PostScript

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 of the less, changes in intraocular pressure also affect the pressure gradient across the lamina cribrosa. Normal intraocular pressures combine with low intraocular pressures produce the same pressure differential across the laminae as elevated intraocular pressures in conjunction with normal intraocular pressures. Failing to factor in both intraocular and intraocular pressures may create an inappropriate distinction in the pathogenesis of glaucomas currently labelled as normal tension glaucoma. The optic neuropathy in glaucoma may be secondary to mechanical deformation and destruction of lamina cribrosa causing axonal degeneration, or conceivably to pressure related ischemic events. A goal of therapy in either situation should be equalisation of prelaminar intraocular pressure with opposing retrodiffusion and cerebrospinal fluid pressure.

Spontaneous venous pulsations occur when intraocular pressure during systole exceeds central retinal venous pressure, which, in turn, reflects intraocular pressure transmitted through the perineural subarachnoid space and retrodiffusion tissue pressure. Lowering intraocular pressure until venous pulsations cease minimises the pressure gradient between mean intraocular and retrodiffusion 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 intraocular 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.

C F Parsa
Wilmer Ophthalmological Institute, Johns Hopkins University School of Medicine

Correspondence to: Wilmer Ophthalmological Institute, Maumenee 517, 600 North Wolfe Street, Baltimore, MD 21287-9237, USA; cparsa@jhmi.edu

Accepted for publication 21 August 2001

References
1 Volkov VV. Essential element of the glaucomatous process neglected in clinical practice [in Russian]. Oftalmol Zh

Acanthamoeba keratitis in Ghana

Suppurative keratitis due to Acanthamoeba spp is most commonly associated with 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 conjunctival irritation (duration of symptoms 31 days) and visual acuity in his affected eye was reduced to perception of hand movements. 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 more than two thirds infiltrate. The lesion was more than 50% of the corneal epithelium and ulcer (greatest diameter 8 mm) involving more than two thirds infiltrate. The lesion was more than 50% of the corneal epithelium and more than one third stroma. The lesion was white, dry in texture, with a well defined margin and raised slough; flare, AC cells, and hypopyon were absent.

No organisms were isolated from culture on blood agar or Sabouraud agar. Non-nutrient agar was not available at this rural hospital. Corneal ulcer material stained with Gram stain and lactophenol cotton blue mountant was examined, retrospectively, by light microscopy at a tertiary microbiology centre. Cysts, morphologically consistent with the appearance of Acanthamoeba were seen (Fig 1) in the stained smear.

At the time of presentation the patient was treated empirically with chloramphenicol, gentamycin, and econazole. After 7 days on this regimen the ulcer had not reduced in size. However, there was a reduction of both infiltrate and flare. All other measurements remained the same. At day 21 the ulcer was reported to have improved and a scar had formed (7.4 mm x 7.0 mm). Visual acuity was hand movements only at presentation. The laboratory report was not received before the patient’s final visit and, sadly, the patient could not be traced for further follow up.

Comment

This report illustrates a case of Acanthamoeba keratitis in a non-contact lens wearer in the tropics. Suppurative keratitis due to Acanthamoeba spp is commonly associated with contact lens wear as a result of poor lens hygiene. However, increasingly, these ulcers are being reported in developing countries in the tropics in patients who have no history of contact lens wear. Sharma et al described 39 cases of Acanthamoeba keratitis, over a period of 2½ years; none of the patients was a contact lens wearer. However, 49% of the patients reported experiences of trauma to the affected eye. The first cases of Acanthamoeba keratitis in non-contact lens wearers in Africa were reported in Mali by Resnikoff et al. This group subsequently reported a further 22 cases between 1990–5. However, there have been no other reports, from Africa, of non-trauma related Acanthamoeba ulcers.

The case presented is the first report of a corneal ulcer caused by Acanthamoeba spp in Ghana 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.

