissues.1,2

This syndrome is both clinically and genetically heterogeneous and is clinically classified into four types.3 Mutations of the PAX3 gene have been identified in WS type 1 and 3, while those of either the endothelin B receptor gene, the endothelin-3 gene or the soxio gene have been identified in WS type 4.4,5 WS type 2 is a heterogeneous group, with about 10% of cases caused by mutations in MITF. But MITF mutations are obviously not the major cause of WS type 2 and for most cases the genetic basis is as yet unknown.

The diagnostic criteria for WS type 2 proposed by Liu et al5 include, in addition to congenital sensorineural hearing loss and pigmentary disturbances of the hair, pigmentary disturbances of the iris but not of the fundus.

In the two affected boys of the Turkish family presented here, the pattern of fundus pigmentation was one of the most striking clinical features, with dense hyperpigmented areas next to hypopigmented areas. We want to emphasise the importance of a thorough observation of the clinical phenotype and especially of the pattern of fundus pigmentation in WS type 2.

CASE REPORT

A Turkish family presented with two of three sons showing clinical symptoms of WS type 2. Firstly, the 5 year old boy, the youngest of the non-consanguineous couple, was referred for ophthalmological evaluation because of constant esotropia in the left eye. The child has worn hearing aids since the age of 16 months; the first reliable audiogram at age 3 years showed profound sensorineural hearing loss which had not changed over the past years. Best corrected visual acuity was 20/20 right eye and 20/400 left eye. Cycloplegic refraction revealed an anisohypermetropia (right eye +0.5D and left eye +4.5D), best corrected visual acuity was 20/20 right eye and 20/200 left eye. Severe fundus pigmentary disturbances were found in the left (blue) eye, with extensive albinoid areas nasally and on the posterior pole, whereas the temporal region showed a homogeneous area of dense hyperpigmentation. In the right (dark brown) eye, the pigmentary disturbances were less extensive with a hyperpigmented peripapillary ring and pigmentary mottling especially in the nasal region (Fig 2, centre). Conventional audiological examinations showed bilateral sensorineural hearing loss with moderate impairment on the right and total deafness on the left side (Fig 2, bottom).

Ophthalmological and audiological evaluations made of the father, the eldest brother, and a son of the father’s first marriage were within normal limits. The mother showed pigmentary mottling in the periphery of the fundus only. No other associated abnormalities (such as hair or skin hypopigmentation, medial eyebrow flare, broad and high nasal root, hypoplasia of alae nasi, or premature greying of hair) were found among the family members. To calculate the W index, a biometric index for dystopia canthorum, we used dystopia indices for WS as reported by Arias,7

Figure 1 (Top) The 5 year old boy (III-5) with bilateral dark brown irides; corneal reflexes demonstrate left esotropia; there is no evidence of dystopia canthorum. (Centre) Left: right fundus with an area of hyperpigmentation in the peripapillary region as well as nasally; pigmentary mottling and spots of hyperpigmentation in the temporal periphery (arrows); (right) left fundus, albinoid in type 2. Audiogram: profound bilateral sensorineural hearing loss.

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Based upon the inner canthal, interpupillary, and outer canthal distances. The W index for this family was 1.45, indicating that none of the individuals had dystopia canthorum. This was consistent with the clinical picture of WS type 2.

The genomic DNA samples, tested for mutations in the PAX3 and MITF genes as described elsewhere, showed no abnormally migrating bands.

COMMENT
Given the classic symptoms of WS type 2 expressed in this Turkish family, we had the opportunity to make some interesting observations on the clinical findings in this syndrome.

In the genomic DNA samples of this family no abnormally migrating bands in the MITF gene or the PAX 3 gene were seen. Only about 10% of patients who fulfil the diagnostic criteria for WS type 2 have an MITF mutation and for most cases the genetic basis is as yet unknown. Dominantly inherited examples of auditory pigmentary syndromes with patchy depigmentation of the skin, hair, eyes or the stria vascularis of the cochlea are usually labelled as Waardenburg syndromes. Expression of clinical findings is extremely variable and the evaluation of a correct history of pedigreed was difficult in this family because of the fact that most of the other family members were living in the Turkey. However, the fundal pigmentary changes of the mother were distinct enough to mark her as affected.

