LETTERS

Spontaneous venous pulsations should be monitored during glaucoma therapy

It is well established that lowering intraocular pressure slows or halts progression of glaucoma. None the less, changes in intracranial pressure also affect the pressure gradient across the lamina cribrosa. Normal intraocular pressures combined with low intraocular pressures produce the same pressure differential across the laminae as elevated intraocular pressures in conjunction with normal intracranial pressures. Failing to factor in both intraocular and intracranial pressures may create an inappropriate distinction in the pathogenesis of glaucomas currently labelled as primary open angle glaucoma. The development of the optic neuropathy in glaucoma may be secondary to mechanical deformation and destruction of lamina cribrosa causing axonal degeneration, or conceivably to pressure-related ischaemic events. A goal of therapy in either situation should be equalisation of prelaminar intraocular pressure with opposing retrolaminar tissue and cerebrospinal fluid pressure.

Spontaneous venous pulsations occur when intraocular pressure during systole exceeds central retinal venous pressure, which, in turn, reflects intracranial pressure transmitted through the perineural subarachnoid space and retrolaminar tissue pressure. Lowering intraocular pressure until venous pulsations cease minimises the pressure gradient between mean intraocular and retrolaminar pressure, and allows a clinical estimation of intracranial pressure. Keeping momentary fluctuations in mind, such end points may guide intraocular pressure lowering strategies to help avoid undertreatment or overtreatment of individuals with glaucoma. Therapies that lower intraocular pressure without also lowering intracranial pressure (such as topical rather than oral carbonic anhydrase inhibitors) should be favoured. The question of whether intracranial pressure raising strategies should be considered may arise in select cases. Finally, a consistent lack of spontaneous venous pulsations in patients with ocular hypertension, especially when venous pulsations can be elicited by digital pressure on the globe, may indicate sufficient counterbalancing intracranial pressure to render intraocular pressure reduction unnecessary.

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References

Acanthamoeba keratitis in Ghana

Suppurative keratitis due to Acanthamoeba spp is most commonly associated with poor contact lens hygiene. However, recently there have been reports of keratitis caused by Acanthamoeba spp in the tropics in non-contact lens wearers. We report one such case of Acanthamoeba keratitis in Ghana, west Africa.

Case report
A 25 year old male driver (from Accra) reported to a hospital in Bawku, northern Ghana. He presented with symptoms of chronic corneal ulceration (duration of symptoms 31 days) and visual acuity in his affected eye was reduced to perception of hand movements only at presentation. The patient did not recall experiencing any trauma to his eye before symptoms. The patient had already taken antibiotics before primary presentation at the hospital but did not bring them with him to clinic and therefore it is not known which they were.

On examination there was a central corneal ulcer (greatest diameter 8 mm) involving the corneal margin and raised slough; flare, AC cells, and hypopyon were absent. No organisms were isolated from culture on previously described in the literature. No organisms were isolated from culture on previously described in the literature. No organisms were isolated from culture on previously described in the literature.

Acanthamoeba spp in the tropics in non-contact lens wearers, and highlights the need to consider Acanthamoeba spp as a potential causative agent of chronic keratitis in patients presenting at rural hospitals in the tropics. In addition, the usefulness of simple stains such as lactophenol cotton blue and Gram stain to visualise Acanthamoeba spp is demonstrated as previously described in the literature.

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Need for measurement of porphyrins in teardrops in patients with congenital erythropoietic porphyria

Con genital erythropoietic porphyria (CEP; Man 
126370) is an extremely rare disorder inherited as an autosomal recessive trait. The cause of this disease is the deficient activity of uroporphyrinogen III synthase (UROS: EC 4.2.1.75). Since a cloning of UROS gene (UROS; Genebank NM000075), efforts have been made to clarify underlying mutations that cause CEP. To date, more than 20 mutations of UROS have been described. Identification of UROS mutations at the molecular level is important for genetic counselling and prenatal diagnosis of affected families.

Clinically, CEP is characterised by severe cutaneous photosensitivity, chronic haemoly sis, and massive porphyrinuria resulting from the accumulation in the bone marrow, peripheral blood, and other org ans of large amounts of predominantly type I porphyrins, which are not substrates for haem synthesis. Red urine may be observed from infancy, and the teeth become stained red. Haemolytic anaemia, an additional complication, may be helped by splenectomy. Besides such classic manifestations ocular involvement, including scleral changes, has been reported in patients with CEP (1). Furthermore, we recently reported the evidence of the accumulation of porphyrins in teardrops in a Japanese patient with CEP who showed scleral changes (2). To confirm whether the accumulation of porphyrins is a common feature and is a direct cause of ocular involvement, we analysed and confirmed the presence of porphyrins in teardrops in an additional three Japanese patients with CEP.

Case reports

We analysed three Japanese patients with CEP, all of whom were diagnosed by their typical clinical manifestations and by the elevation of porphyrins (uroporphyrin I and coproporphyrin I) in urine (Table 1). For case 2, we performed sequence analysis of UROS and identified a T to C transition of nucleotide 634, which predicted a serine to proline substitution at residue 212 (S212P), and a C to T transition of nucleotide 745 that predicted a glutamine to premature stop codon (Q249X). First cases of keratitis caused by free-living amoebae of the genus Acanthamoeba diagnosed in Mal Volume 91 Part 1 1998 pp 1387-92

The histological changes at the body surface lesions in CEP are mainly caused by the accumulation of porphyrins. Typically, an extremely elevated accumulation of porphyrins, especially of uroporphyrin I and coproporphyrin I, were observed. Interestingly, in case 4, the accumulation of porphyrins was relatively mild compared with other patients.