A K Leck
Department of Epidemiology and International Eye Health, Institute of Ophthalmology, UCL, London EC1V 9EL, UK

M M Mathison
Institute of Ophthalmology, UCL, London EC1V 9EL, UK

M Hagan
E Ackuaku
Department of Ophthalmology, Korle Bu Teaching Hospital, Accra, Ghana, West Africa

Correspondence to: Dr A K Leck; a.leck@ucl.ac.uk

Accepted for publication 4 February 2002

References
1 Sharma S, Garg P, Rao GN. Patient characteristics, diagnosis and treatment of

www.bjophthalmol.com
Need for measurement of porphyrins in teardrops in patients with congenital erythropoietic porphyria

Congenital erythropoietic porphyria (CEP: MIM#263700) 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), which predicted a serine to proline change, has been reported in patients with CEP.

To date, more than 20 mutations of UROS have been identified underlying mutations that cause CEP. To date, more than 20 mutations of UROS have been identified. 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 haemolytic anaemia, and accumulation of porphyrinuria resulting from the accumulation in the bone marrow, peripheral blood, and other organs 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 may be 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.

Furthermore, we recently reported the evidence of the accumulation of porphyrins in teardrops in a Japanese patient with CEP who showed scleral changes. 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 (GQ246X). All patients who were observed to have sclerotic necrosis of the limbus and pigmentation of eyelids (Fig. 1), but in case 4 (KT), these changes were relatively mild. No patients showed visual disturbance and other ocular changes, such as pigmentation of eye lids and cornea.

Analysis of teardrop porphyrins was performed in three patients, after obtaining informed consent. In normal controls, no porphyrin isomer was observed, whereas in all patients remarkable elevation 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.

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

<table>
<thead>
<tr>
<th>Isomer</th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
<th>Case 4</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uroporphyrin</td>
<td>1302.6 (ng/dl)</td>
<td>1235.3</td>
<td>3345.9</td>
<td>91.4</td>
<td>0</td>
</tr>
<tr>
<td>Heptaporphyrin</td>
<td>49.1</td>
<td>302.5</td>
<td>141.5</td>
<td>3.6</td>
<td>0</td>
</tr>
<tr>
<td>Hexaporphyrin</td>
<td>27.4</td>
<td>0</td>
<td>35.8</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pentaporphyrin</td>
<td>24.6</td>
<td>67.9</td>
<td>109.5</td>
<td>4.9</td>
<td>0</td>
</tr>
<tr>
<td>Coproporphyrin I</td>
<td>108.1</td>
<td>348.8</td>
<td>285.9</td>
<td>21.4</td>
<td>0</td>
</tr>
<tr>
<td>Coproporphyrin II</td>
<td>11.2</td>
<td>32.5</td>
<td>28.6</td>
<td>6.4</td>
<td>0</td>
</tr>
<tr>
<td>Protoporphyrin</td>
<td>1363.3</td>
<td>59.9</td>
<td>59.2</td>
<td>16</td>
<td>0</td>
</tr>
</tbody>
</table>

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 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 phenotype of ocular involvement, also showed mild accumulation of porphyrins, suggesting that the accumulation of porphyrins, especially uroporphyrin and coproporphyrin 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.

![Figure 1 Scleral involvement shown in case 2.](http://bjo.bmj.com)

References


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 septicemia secondary to a urinary tract infection treated with a course of intravenous fluocoxacin 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 he was apyreal. 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 keratitic 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 level of the retinal pigment epithelium (RPE) which could represent drusen. In the left eye he had ++ cells in the vitreous, and similar white lesions in the fundus. There were no haemorrhages or cotton wool spots.

The fluorescein angiogram of the right eye (Fig 1) showed multiple dots of hyperfluorescence under the neural retina 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, ANA, ANCA, ENA, and complement C3 and C4. The lumbar puncture results were also normal with no growth and three early morning urine samples were also clear. The chest x ray was normal and a magnetic resonance imaging (MRI) of the orbits and head showed generalised ischaemia only. The Mantoux test was negative.