Complete heterochromia irides and especially the brilliant sapphire-blue eye colour were one of the most impressive clinical findings in WS type 2 family in which no mutations of the MITF gene could be found. The affected family members showed a conspicuous fundus picture with ipsilateral connections between iris, fundus, and perhaps, inner ear pigmentation. Therefore, one might suggest, that the clinical signs in WS type 2 could be a consequence of a failure in distribution of pigmented melanocytes in their final location. The genetic basis, as yet unknown for most cases of WS type 2, might be found in a very late step of the pigmentation pathway.

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Depression and anxiety frequently accompany adolescence, and a chronic course is typical. Trichotillomania is characterised by an irresistible urge to pull one’s hair. Any body hair may be targeted. Scalp and eyelashes are most commonly affected. Onset is generally in childhood or adolescence, and a chronic course is typical. Depression and anxiety frequently accompany this disorder. An increased incidence of comorbid obsessive-compulsive disorder (OCD) has been noted. The estimated lifetime prevalence is 1.5% for male and 3.4% for female college students. In very young patients, a more equal sex ratio is observed. On the whole, women show 5–10 times higher prevalence rates than men. The majority of the sufferers disguise their hair loss very well. Because of the secrecy and shame about their behaviour, many remain silent sufferers and treatment is often delayed. It is a chronic mental illness that imposes severe limitations on the patient’s social, emotional, and occupational adjustment. The pathophysiology of trichotillomania is not well understood. Treatment options include: medications such as serotonin reuptake inhibitors with or without haloperidol, paroxetine, clomipramine, pimozide, risperidone in serotonin reuptake inhibitor refractory trichotillomania, valproaxine; behaviour therapy habit reversal training and hypnotherapy.

Trichotillomania has been infrequently reported in the ophthalmic literature. Management can be difficult. Many of these patients are aware of their behaviour, but are unable to curtail it. Others may conceal or deny their habit. Psychiatric counselling may be of benefit if patients are willing to undergo it.

COMMENT

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Trichotillomania has been infrequently reported in the ophthalmic literature. Management can be difficult. Many of these patients are aware of their behaviour, but are unable to curtail it. Others may conceal or deny their habit. Psychiatric counselling may be of benefit if patients are willing to undergo it.
Herman Knapp Testimonial Fund fellowship, the ophthalmic Physician fellowship, Boston, MA. Dr Read is the recipient of an American Physician grant EY03040 and by an unrestricted grant Supported in part by National Institute of Health therapy.

Assessment of possible systemic toxicity is continuously followed, since stromal inflammation, but fine golden granules are still evident.

The second variant of keratopathy is rare, presenting with inflammatory symptoms and signs. Examination reveals marginal interstitial keratitis that may ulcerate, with white, subepithelial limbal infiltration and deep, brush-like stromal vascularisation. It is presumed to be an idiosyncratic reaction. It may be unilateral or bilateral, and is considered an indication to stop gold therapy. The underlying pathogenic mechanism, as well as the possible associations with other systemic gold toxicity, is unknown. However, it is notable that the keratitis in our case was responsive to topical corticosteroids and recurrent after their withdrawal. A similar response has been reported in systemic manifestations of gold toxicity.

The diagnosis of gold keratopathy should be considered in patients with rheumatoid arthritis who present with marginal keratitis. Assessment of possible systemic toxicity is warranted and cessation of therapy should be considered in such cases. Patients should be continuously followed, since stromal inflammation may recur even after cessation of gold therapy.

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COMMENT

Two variants of gold induced keratopathy (corneal chrysiasis) have been described. The more common variant manifests as asymptomatic deposition of fine brown or purple granules in the central posterior cornea, sparing the periphery. Other patterns include peripheral deposition with extension towards the central cornea, superficial and deep stromal deposition. Corneal marginal granule deposition correlates with duration and dosage of therapy and occurs in most, if not all patients after a cumulative dose of 1 g has been reached. Corneal gold deposition by itself is not considered an indication to discontinue gold therapy.

Orbital metastases from malignant neoplasms are rare and can originate from anywhere in the body. In adults, the primary tumour is almost always a carcinoma, with breast and lung accounting for the vast majority of orbital metastases, followed in frequency by gynaecological and gastrointestinal primaries. In children with orbital metastases the primary tumours in descending order of frequency are neuroblastoma, Ewing's sarcoma, and Wilm's tumour. They have reported single cases of osteosarcoma, demonstrating a soft tissue density mass in the right orbit displacing the eyeball. Fine needle aspiration cytology from the mass showed malignant spindle cells. A diagnosis of osteosarcoma with metastasis to right orbit was made. The patient was offered palliative chemotherapy but refused further treatment and was discharged from the hospital.