Comment

Sclerotic changes at the body surface lesions in CEP are mainly caused by the accumulation of porphyrins. Here, we demonstrated the first evidence that the accumulation of porphyrins in teardrops is a common feature in patients with CEP. No accumulation of porphyrins was observed in normal control, whereas the elevation of porphyrins in teardrops was observed in all patients with CEP. Furthermore, in case 4, who manifested relatively mild elevation of porphyrins, especially uroporphyrin I and coproporphyrin I in teardrops directly causes ocular involvement, and that its severity depends on the level of porphyrins accumulated in teardrop. Therefore, it is important to measure porphyrins in teardrops of patients with CEP. We strongly recommend the use of ultraviolet spectacles to protect against sunlight and to prevent the initiation and progression of scleral lesions, although some patients do not have eye involvement.

Table 1 Tear drop analysis of porphyrins in Japanese patients with CEP. Case 1 has been reported previously.

<table>
<thead>
<tr>
<th>Case</th>
<th>Uroporphyrin (ng/dl)</th>
<th>Coproporphyrin I (ng/dl)</th>
<th>Coproporphyrin III (ng/dl)</th>
<th>Protoporphyrin (ng/dl)</th>
</tr>
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<tr>
<td>Case 1</td>
<td>1302.6</td>
<td>1235.3</td>
<td>3345.9</td>
<td>91.4</td>
</tr>
<tr>
<td>Case 2</td>
<td>49.1</td>
<td>302.5</td>
<td>145.1</td>
<td>3.6</td>
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<tr>
<td>Case 3</td>
<td>27.4</td>
<td>0</td>
<td>35.8</td>
<td>0</td>
</tr>
<tr>
<td>Case 4</td>
<td>24.6</td>
<td>67.9</td>
<td>109.5</td>
<td>4.9</td>
</tr>
</tbody>
</table>

Figure 1 Scleral involvement shown in case 2.

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Uveitis initiating an autoimmune reaction resulting in Goodpasture’s syndrome in a Chinese man

Goodpasture’s syndrome is an autoimmune disease caused by IgG directed against the alpha-3 chain of type IV collagen found in basement membrane. It causes pulmonary haemorrhage and renal failure. The antibody has been demonstrated in the basement membranes in the eye. However, ophthalmological complications in Goodpasture’s syndrome are rare. As with other autoimmune diseases, Goodpasture’s syndrome patients have a strong susceptibility based on a genetic background. Much evidence supports the concept that cross reactivity with exogenous epitopes or insult to the basement membrane can initiate the process of autoimmunity resulting in Goodpasture’s syndrome. We present a case of a Chinese man in whom we believe uveitis precipitated the autoimmune reaction causing Goodpasture’s syndrome

Case report

A 77 year old Chinese man from Hong Kong presented to the eye casualty department...
with a 1 month history of a black patch in the centre of his visual field in the left eye. Before this he noticed floaters and a “black cloud” in the left eye. He did not complain of pain or photophobia.

Three months earlier he had an episode of acute anterior uveitis, which resolved with dexamethasone and cyclopentolate drops. His vision at that episode was 6/24 in the right eye and 6/12 in the left eye. Six months earlier he had developed septicaemia secondary to a urinary tract infection treated with a course of intravenous flucloxacillin and fusidic acid and he made a good recovery.

He came to the United Kingdom 30 years ago and returned to Hong Kong for holidays every few years. There was no family history of note.

He looked well on examination and was afebrile. Systemic examination was unremarkable apart from an itchy rash on both his legs and his blood pressure was 104/60. His visual acuity was 6/9, N6 in the right eye and CF, N36 in the left eye. His right eye was white and quiet with evidence of old keratic precipitates (KPs) only. His left eye had mutton fat KPs with ++ cells in the anterior chamber. The right fundus had a healthy disc and retinal vessels, but there were tiny white lesions at the disc and retinal vessels. There were no haemorrhages or cotton wool spots. The fluorescein angiogram of the right eye (Fig 1) showed multiple dots of hyperfluorescence under the neuroretina at the level of the RPE, which looked more like inactive disease of the RPE and choroid rather than drusen. There was no leakage from the disc, vessels, or macula. The left eye had a similar picture with a few dilated capillaries at the disc but no leakage at the disc or the vessels. Late pictures of the left macular reveal minimal cystoid macular oedema which was confirmed by OCT. The clinical differential diagnosis was sarcoid or tuberculosis.

Investigations revealed a raised erythrocyte sedimentation rate (ESR) of 64 in the first hour and C reactive protein (CRP) of 14, but all other blood tests were normal including his full blood count, liver function tests, urea and electrolytes, serum ACE, VDRL/TPHA, all other blood tests were normal including a renal biopsy showed Goodpasture’s disease (Fig 2). His glomerular basement membrane antibodies (ELISA confirmed by western blot) were also positive with a level of 77% (0–15 reference range), as were his PEG immune complexes. ANA, ANCA, and anti-DNA were all negative. He was given high dose steroids and had a course of plasma exchange (three 3 litre volume exchanges with FFP/PPF replacement).