Investigations were unhelpful so he was treated symptomatically with dexamethasone 0.1% and cyclopentolate drops and an orbital floor injection of 40 mg of Kenalog (triamcinolone) in 1 ml.

The following week he was reviewed in clinic. His left eye had improved to 6/12, N8. However, he complained of generally feeling unwell with dizziness and nausea. There was no temperature or vomiting.

A blood test revealed that he was in acute renal failure with sodium of 125, potassium 6.9, urea 56.9, and creatinine 1681. ESR was 120, FBC 8.0, WCC 10.2, and platelets of 610. Liver function tests were normal apart from albumin of 21. He underwent haemodialysis and 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 NCI 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 antibasement membrane antibodies possibly because of the small percentage of alpha-3 chain or its NCI 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 antibasement membrane 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 choroidal plexus, the uveitis may have opposed 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 insulin to the basement membrane or cross reactivity with exogenous.

Figure 1 Fluorescein angiogram of the right eye showing multiple dots of hyperfluorescence under the neuroretina at the level of the RPE. These dots look more like inactive disease of the RPE and choroid rather than drusen. There is no leakage from the disc, vessels, or macula.

Figure 2 (A) Renal biopsy stained with MSB (Martius scarlet blue) stain shows a circumferential active cellular crescent that has obliterated urinary space. Almost all glomeruli showed similar lesions. The presence of fibrin (stained red, in the centre of the glomerulus) and marked infiltration by inflammatory cells indicates acute damage. The collagen stains blue and extensive blue staining reflects scarring and chronic damage. The features are therefore of a fulminating acute crescentic glomerulonephritis superimposed on chronic damage, consistent with injury inflicted by recurrent acute episodes. (B) Renal biopsy stained by anti-IgG antiserum by immunoperoxidase method. The linear (brown) labelling of the capillary wall is pathognomonic of antibody against glomerular basement membrane.
epitopes can initiate the process of autoimmune
reactivity resulting in Goodpasture's syndrome.1
Interestingly, uveitis and Goodpasture's share
some similar characteristics. The immuno-
ological profiles both involve the cytokines
IL-6, IL-12, and TGFβ, and both are associ-
ated with HLA B7 (indicating a particularly
poor prognosis in Goodpasture's) and HLA DR
15.4
This case is extremely rare. Other events
associated with the induction of anti-GBM
disease in humans have included lung dam-
age 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.5
To our knowledge this is the first reported case
where uveitis was the likely precipitating fac-
tor for the induction of Goodpasture's disease.
Moreover, ophtalmologists should keep
aware of all blood test results and check the
results of ordered tests. They should follow up
the patient with repeated history and exam-
ination and repeat tests if the diagnosis is
uncertain. Unsuspected fatal diseases as we
have seen in this case, may occasionally
present to ophthalmologists.

M Chak, M R Stanford, W Poon,
E M Graham
Department of Ophthalmology, GKT, St Thomas’s
Hospital, London, UK

M F Tungekar
Department of Histopathology, GKT, St Thomas’s
Hospital, London, UK

D Goldsmith
Renal Unit, GKT, Guy’s Hospital, London, UK

Correspondence to: Miss Melanie Chak, Centre for
Paediatric Epidemiology and Department of
Ophthalmology, Institute of Child Health, 30
Guildford Street, London WC1N 1EH, UK

Accepted for publication 17 April 2002

References
1 Bolton WK. Goodpasture’s syndrome. Kidney
Molecular cloning of the human Goodpasture
antigen demonstrates it to be the alpha-3
chain of type IV collagen. J Clin Invest
3 Cashman SJ, Pusey CD, Evans DJ.
Extraglomerular distribution of immunoreactive
Goodpasture antigen. J Pathol
1988;155:61–70.
4 Kelly PT, Haponik EF. Goodpasture’s
Ocular clinical findings and basement
membrane changes in Goodpasture’s syndrome.
6 Rowe PA, Morrisfield DC, Dutton GN.
Ophthalmic features of fourteen cases of
Goodpasture’s syndrome. Nephron
7 Boucher MC, et Taubky EA, Cormier G.
Bilateral serous retinal detachments associated
with Goodpasture’s syndrome. Can J
8 Kolluri R. Goodpasture syndrome. Kidney Int