COMMENT

Osteosarcoma is the most common primary malignant tumour of bone. Most cases occur in children, adolescents, and young adults with a male predominance. The classic site of occurrence is the medulla of the long bones, particularly the distal femur, proximal tibia, and proximal humerus. Metastases of osteosarcoma typically involve the lungs. Recent studies indicate, however, that the incidence of non-pulmonary metastases is increasing.

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demonstrates an opaque left maxillary antrum

Oscillopsia is an illusion that the world is in

A 26 year old woman was referred with a 6

An unusual cause of oscillopsia

Editor,—Chronic maxillary atelectasis (CMA), also known as silent sinus syndrome (SSS), describes the same condition. Typically, the patient presents with acute enophthalmos and hypoglobus in the absence of previous trauma or surgery. Past sinus disease may be present and computed tomograph (CT) scans demonstrate ipsilateral sinus contraction, orbital floor resorption, and thinning with inferior prolapse into the maxillary sinus. We present a patient who noted oscillopsia while jogging 1 year after being diagnosed with SSS.

CASE REPORT
A 26 year old woman was referred with a 6 month history of painless gradual sinking of the left eye (Fig 1). She had suffered two episodes of mild sinusitis, one at the age of 12 and one at a year before presentation. Visual acuity was 6/6 in each eye and there was no evidence of optic neuropathy. There was 4 mm of left relative enophthalmos, no manifest deviation, and full extraocular movements. The height of the palpebral aperture was 1 mm less on the left. Orbital CT scans showed a unilaterally opaque maxillary antrum and ethmoid sinus, a collapsed inferior prolapse into the maxillary sinus, and Lockwood's ligament, while the levator palpebrae superioris and Whitnall's ligament remain in their normal position. Patients with SSS may also develop vertical diplopia, lid retraction, lagophthalmos, or blurred vision.

Spontaneous enophthalmos unrelated to trauma, surgery, local malignancy, or systemic disease is uncommon. The presence of diplopia may suggest an underlying neuro-ophthalmic disorder; however, hypoglobus and enophthalmos point to the orbital/maxillary area as the primary site of pathology.

An unusual cause of oscillopsia

Letters

An unusual cause of oscillopsia

Editor,—A 56 year old man was referred to the oculary oncology service with complaints of pain, redness, and blurring of vision in his left eye for the previous 2 months. He had no significant past ocular history. He was a known hypertensive with no known allergies.

On examination his visual acuity was 6/18 in the right eye and 6/6 in the left eye. There was 2 mm of relative enophthalmos on the right side. A pink subconjunctival patch was noticed in the superior quadrant (Fig 1). He had a shallow anterior chamber. Gonioscopy showed that anterior bowing of the iris closed 270 degrees of the angle. A YAG iridotomy was performed and pupils dilated for fundus evaluation. Funduscopy showed extensive peripheral elevation of the ciliary body and pars plana, which appeared to extend subretinally to the disc with an overlying retinal detachment in places (Fig 2). Ultrasound biomicroscopy along with B scan of the globe confirmed diffuse infiltration of the ciliary body and choroid (Fig 3A). Diffuse extension of this abnormal tissue behind the globe was also evident. The left eye was normal. A working diagnosis of benign reactive lymphoid hyperplasia was made and an incisional biopsy planned. The patient was subsequently admitted for an incisional biopsy and investigations to rule out systemic disease. No systemic evidence of lymphoma was found, however. Histopathology confirmed the diagnosis of well differentiated B cell lymphoma (diffuse large cell lymphoma (REAL classification)) (Fig 4).

A cytogenetic analysis was also performed as detailed previously. Only a partial analysis was possible, but from analysis of 12 divisions the karyotype was determined to be: 2 cells, 46 XY; 10 cells, 43–46 X; add (1) (q27)[10], add (6) (p22)[10], +10[10], −14[10], +2mar[5].

The patient was subsequently started on 30 mg of prednisolone and was referred to the radiotherapy department where he received 30 Gy in 15 sessions over a 3 week period. Follow up at 4 months and further 3 months following the radiotherapy showed resolution of conjunctival lesion at presentation.