His eyes continued to improve during the following month and the inflammation settled. At last review his visual acuity was 6/9 right eye and 6/12 left eye. Unfortunately, he developed haemoptysis and overwhelming septicemia and died 2 months later. A post mortem was declined.

Comment

In 1919 Ernest Goodpasture described a patient with haemoptysis, anaemia, and proteinuria and a post mortem showing pulmonary alveolar haemorrhage and proliferative glomerulonephritis. Goodpasture’s disease, a rare autoimmune organ specific disease in which IgG antibodies are directed against the NCl domain of the alpha-3 chain of type IV collagen leading to pulmonary haemorrhage, glomerulonephritis, and renal failure. Goodpasture’s syndrome, however, describes Goodpasture’s disease with either haemoptysis or crescentic glomerulonephritis, or both. Clearly, this patient had the complete syndrome. Thirty per cent of patients are ANCA positive and lung or kidney biopsy shows linear immunofluorescent staining for IgG along the basement membrane. The death rate has drastically improved from 75% to 25% with the advent of plasmapheresis combined with immunosuppressants. However, it is rare to escape irreversible dialysis dependency unless the disease is detected and anti-GBM antibody levels are reduced before oliguria has ensued.

Immunofluorescent and immunohistochemistry studies show that the deposition of the antibasement membrane antibodies can also occur in the eye in the basement membrane of the choroidal vessels, ciliary body, lens capsule, and Bruch’s membrane. The pathogenic significance of this is still unknown. Furthermore, there have not been any studies confirming the actual presence of type IV collagen or of the alpha-3 epitope in the eye, although it is widely assumed that they are both present.

Documented ophthalmological abnormalities in Goodpasture’s include retinal haemorrhages and exudates and serous retinal detachment. It is possible that these signs may reflect hypertension or ANCA positivity rather than direct damage from antiglomerular basement membrane antibodies possibly because of the small percentage of alpha-3 chain or its NCl domain in the eye. As the disease is so florid in the kidneys and the lung, one would expect a disease of similar severity in the eye if the antibasement membrane antibodies were pathogenic in the eye.

This man had a granulomatous panuveitis with choroidal infiltrates. These ophthalmic features have not previously been described in Goodpasture’s syndrome. The serum from his initial admission with uveitis in February, 2 months after his episode of septicemia, was normal apart from raised ESR and CRP levels and his antiglomerular basement membrane antibodies were 9%, which is within normal limits. Four weeks later in March, the titre of antibodies had risen to a grossly abnormal level of 77%. The temporal relation of developing antiglomerular basement membrane antibodies and disease means it is likely that these complexes occurred in response to his septicemia and produced a reactive uveitis. As type IV collagen is also found in the choroidalplexus, the uveitis may have been the type IV collagen to the immune system causing antibody production which results in cross reactivity with the glomerular basement membrane in the kidney to produce Goodpasture’s syndrome. As with other autoimmune diseases, Goodpasture’s syndrome patients have a strong susceptibility based on a genetic background. Much evidence supports the concept that insul in the basement membrane or cross reactivity with exogenous...
epitopes can initiate the process of autoreactivity resulting in Goodpasture's syndrome. Interestingly, uveitis and Goodpasture's share some similar characteristics. The immunological profiles both involve the cytokines IL-6, IL-12, and TGFβ, and both are associated with HLA B7 (indicating a particularly poor prognosis in Goodpasture's) and HLA DR 15. This case is extremely rare. Other events associated with the induction of anti-GBM disease in humans have included lung damage by infections such as influenza and toxin exposure with tobacco and hydrocarbons. Renal injury by ischaemia and membranous nephropathy can also induce disease. Other causes include lymphoma and adenoma. To our knowledge this is the first reported case where uveitis was the likely precipitating factor for the induction of Goodpasture's disease.

Moreover, ophthalmologists should be aware of all blood test results and check the results of ordered tests. They should follow up the patient with repeated history and examination and repeat tests if the diagnosis is uncertain. Unsuspected fatal diseases as we have seen in this case, may occasionally present to ophthalmologists.

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References


Fusarium solani keratitis following LASIK for myopia

Fungal keratitis is a rare complication of photorefractive keratectomy (PRK), 1–3 LASIK, 4–6 and LASIK enhancement. 7 We describe a patient who developed keratitis in one eye after bilateral LASIK procedures. The keratitis progressed despite intensive topical and systemic antibacterial and antifungal treatment.

Initial cultures were negative, but a diagnosis of fungal keratitis was suggested by confocal microscopy. Fusarium solani was isolated following penetrating keratoplasty.