Fusarium solani keratitis
following LASIK for myopia

Fungal keratitis is a rare complication of pho-
torefractive keratectomy (PRK),1 2 LASIK,3
and LASIK enhancement.4 We describe a
patient who developed keratitis in one eye
after bilateral LASIK procedures. The keratitis
progressed despite intensive topical and sys-
temic antibacterial and antifungal treatment.
Initial cultures were negative, but a diagnosis
of fungal keratitis was suggested by confocal
microscopy. Fusarium solani was isolated fol-
lowing penetrating keratoplasty.

Case report
A 45 year old woman noted blur and discom-
fort of the right eye 3 days after bilateral
LASIK procedures for myopia. The visual acu-
ity 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 dexam-
ethasone 0.1% four times daily was contin-
ued.

After a further 4 days the vision had
progressed to 6/24 and there was ulceration
through the flap over the infiltrate; treatment
was changed to hourly gentamicin 1.5%,
cefuroxime 5%, and econazole 1%, and dexam-
ethasone (2.5%) was started with oral
clarithromycin 500 mg twice daily. Confocal
microscopy of the edge of the lesion dem-
onstrated 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 na-
tamycin (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 cor-
nect graft was performed and the anterior
chamber was irrigated with amphotericin (5
µg in 0.1 ml). Dexamethasone 0.1% times daily
was continued after surgery to treat severe
intraocular inflammation. Histology of the
excised corneal tissue showed filamentary
fungalgrowth in the anterior to Descemet’s
membrane but no evidence of hyphae extend-
ing to the margin of the excised tissue. Fusarium solani was subsequently grown from
the corneal button and the isolate was
reported cases of fungal keratitis after LASIK
have been due to filamentary organisms.2 3
The diagnosis may be difficult to confirm as
cultures and biopsies of the anterior stroma
can be negative because of the tendency of
filamentary fungi to proliferate in the poste-
rior 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,2 3
and perforation and vascularisation of the
corneal occurred in one.5 The only case
with a medical cure had a surface infection of
a persistent epithelial defect.1

The origin of this infection is uncertain. The
patient had visited Florida 2 months previ-
ously, where Fusarium sp is the most common
isolate from cases of fungal keratitis.6 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. Be-
cause of a reluctance to disturb the LASIK flap
there is a temptation to treat infiltrates
empirically with broad spectrum antibiotics
and steroid,5 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.2 A
further negative biopsy then delayed a decision
for surgical intervention. Corticosteroid may
www.bjophthalmol.com
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.

Acknowledgement
Mr John Dart provided helpful advice with the management of this case.

S Verma, S J Tuft
Moorfields Eye Hospital, City Road, London
EC1V 2PD, UK

Correspondence to: Mr Stephen Tuft, stuf@ucl.ac.uk

Accepted for publication 17 April 2002

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 mass lesion located superiorly with 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 haemangioma versus nevus. Differential diagnoses in the right eye included ciliary body peripheral choroidal melanoma, retinal pigment epithelioma (RPE) adenoma, adenocarcinoma, and metastatic lesion. The patient underwent an iridectomy with peripheral chordectomy 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 nuclei 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 polyepitope, and negative for serotonin. Occasional tumour cells stained for Ki-67 but were negative for p53 and thyroid transcription factor (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 surrounding 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, cord-like 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).

www.bjophthalmol.com
Notwithstanding their metastatic potential, carcinoids are compatible with long term survival as (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 metastasis 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. Proliferation of uveal carcinoid led to the clinical impression of the 43 year long interval since resection of the tumour. Its expression may be useful in determining tumour's histological trabecular pattern and tumour growth. It is regarded as a fractional measure of tissue and tumour growth.