Figure 1 Photograph showing the conjunctival lesion at presentation.

Cytenetic analysis in ocular lymphoma

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of the mass. The patient has since been asymptomatic.

COMMENT

Characteristic cytogenetic abnormalities are known to be associated with certain types of lymphoma. In addition to classic translocation of chromosome 8 and 14 in Burkitt's lymphoma, other chromosome rearrangements are related to subsets of lymphoma. To our knowledge this is the first report of chromosome abnormalities in ocular lymphoma. We observed abnormalities frequently associated with non-Hodgkin's lymphoma (NHL), including rearrangements of chromosome 1 and 6, which are found in both B and T cell NHL, as is a loss of the Y chromosome. Trisomy of chromosome 12 was also observed in this ocular lymphoma, and has been linked with small lymphocytic or diffuse large cell B NHL, and from a study of diffuse large cell lymphomas of stomach, chromosome 12 was again found to be the most consistent abnormality. Although its too early to identify which abnormalities are specifically related to the development of this eye lymphoma, it is apparent that certain alterations are characteristic of lymphoma in general, suggesting that similarities exist between development of ocular and other lymphomas.

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Grotesque bilateral eyelid swelling as a symptom of Munchausen's syndrome

EDITOR,—Eyelid swelling can be diffuse or solid, acute or chronic, isolated or part of a syndrome. The differential diagnosis of solid, chronic, and isolated eyelid swelling comprises tumours of multiple origin. We report a case of eyelid swelling which was caused by automutilation as part of Munchausen's syndrome.

CASE REPORT

A 44 year old white woman presented with bilateral lower eyelid swelling that had been present for 6 months, which made reading impossible (Fig 1). In the past she had undergone several paranasal sinus operations and 3 years earlier she had been treated for a preseptal orbital cellulitis and pansinusitis. For the past 4 years she had been bedridden because of fibromyalgia.

The swellings measured 7 × 5 × 2 cm and felt solid on palpation. Complete ocular, internal, otolaryngological, dermatological, parasitological, and psychological examination revealed no clues for the diagnosis. The swellings were surgically removed to the level of the orbital septum, the defects being covered with full thickness skin grafts. Histological examination showed chronic lymphoedema with lymphangiectasia, inflammation, and striking eosinophilia, but no conclusive diagnosis could be made at this time. During uneventful healing of the lower lids, the patient developed bilateral upper eyelid swelling. These swellings were removed as well and replaced by split skin grafts. Histology of the upper lids showed densely packed empty spaces, which almost obscured pre-existent structures such as the orbicularis muscle (Fig 2). In between a patchy infiltrate of lymphocytes, neutrophils, eosinophils, and many macrophages was seen. At high magnification (Fig 3), the empty spaces revealed a lining of macrophages as was demonstrated by positivity for the CD 68 antibody, a reaction pattern highly suggestive of a factitial process. The diagnosis of Munchausen's syndrome was made.

COMMENT

The patient was confronted with these results and admitted having pin-pricked herself after putting fatty ointments on her eyelids. She thought this would help the “blisters” to disappear more rapidly. After an emotional conversation, she was able to get up and walk for the first time in 4 years. The repeated psychiatric evaluation resulted in a diagnosis of a factitious disorder with physical signs superimposed on a somatisation disorder. The complaints seemed to have a function in the maintenance of the balance of power in the matrimonial relationship. The patient refused psychiatric treatment.

Factitious disorders, such as the Munchausen's syndrome, are under the patient's voluntary control and are intended to get or maintain the role of patient. Self inflicted enucleation and corneal perforation are described ophthalmological representatives of these disorders and easy to recognise. The above described swellings are a less common
and more difficult to prove example of an ocular factitious disorder, although the patient’s medical history might make the doctor suspicious. In summary, self inflicted disorders must be considered as a cause of cyeld swelling.

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Angle closure glaucoma secondary to hemiretinal vein occlusion

EDITOR.—Central retinal vein occlusion (CRVO) has been reported to cause shallow-
ing of the anterior chamber with acute angle closure glaucoma. 1–3 This is due to anterior displacement of the lens-iris diaphragm caused by either the transudation of fluid from retinal vessels into the vitreous cavity or swelling of the ciliary body due to spasms, oedema, or detachment which may cause relaxation of lens zonules with subsequent crowding and closure of the angle. 1 We describe a patient who developed angle closure glaucoma without neovascularisation of the angle secondary to hemiretinal vein occlusion which responded to miotics and iridotomy suggesting a “pupillary block” mechanism. This is the first report of angle closure glaucoma following a hemiretinal vein occlusion.