Case report

A 45 year old woman noted blur and discomfort of the right eye 3 days after bilateral LASIK procedures for myopia. The visual acuity was 6/9–3 unaided and there was a 1.5 mm diameter infiltrate beneath the flap (Fig 1A). The left eye was unaffected with an unaided visual acuity of 6/6. Cultures were not taken but her topical antibiotic was changed from chloramphenicol to ofloxacin, and dexamethasone 0.1% four times daily was continued. After a further 4 days the vision had reduced to 6/36 and there was ulceration through the flap over the infiltrate; treatment was changed to hourly gentamicin 1.5%, cefuroxime 5%, and econazole 1%, and dexamethasone was continued to reduce the risk of further flap melt. A culture from the ulcerated corneal surface over the infiltrate was negative. There was continued deterioration and treatment was therefore stopped for 24 hours before the flap was lifted and cultures taken for routine bacteriology, acid fast bacilli (Mycobacterium), and fungi. No organism was identified. Because of the uncertain diagnosis a loading oral dose of fluconazole 200 mg was given followed by 100 mg daily, and a 7 day course of intensive topical vancomycin (5%) and amikacin (2.5%) was started with oral clarithromycin 500 mg twice daily. Confocal microscopy of the edge of the lesion demonstrated filamentary structures in the deep stroma (Fig 1B), but a subsequent tissue biopsy of the flap and the deeper stroma was again negative. Despite intensive treatment with topical amphotericin (0.15%) and nata霉素 (5%), and courses of oral itraconazole (400 mg daily) and voriconazole (400 mg daily) there was continued deterioration and the cornea perforated (Fig 1C). On the 32nd day following LASIK a 9 mm penetrating corneal graft was performed and the anterior chamber was irrigated with amphotericin (5 µg in 0.1 ml). Dexamethasone 0.1% four times daily was continued after surgery to treat severe intraocular inflammation. Histology of the excised corneal button showed filamentary fungal elements anterior to Descemet's membrane but no evidence of hyphae extending to the margin of the excised tissue. Fusarium solani was cultured from the corneal button and the isolate was reported sensitive in vitro to amphotericin (1.0 µg/ml), partially sensitive to clotrimazole (8 µg/ml), econazole (4 µg/ml), and miconazole (8 µg/ml), and resistant to itraconazole (>16 µg/ml) and fluconazole (>16 µg/ml). Despite continued topical and oral antifungal treatment, two further penetrating grafts were necessary to remove recurrences at the graft interface. Following the last graft topical steroid was substituted with topical cyclosporin A 2% four times daily for 4 weeks, after which fluorometholone 0.1% four times daily was started to control inflammation and prevent vascularisation. All topical antifungal treatment was stopped after 3 months. The final vision at 8 months was reduced to 6/60 as a result of irregular corneal astigmatism, cataract, and graft oedema.

Comment

Fungal keratitis is rare in the United Kingdom but accounts for 17–37% of microbial keratitis isolates in warmer countries. 2 To date all reported cases of fungal keratitis after LASIK have been due to filamentous organisms. 4–6 The diagnosis may be difficult to confirm as cultures and biopsies of the anterior stroma can be negative because of the tendency of filamentous fungi to proliferate in the posterior corneal stroma. A delay in identification of the causative agent often contributes to the poor outcome. Of the four previous reported cases of presumed flap interface infection, excisional keratoplasty was required in three, 4–6 and perforation and vascularisation of the corneal occurred in one. 3 The only case with a medical cure had a surface infection of a persistent epithelial defect. 7 The origin of this infection is uncertain. The patient had visited Florida 2 months previously, where Fusarium sp is the most common isolate from cases of fungal keratitis. 7 On the day of treatment the ambient temperature in London was 80°F, but subsequent air culture plates from the treatment area and from the air conditioning system were negative. Because of a reluctance to disturb the LASIK flap there is a temptation to treat infiltrates empirically with broad spectrum antibiotics and steroid, 3 rather than lifting the flap to culture the lesion directly. Unfortunately, in this case, two cultures were negative, and the diagnosis of a filamentous fungal infection was suggested by confocal microscopy. 3 A further negative biopsy then delayed a decision for surgical intervention. Corticosteroids may

Figure 1 (A) Infiltrate beneath the flap (arrow) on the third day following LASIK. (B) Confocal image showing branching filamentary structures (arrows) in the deep stroma adjacent to the area of infiltrate. (C) Advanced abscess before 9 mm penetrating keratoplasty 32 days after LASIK.
increase the virulence of pathogenic fungi and it is normally contraindicated in fungal keratitis, although it has a role in reducing inflammation after antifungal treatment has been started. The role of cyclosporin A as an alternative to steroid after surgery for fungal keratitis requires further evaluation.  

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References

Uveal metastasis 43 years after resection of bronchogenic carcinoid

Carcinoids are a heterogeneous group of tumours believed to arise from enteroendocrine cells scattered primarily throughout the gastrointestinal tract, but these tumours are also found at other sites such as the lungs. Although the term carcinoid underscores the benign nature of the tumour with an indolent course, its potential for metastasis is widely recognised. The most frequent sites for metastasis include the lymph nodes, liver, and bone. Metastasis to the eye and orbit is rare. Gastrointestinal carcinoids tend to metastasise to the orbit while bronchial carcinoids have the propensity to metastasise to the uvea. The interval between diagnosis of the primary tumour and the recognition of ocular or orbital metastasis varies. The longest reported interval is 24 years for intraocular metastasis, and 15 years for orbital metastasis. We report on a patient with metastatic carcinoid to the uvea occurring 43 years after excision of the primary bronchial carcinoid and confirmed by histological and immunohistochemical tests, and we propose a mechanism for such delayed metastasis.

Case report

A 63 year old white woman was found to have a superiorly located choroidal mass in the right eye and an inferonasal elevated mass in the left eye on routine examination. Medical history is significant for the diagnosis in 1958 of bronchial adenoma, presently known as bronchial carcinoid. The patient underwent lung surgery, details of which are unavailable. She denies any history of smoking. The bronchial carcinoid recurred in 1965 and a right lower lobectomy was performed. The histopathological diagnosis was bronchial adenoma, cylindroid type, with metastasis to the peribronchial lymph node of the basilar segments.