CASE REPORT
A 63 year old African American man with controlled systemic hypertension noted reduced vision in his right eye for 1 month. Best corrected visual acuity was 20/200 right eye with +1.75 −0.75 × 85 and 20/25 left eye with +2.25 −1.00 × 95. Slit lamp examination was unremarkable, pupils were equally reactive without an afferent pupil defect. Intraocular pressure (IOP) was 26 mm Hg right eye and 25 mm Hg left eye. Gonioscopy revealed grade 3 angles in both eyes. The superior half of the retina right eye had dilated tortuous veins and multiple superficial haemorrhages. The right optic nerve was oedematous and hyperaemic. Retinal examination was unremarkable left eye with a cup to disc ratio of 0.4 horizontally by 0.5 vertically. The patient was diagnosed with a hemiretinal vein occlusion right eye, elevated IOP in both eyes, and treated with betaxolol 0.25% twice daily in both eyes.

Two weeks later visual acuity was counting fingers right eye and unchanged left eye. IOP was 42 mm Hg right eye and 20 mm Hg left eye, on betaxolol. The patient was referred to our office.

On examination the anterior chambers were shallow right eye and deep left eye. IOP was 45 mm Hg right eye and 21 mm Hg left eye. The angle right eye remained open to scleral spur and grade 2 left eye. B scan ultrasonography revealed an unremarkable posterior segment without chorioidal detach-
ments right eye. Brimonidine 0.2% and Cosopt were administered to the right eye. Thirty minutes later the IOP was 36 mm Hg right eye. Three hours later IOP right eye was 28 mm Hg. Mydriacyl 1%, neosynephrine 2.5%, and Cyclogyl 2% were administered and the IOP increased to 37 mm Hg. The patient was discharged on acetazolamide 250 mg by mouth four times daily, brimonidine 0.2% three times daily right eye, Cosopt twice daily right eye, and pilocarpine 2% four times daily right eye.

The following day, the anterior chamber had deepened and the IOP was 24 mm Hg right eye. Gonioscopy revealed a closed angle (Fig 1). Pilocarpine 2% was instilled and a laser iridotomy performed right eye. The following day the IOP was 16 mm Hg right eye. Gonioscopy revealed a grade 2 angle. Acetazolamide was discontinued, pilocarpine 4% four times daily and a laser iridotomy was performed left eye. Four days later the IOP had deepened and the IOP was 24 mm Hg right eye. Pilocarpine 2% was instilled and a laser iridotomy performed right eye. The following day the IOP was 16 mm Hg right eye. Gonioscopy revealed a grade 2 angle. Acetazolamide was discontinued, pilocarpine 4% four times daily and Timoptic XE four times daily 0.5% IOP on subsequent visits remained below 20 mm Hg, and the angle remained open (Fig 2). Visual acuity did not improve.

COMMENT
Transient angle closure glaucoma, an infre-
quent sequel of CRVO, has not been reported following hemiretinal vein occlusion (HRVO). Angle closure may occur days to months following a CRVO. Neovascular glau-
coma may develop weeks or months following a CRVO. 4–6 Determining the mechanism of angle closure in an individual patient following a retinal vascular occlusion will guide the ophthalmologist to the appropriate treatment options, miotic or miotic therapy. Ultrasound biomicroscopy may be of benefit in differentiating between a ciliary block mechanism and a pupillary block mechanism. 7

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Varicella zoster virus immune recovery stromal keratitis in a patient with AIDS

EDITOR.—The advent of potent antiretroviral therapy has resulted in the recognition of the syndrome of immune recovery uveitis in patients with AIDS and a history of cytomegalo-
lovirus (CMV) retinitis. 8 Although the patho-
genesis of this disease is poorly understood, it is hypothesised to be a consequence of an improved immune response to viral antigen
already present in the eye, with or without active viral replication. We describe a case of immune recovery varicella zoster virus (VZV) stromal keratitis in a patient with AIDS.