On initial examination, visual acuity was 20/25 in each eye. Fundus examination of the right eye revealed a lightly pigmented dome-shaped golden brown mass at the 12 o'clock position involving the pars plana ciliaris and peripheral choroid. Echography revealed a solid ciliary body and peripheral choroidal mass lesion located superiorly with an elevation of 4 mm and a base diameter of 8 mm. Internal reflectivity was medium to high, with a moderately internal reflective structure. The left fundus revealed an inferonasal non-pigmented orange-reddish choroidal lesion with overlying subretinal fluid and calcification (Fig 1). Echography of this lesion showed an elevation of 2.2 mm and a base diameter of 7 mm with medium internal reflectivity.

The metastatic examination included magnetic resonance imaging of the brain, computed axial tomography of the chest, abdomen and pelvis, positron emission tomography scan, and mammography. It did not show any evidence of metastasis. Clinical diagnosis in the left eye was choroidal naevomelanoma versus naevus. Differential diagnoses in the right eye included ciliary body-peripheral choroidal melanoma, retinal pigment epithelium (RPE) adenoma, adenocarcinoma, and metastatic lesion. The patient underwent an iridocyclectomy with peripheral chordoidectomy in the right eye.

The gross specimen consisted of an oval-shaped dark mass measuring 10 × 9 mm. Microscopic examination revealed a well circumscribed mass within the ciliary body and peripheral choroid with morphological evidence of infiltrating cells with trabecular, tubular, cord-like, or rosette-like patterns (Fig 2A). These cells showed moderate amounts of cytoplasm containing uniform nuclei displaying granular material. Distinct nucleoli were noted and occasional mitotic figures were detected. The tumour stroma also showed prominent vascularity. Immunohistochemical studies were positive for neuron specific enolase, synaptophysin (Fig 2B), chromogranin (Fig 2C), and CD 57. They were focal positive for neuroendocrine, weak positive for nonsquamous keratin, variable for vasointestinal poly peptide, and negative for serotonin. Occasional tumour cells stained for Ki-67 but were negative for p53 and thyroid transcription factor protein (TTF-1). Upon electron microscope examination, the formalin fixed tissue showed tumour cells displaying electron dense intracytoplasmic granules measuring 100–125 nm. Electron lucent space and a membrane surround these central electron dense granules (Fig 2D). The histopathological diagnosis was metastatic carcinoid, involving ciliary body and peripheral choroid.

Figure 1 Fundus photograph of the left eye with a non-pigmented orange-reddish lesion.

Figure 2 Carcinoid tumour showing infiltrating cells with trabecular, tubular, cordlike or rosette-like pattern [haematoxylin and eosin; original magnification ×100] (A). Carcinoid tumour showing immunoreactivity with synaptophysin [original magnification ×100] (B). Immunoreactivity with chromogranin [original magnification ×100] (C). Tumour cells showing membrane bound electron dense intracytoplasmic granules [original magnification ×30 000] (D).
Notwithstanding their metastatic potential, carcinoids are compatible with long term survival\(^1\) (as attested by our patient’s case). To our knowledge, the 43 year interval between diagnosis of the patient’s primary tumour and recognition of uveal metastasis is the longest interval reported to date. Low immunoreactivity to Ki-67 and non-reactivity to p53 may possibly explain the indolent course of this tumour and its metastatic many years after the resection of the original tumour. Ki-67 is a DNA binding nuclear protein that is expressed in proliferating cells but not in quiescent cells. It is regarded as a fractional measure of tissue and tumour growth.\(^2\) P53, a tumour suppressor gene, is the most commonly mutated gene in tumours; its functional inactivation can bring about abnormal cell proliferation. Occasional staining of the patient’s tumour to Ki-67 and the negative staining of the tumour to p53, as well as its histologically well circumscribed appearance, demonstrate low proliferative activity and low aggressiveness. These biological factors may have played a part in the delayed metastasis of the patient’s tumour.

TTF-1 is a nuclear transcription factor primarily expressed in the lungs and thyroid. Its expression may be useful in determining the site of origin of a metastatic neuroendocrine tumour.\(^3\) However, expression of TTF-1 in primary or metastatic pulmonary carcinoids varies anywhere from completely negative\(^4\) to 44% to a high of 80%.\(^5\) Despite a clinical history of the primary tumour arising from the bronchus, the patient’s metastatic lesion like those reported by Fabbro et al\(^6\) exhibited no staining to TTF-1. Likewise, the patient’s tumour’s histological trabecular pattern and negative serotonin staining favour the bronchus as its site of origin.

Although bilateral ocular involvement suggests the diagnosis of a metastatic process, the 43 year long interval since resection of the bronchial carcinoid led to the clinical impression of uveal melanoma. Consequently, this case suggests that carcinoid tumours can metastasise as much as four decades after removal of the primary tumour. The prognosis for metastatic uveal tumour is generally poor; uveal carcinoids, however, are compatible with long term survival.\(^6\) Consequently, awareness and recognition of carcinoid’s delayed metastatic potential can translate to maximisation of the patient’s visual, systemic and overall prognosis.

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References


**Recurrent corneal ulcerations with perforation in keratosis follicularis (Diarier-White disease)**

Diarier-White disease, also known as keratosis follicularis, is a relatively common genodermatosis (frequency between 1 in 36 000 and 1 in 100 000) with autosomal dominant inheritance and late age of onset.\(^7\) Clinical features consist of disseminated warty papules and plaques with an affinity to the seborrhoeic areas of the body. The disease may be exacerbated by sun exposure or sweating and never remits.