CASE REPORT
A 37 year old man with AIDS (CD4 = 180 cells x 10^9/l) developed right sided opthamalic zoster and was treated with aciclovir (800 mg by mouth five times a day). Twelve days after onset of the rash, topical prednisolone acetate (one drop every 2 hours) was prescribed to treat multiple anterior stromal corneal infiltrates. The keratitis promptly resolved, and aciclovir (800 mg by mouth five times a day). Twelve days after treatment, systemic aciclovir was prescribed to prevent recurrent VZV keratitis.

The incidence of recurrent VZV keratitis has been recognised following immune recovery following systemic antiretroviral therapy and while the patient's immune status improved on combination antiretroviral therapy. Immune recovery keratitis has been reported in patients with previously inactive varicella zoster virus infection. Immune recovery keratitis is a rare condition and has been reported in patients with immunocompromise and those with immune reconstitution.

COMMENT
VZV associated anterior stromal keratitis is thought to be due to immune recognition of residual viral antigen in the corneal stroma. The incidence of recurrent VZV stromal keratitis has not been well characterised, nor have factors which might precipitate recurrences. Recurrent keratitis related to immune system activation has been recognised following adenoviral infection. In that case, subepithelial opacities associated with a previous adenoviral follicular, keratoconjunctivitis recurred 9 months following the original infection in association with a severe upper respiratory infection. In this report, a patient with AIDS and a history of opthamalic zoster had a recurrence of anterior corneal stromal infiltrates almost 3 years after the initial skin eruption. Recurrence of the keratitis was not associated with skin or corneal epithelial disease and occurred despite aciclovir prophylaxis.

Although the recurrence of the keratitis with this patient’s immune recovery may be coincidental, the significant delay between his initial zosteriform eruption and the recurrence of his stromal disease, as well as the close temporal relation between the recurrence and the patient’s immune recovery, suggest that this is a case of immune recovery zoster keratitis in a patient with opthamalic zoster.

Other examples of immune recovery disease in patients with AIDS include recurrent antiretroviral therapy and while the patient's immune status improved on combination antiretroviral therapy. Immune recovery keratitis may be increasing in frequency in patients with immune reconstitution.

TPM is the recipient of a Research to Prevent Blindness (NY, NY) Lew Wasserstein Award.

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References

Figure 1 Slit lamp photograph of the temporal aspect of the patient’s right eye shows stromal infiltrates with an intact corneal epithelium.
includes the United States, Italy, and Africa. Its infestation in dogs, the only definitive host, is not clinically significant, although they may manifest an elevated eosinophil and leucocyte count. This manifestation may result in false positives in test for circulating *Dirofilaria immitis* microfilariae, also known as the dog heartworm. The differentiation of these two worms is important as *Dirofilaria* is pathogenic to canines. Knott’s test is used to detect these microfilariae serologically. Identification of these two adult worms is by their staining patterns with acid phosphatase: *Diptelotamena* stains evenly while *Dirofilaria* concentrates the acid phosphatase in two regions. *Diptelotamena* reconditum microfilariae averages about 250–270 µm in length and 4.4–5.4 µm in width with a round curved body, a distinguishing cephalic hook, and a blunt anterior end. Male adults average 13 mm in length and females 17–32 mm. *Diptelotamena* has an indirect life cycle with development of infective larvae that are carried by fleas (genus *Ctenocephalides*, *Pulex*), ticks (*Rhipicephalus sanguineus*), and lice (*Linognathus canines*). Knott’s test was recommended. Other control measures in-...

**Table 1** Immunohistochemical staining of epithelial cells for *Hsp27* and Ki-67 in pterygium and normal conjunctiva

<table>
<thead>
<tr>
<th></th>
<th><em>Hsp27</em> immunoreactivity (%)</th>
<th>Ki-67 immunoreactivity (%)</th>
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<tbody>
<tr>
<td><strong>Pterygia</strong></td>
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<td>17</td>
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<tr>
<td><strong>Mean</strong></td>
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**SD (14.84)**  

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<tr>
<th><strong>Normal conjunctiva</strong></th>
<th><em>Hsp27</em> immunoreactivity (%)</th>
<th>Ki-67 immunoreactivity (%)</th>
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**Mean**  

<table>
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<th><strong>SD (7.75)</strong></th>
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<td>36.7</td>
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<td>Mean: 36.7</td>
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**Website extra**