Ocular involvement in keratosis follicularis is relatively uncommon. Of the affected patients have dry eye syndrome with and without Sjogren’s syndrome. Possible corneal manifestations are peripheral arcus lipoides-like opacifications, asymptomatic neublar dot-like opacities of the peripheral corneal epithelium, and central epithelial surface irregularities.\(^8\) Involvement of the eyelids and association with retinitis pigmentosa, subnornial dark adaption, and post-cataract extraction staphyloccal endophthalmitis may also occur.\(^9\)

We describe the first case of recurrent severe bilateral corneal ulcerations with perforation in a female patient with keratosis follicularis.

**Case report**

A 74 year old woman was referred to the university eye hospital with complaints of redness and reduced visual acuity in the left eye. She had no significant ocular history. She and her two daughters have been suffering from keratosis follicularis (Diarier-White disease) for many years.

On first examination (February 2001) best corrected visual acuity was 0.8 in the right eye and 0.3 in the left eye. Both eyes showed pathohiological Schirmer’s tear test.

Slit lamp examination showed blepharitis marginalis on both eyes, thickened, knobbly lid margins, and a rarefication of the eyelashes. In the left eye there was a descemetocele without corneal perforation or intraocular inflammation (Fig 1A).

Microbiological examination of the conjunctiva indicated Staphylococcus aureus, Staphylococcus epidermidis, and Streptococcus viridans. The left eye was treated with ofloxacin and cyclosporin A eye drops. Additionally, both eyes were treated with artificial tears, and the clinical picture slowly improved over the next 9 days.

Four weeks later (March 2001) visual acuity was 0.7 in the left eye. Examination of the left eye revealed corneal staining and thinning at the 6 o’clock position. There were no signs of inflammation. Antibiotic therapy was discontinued.

Seven weeks later (April/May 2001) the patient reported foreign body sensation in the right eye. Slit lamp examination demonstrated 3+ conjunctival injection, 3+ anterior chamber cells, ulceration of the cornea at the peripheral 6 o’clock position, a descemetocele, and anterior and posterior synechiae (Fig 1B). The aspect of the left eye was similar to the previous examination 7 weeks earlier.

The patient was again hospitalised and placed on topical ofloxacin and mydriatics. Microbiological examination indicated again Staphylococcus aureus, and additionally Candida albicans and Blastomyces. Therefore, topical antimycotic eyedrops were added. During follow up the corneal infiltration and intraocular inflammation in the right eye slowly reduced.

Nine weeks after discharge (August 2001) the patient returned to the hospital. She reported burning of the right eye for 5 days. The therapy with ofloxacin had been discontinued 3 weeks previously, only the therapy with artificial tears had been continued.

Figure 1  (A) Left eye, February 2001: clinical aspects of the first examination: blepharitis marginalis, thickened, knobbly lid margin, and a rarefication of the eyelashes. Descentemetecele without corneal perforation or intraocular inflammation. (B) Right eye, May 2001: conjunctival injection, intraocular inflammation, anterior and posterior synechiae, and ulceration of the cornea.
Visual acuity was 0.02 in the right eye and 0.7 in the left eye. The right eye showed 3+ conjunctival injection, 3+ anterior chamber cells, and ulceration of the cornea. A corneal perforation at the peripheral 6 o’clock position was closed by an incarceration of the iris. The anterior chamber was flattened.

After intensive topical and intravenous antibiotic therapy and insertion of punctum plugs infection and inflammation slowly resolved. Visual acuity did not improve. The patient was discharged and was again controlled by her ophthalmologist.

Comment
We report a 74 year old woman patient with recurrent bilateral corneal ulceration and uniconular perforation probably associated with keratosis follicularis.

Keratosis follicularis (Darier-White disease) is caused by mutations in the ATP2A2 gene, which encodes the Ca"++ ATPase 2 isoform. This defect results in disturbed cell to cell adhesion and differentiation of the epithelium.2

Histopathological hallmarks of the disease are focal suprabasal clefting due to acantholysis, and subsequent dyskeratotic round epithelial cells, and ulceration of the cornea. A corneal epithelial lesion in keratosis follicularis was found in 184 uveal melanoma cases we found only 71 cases of uveal melanoma in 12 years (0.02% incidence). The mode of presentation and the implication of uveal melanoma. Whether this has any bearing on the prognosis and the implication of uveal melanoma. Whether this has any bearing on the prognosis and the implication of uveal melanoma. Whether this has any bearing on the prognosis and the implication of uveal melanoma. Whether this has any bearing on the prognosis and the implication of uveal melanoma. Whether this has any bearing on the prognosis and the implication of uveal melanoma. Whether this has any bearing on the prognosis and the implication of uveal melanoma. Whether this has any bearing on the prognosis and the implication of uveal melanoma.

In our patient the recurrent corneal ulcerations with subsequent perforation could be explained by the participation of the ectodermal ocular tissues in keratosis follicularis: the lacrimal gland, the eyelids, and the corneal epithelium. A combination with Sjögren’s syndrome, dry eyes, oral mucosal lesions, and involvement of the salivary gland is known from the literature. A histological examination of the eyelids in one patient showed a characteristic epidermal involvement, but no participation of the specific adnexal glands of the lid margin. It was presumed that the knobly, scaling lid margin could provoke symptoms and sequelae similar to seborrhoic blepharitis. Recurrent localised or widespread cutaneous viral infections and secondary bacterial overgrowth is also common. Bacteria and fungi seem to cause the keratotic debris.

In our patient keratosis follicularis probably resulted in dry eye syndrome with reduced corneal protection and microbiological colonisation of the skin and ocular surface. Impaired functioning of these adnexal glands of the corneal epithelium caused the recurrent corneal ulcerations with perforation. Therefore it can be concluded that the increased risk of ocular complications in keratosis follicularis may include severe corneal infection. Beside the long term dermatological medical care an intensive ocular therapy with lubricants and antibiotics may help to avoid this ocular complication.

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References

We have read with great interest the article by Eskelin and Kivelä. This study provides information as to how uveal melanoma can be diagnosed and treated early if fundus examination is done by an ophthalmologist and also emphasised that the indirect ophthalmoscopy should be done even in asymptomatic patients having an ophthalmic check up. We feel that indirect ophthalmoscopic evaluation of the dilated fundus is essential for the identification of malignant uveal melanoma. This method of examination offers the best chance of detecting early retinal pathology and also allows follow up of progressive benign lesions suspected of potential malignancy.

In the Finnish population Eskelin and Kivelä have found 184 uveal melanoma cases. Another crucial area of concern is the risk of infection with xenografts, which cannot be totally eliminated even by highly stringent screening and processing procedures. We are referring to the group of bovine spongiform encephalopathies including Creutzfeldt-Jakob disease (CJD) and its variant found in the United Kingdom (vCJD). Therefore, the quest for a comparable wrapping material and better implants which do not require wrapping continues, and bovine pericardium should be considered, bearing in mind its above mentioned shortcomings.

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References
TTT for occult CNV: the power!

Transpupillary thermotherapy (TTT) was originally introduced for the treatment of small choroidal melanoma. Although the precise mechanism of action for this treatment is unknown yet, the reported data appear to be beneficial compared to the natural course of the disease.

Currently, the following treatment parameters are recommended to treat occult choroidal neovascularisation (CNV) with TTT: one exposure, 60 second exposure time, 800 mW power for the 3 mm spot, 320 mW for the 2 mm spot, and 320 mW for the 1.2 mm spot. With these parameters applied via the Goldmann fundus lens the power per field is calculated to 247 mW/mm². This usually results in no visible change of the treated area at the end of exposure. Thus, if the applied power would be inappropriately lowered (e.g. 800 mW for the 3 mm spot) the power per field would be inappropriately lower (e.g. 80 mW/mm²). This might at regular intervals depending on the frequency of the instrument’s use. This might be beneficial for the power level.

However, we did not observe satisfactory functional results in the majority of the first consecutive 28 cases treated and in most cases no effect at all could be demonstrated in the fluorescein angiography or OCT.

Lacking any possible explanation other than that the treatment method didn’t work, we finally asked a technician to check the laser system. Immediately he noticed barely visible defects at the artefact of the fibreoptic resulting in a measurable reduction of power output from the 800 mW on the display to 560 mW at the end of the fibreoptic. Apparently the fibreoptic had been damaged by its frequent use in treating patients with choroidal tumours. However, this remained unnoticed by the oncologist because in treating choroidal melanomas the end point of an exposure is invisible to grey scale lesion. If this is not achieved with the initially chosen power level, the physician usually increases the power in a stepwise manner until this end point is reached.

In summary, we highly recommend to all physicians who are treating occult CNV with subthreshold TTT to check their aiming spot regularly, especially if the system has been in use for a longer time. Additionally, the output power of the entire application system (laser and fibreoptic) should probably be rechecked at regular intervals depending on the frequency of the instrument’s use. This might prevent future reports of the (“false negative”) ineffectiveness of this possible beneficial treatment method.

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References

Sight Savers International Honoured by American Medical Association Award

Sight Savers International, the UK’s leading charity tackling blindness in the developing world, is the first ever non-US organisation to receive this prestigious Award.

The panel of judges made a unanimous decision to award the $25,000 prize in recognition of Sight Savers’ support for the provision of vital eye care services in some of the poorest countries around the world over the last 50 years.

Richard Porter, Executive Director of Sight Savers who received the award in Chicago commented: “We are delighted and honoured to receive the Dr Nathan Davis International Award. Our vision is of a world where no-one is needlessly blind and where irreversibly blind people share the same opportunities as everyone. This award recognises the enormous difference Sight Savers make to the lives of people in poor communities through some of the most simple and cost effective treatments available. Sight Savers is dedicated to combating avoidable blindness in developing countries. The charity works with partner organisations in poor and under served communities to develop and support healthcare programmes that prevent and cure blindness, and provide services to irreversibly blind people.

Technology for Vision 2000

The latest issue of Community Eye Health (No 42) focuses on technology and training, with an editorial by Catherine Cross, chairperson of the International Agency for the Prevention of Blindness (IAPB). For further information please contact: Journal of Community Eye Health, International Centre for Eye Health, Institute of Ophthalmology, 11–43 Bath Street, London EC1V 9EL, UK (tel: +44 (0)20 7608 4900; fax: +44 (0)20 7250 3207; email: eyeresource@ucl.ac.uk; website: www.jceh.co.uk). Annual subscription (4 issues) £23/US$40. Free to workers in developing countries.