*A video report is on the BJO website. It shows the undulating appearance of the right bulbar conjunctiva of a 52 year old white male as the Dipetalonema reconditum remains mobile immediately before removal following localised peritomy.*

www.bjophthalmol.com

**Immunohistochemical detection of heat shock protein 27 and Ki-67 in human pterygium**

Eystro,–Pterygium, a disorder of the ocular surface, consists of atrophic conjunctival epithelium and a highly vascularised hypertrophic and elastic degenerated connective tissue. Ultraviolet irradiation is considered to be the principal environmental factor through an effect on the basal stem cells on the nasal limbus and activation of the fibroblasts.12 Previous studies have detected chromosomal allelic loss in slightly over 50% of pterygia and a low frequency of microsatellite instability.14 However, no differences in cellular proliferation between pterygial and normal conjunctival tissue have been detected with flow cytometry.4 On the other hand, a recent report suggests that pterygium may be the result of a failure of appropriate cellular apoptosis.6 We studied 17 pterygia and 12 normal conjunctival tissue samples from the nasal conjunctiva for the expression of heat shock protein 27 (Hsp27) and cell proliferation associated nuclear antigen Ki-67.

Hsp27, a member of the small heat shock proteins family, is overexpressed in response to many environmental and pathophysiological stresses including ultraviolet radiation, hormones, growth factors, infection and axon, and may be important in surveillance of cell integrity acting as a “molecular chaperon.” Recently it has been found that Hsp27 constitutive overexpression in embryonic stem cells enhances the differentiation-mediated decreased rate of cell proliferation and prevents these cells from undergoing apoptosis.15 Specimens from 17 patients (seven males and 10 females) (mean age 73.6) undergoing primary pterygium excision and 12 healthy people (three male and nine female) (mean age 77.7) undergoing cataract surgery were studied. None of these patients had an ophthalmic or systemic disease or used topical or systemic medication. Informed consent was obtained from patients participating in this study. Formalin fixed, paraffin embedded serial sections were immunostained using monoclonal antibodies against Hsp27 (clone G3.1) and Ki-67 (clone MIB-1). Morphological assessment of immunostained tissue preparations and manual cell counting of immunolabelled cells were performed. Hsp27 and Ki-67 labelled cell fractions were expressed in percentages.

Hsp27 cytoplasmic immunoreactivity was observed only in basal and suprabasal layers of normal conjunctival epithelium (mean 36.7) (Fig 1A). On the other hand, strong Hsp27 immunoreactivity was obtained in nuclei of scattered cells, situated mostly in the basal layers of epithelium, in normal conjunctival epithelium (mean 5.2) as well as in pterygium (mean 9.4) (Table 1). No staining of Hsp27 and/or Ki-67 was observed in substantia propria in normal conjunctiva tissues and pterygia but in pterygia, Hsp27 strong immunoreactivity was observed in endothelial cells and smooth muscle cells of vessels. There was a statistically significant difference in expression of Hsp27 between normal conjunctival epithelium and pterygia (p<0.001) but no difference in Ki-67 immunoreactivity (p>0.1) although some pterygia contained large number of proliferative cells. There was no correlation between Hsp27 and Ki-67 labelling percentage in pterygia (p=0.7) and normal conjunctiva (p=0.9).

Our findings concerning Ki-67 expression are consistent with previous results suggesting that pterygium may not be a disorder of cell proliferation.7 Overexpression of Hsp27 in all...
pterygia is interesting because this protein is known to be related to differentiation when expressed in other epithelial tissues—for example, skin,

and in view of the recent report that Hsp27 transient expression seems essential for preventing embryonic stem cells from undergoing apoptosis. Furthermore, Tan et al. recently proposed that pterygium may be related to faulty apoptosis. The role of Hsp27 in pterygium remains to be elucidated since Hsp27 is expressed in basal epithelial cells of normal conjunctiva, where the cells are mainly differentiating stem cells and in all layers of epithelium in pterygia. Further studies would provide valuable information regarding the possible role of Hsp27, and the involvement of heat shock proteins generally in the pathogenesis of pterygium.

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Figure 1 (A) Normal conjunctiva: Hsp27 cytoplasmic immunoreactivity in basal and subbasal layers of epithelium (×400). (B) Pterygium: Hsp27 positive cells in all layers of epithelium. Cells of subepithelial connective tissue are Hsp27 negative while vessels are Hsp27 positive (arrows) (×400).