International Centre for Eye Health

The International Centre for Eye Health has published a new edition of the Standard List of Medicines, Equipment, Instruments, and Technical Supplies (2001) for eye care services in developing countries. It is compiled by the Task Force of the International Agency for the Prevention of Blindness. Further details: Sue Stevenson, International Centre for Eye Health, 11–43 Bath Street, London EC1V 9EL, UK (tel: +44 (0)20 7608 6910; email: eyeresource@ucl.ac.uk).

Second Sight

Second Sight, a US based charity whose aims are to eliminate the backlog of cataract blind in India by the year 2020 and to establish strong links between Indian and British ophthalmologists, is regularly sending volunteer surgeons to India. Details can be obtained from the charity website (www.secondsight.org.uk) or by contacting Dr Lucy Mathen (lucymathen@yahoo.com).

Specific Eye Conditions (SPECS)

SpecEye ConditionS (SPECS) is a not for profit organisation which acts as an umbrella organisation for support groups of any conditions or syndrome with an integral eye disorder. SPECS represents over fifty different organisations related to eye disorders ranging from conditions that are relatively common to very rare syndromes. We also include groups who offer support of a more general nature to visually impaired and blind people. Support groups meet regularly in the Boardroom at Moorfields Eye Hospital to offer support to each other, share experiences and explore new ways of working together. The web site www.eyeconditions.org.uk acts as a portal giving direct access to supported eye care sites. The SPECS web page is a valuable resource for professionals and may also be of interest to people with a visual impairment or who are blind. For further details about SPECS contact: Kay Parkinson, SPECS Development Officer (tel: +44 (0)1803 524238; email: k@eyeconditions.org.uk; www.eyeconditions.org.uk).

The British Retinitis Pigmentosa Society

The British Retinitis Pigmentosa Society (BRPS) was formed in 1975 to bring together people with retinitis pigmentosa and their families. The principle aims of BRPS are to raise funds to support the programme of medical research into an eventual cure for this hereditary disease, and through the BRPS welfare service, help members and their families to cope with the everyday concerns caused by retinitis pigmentosa. Part of the welfare service is the telephone helpline (+44 (0)1280 860 363), which is a useful resource for any queries or worries relating to the problems retinitis pigmentosa can bring. This service is especially valuable for those recently diagnosed with retinitis pigmentosa, and all calls are taken in the strictest confidence. Many people with retinitis pigmentosa have found the Society helpful, providing encouragement, and support through the Helpline; the welfare network and the BRPS branches

throughout the UK. (tel: +44 (0)1280 821 334; email: lynda@brps.demon.co.uk; web site: www.brps.demon.co.uk)

BEAVRS Meeting
The next BEAVRS meeting will be held in the Dalmahoy Hotel near Edinburgh on 31 October to 1 November 2002. Further details: Susan Campbell, Medical Secretary, Gartnavel General Hospital (email: susan.j.campbell.wg@northglasgow.scot.nhs.uk).

Cornea 2002—Celebrating 50 Years of Eyebanking
The Cornea 2002 meeting will be held in Le Meridien Hotel, London, Gatwick on 14–15 November 2002. Subjects to be covered will include eye banking, penetrating and lamellar keratoplasty, stem cell restoration, keratopros thesis, advanced keratoplasty techniques, paediatric cornea, keratorefractive surgery, and intraocular refractive surgery. Spaces are limited and a beneficial package rate is available prior to 30 September 2002. Further details: CORNEA 2002 organiser at the Corneo Plastic Unit, The Queen Victoria Hospital, Holtye Road, East Grinstead, West Sussex, RH19 3DZ, UK (tel: 01342 410 210 ext 560; fax: 01342 317 181; email: Cornea2002@hotmail.com).

Introductory Course in Osteo-odonto-keratoprosthesis (OOKP)
The University of Brighton Postgraduate Medical School is holding an introductory course in osteo-odontokeratoprosthesis (OOKP) 20–21 November 2002 in the New Seminar Room, Sussex House, Brighton & Sussex University Hospitals Trust in Brighton. The course will comprise of a variety of lectures with live surgery, two way audio and video links (Stage 1 and Stage 2 OOKP surgery), and examination of patients. Further details: Mrs Erica Strange, University of Brighton, Postgraduate Medical School, Falmer Campus, Brighton, East Sussex BN1 9PH, UK (tel: +44 (0)1273 644 005; fax: +44 (0)1273 644 002; email: e.strange@brighton.ac.uk).

23rd Annual Conference and Dinner Glaucoma Society (UK & EIRE)
The 23rd Annual Conference and Dinner of the Glaucoma Society will be held on Thursday 21 November 2002, 8.30am to 5.00pm at the Central Conference Centre, London. The Annual Dinner is from 6.30pm to 10.00pm at The Royal College of Surgeons, London. Conference charges: £60 members; £80 non-members. Price entitles delegates to refreshments, lunch, abstract book, programme, and annual dinner. (Maximum number of places 250—apply now to secure your place). Further details: Janet Flowers, Administrator, 29 Quarry Hill, Grays, Essex, RM17 3BT, UK (tel/fax: 01375 383172; email: glausoc@ukeire.freeserve.co.uk).
Recurrent corneal ulcerations with perforation in keratosis follicularis (Darier-White disease)

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