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. Consequentially, awareness and recognition of carcinoid's delayed metastatic potential can translate to maximisation of the patient's visual, systemic, and overall prognosis.

We thank Dr James D Sanchez, medical oncologist, Southwest Cancer Clinic, Las Vegas Nevada.

Supported in part by grant no EY00340 from the National Institutes of Health and the Research to Prevent Blindness Inc, New York, NY, USA.

Kaiser DE, See FR, Rechdouni AK, Irvine AR. Ocular Pathology Laboratory, the Doheny Eye Institute, the Doheny Retina Institute, and the Department of Ophthalmology, Keck School of Medicine of the University of Southern California, Los Angeles, CA, USA.

Correspondence: Narsing A Rao, MD, Doheny Eye Institute, 1450 San Pablo Street, DVC221, Los Angeles, CA 90062, USA; narao@hcom.us

Accepted for publication 23 April 2002

References

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

Darier-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. 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 unusual. In 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. Involvement of the eyelids and association with reitinitis pigmentosa, subnormal dark adaption, and post-cataract extraction staphylococcal endophthalmitis may also occur. 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 (Darier-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 pathological Schirmer's tear test.

Slit lamp examination showed blepharitis marginalis on both eyes, thickened, knobbly lid margins, and a rarefaction 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 thickening 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, anterior and posterior synchiae (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 Blastomonas. Therefore, topical antmyotic eye drops 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.

www.bjophthalmol.com
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 flat.

After intensive topical and intravenous antibiotic therapy and insertion of punctum plug 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 unilateral perforation probably associated with keratitis follicularis.

Keratitis follicularis (Darier-White disease) is caused by mutations in the ATP2A2 gene, which encodes the Ca\(^{2+}\) ATPase 2

In our patient the recurrent corneal ulcerations with subsequent perforation could be explained by the participation of the ectodermal ocular tissues in keratitis follicularis: the lacrimal gland, the eyelids, and the corneal epithelium. A combination with Sjögren’s syndrome, dry eyes, oral mucosal lesions, and keratitis follicularis associated with retinitis pigmentosa and genotype-phenotype correlation. Darier disease—novel mutations in ATP2A2 gene, which encodes the Ca\(^{2+}\) ATPase 2

In the Finnish population Eskelin and Kivelä have found 184 uveal melanoma cases in 5 years. Interestingly, in a study done by us on the Asian Indian population at the ocular oncology department of a tertiary eye care institute, we found only 71 cases of uveal melanoma in 12 years (0.02% incidence). The mean age of presentation in the Finnish population was found to be 60 years (range 14–87) and in the British 59.7 years. However, the mean age at presentation of uveal melanoma in the Asian Indian population was found to be 46.1 (range 13–75) years in the 71 cases studied by us. Similar low mean age of presentation (43.7 years) has been reported earlier in the Chinese population.

In addition, there may be a difference between the Finnish and Asian Indian population in the mean basal diameter of the uveal melanoma at the time of presentation. In the Asian Indian population, the mean basal diameter of the tumour was 12.44 (SD 4.41) mm compared to 11.3 and 6.4 mm in the Finnish population and 11.6 mm and 4.9 mm in the British population. We feel that the Asian Indians present at an earlier age with larger tumours in comparison with the Western population. The difference is more pronounced in the Asian India population. The comparison also emphasizes the racial differences in presentation of uveal melanoma. Whether this has any bearing on the prognosis and the implication of early onset melanoma in pigmented populations remains to be seen.

**References**
8. M S Bajaj, N Pushker. Dr Rajendra Prasad Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, Ansari Nagar, New Delhi - 110 029, India
9. Correspondence to: Dr Neelam Pushker, Oculoplast and Paediatric Ophthalmology Services, Dr RP Centre for Ophthalmic Sciences, AIIMS, Ansari Nagar, New Delhi - 110 029, India; msbajaj32@hotmail.com

**References**
4. M S Bajaj, N Pushker. Dr Rajendra Prasad Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, Ansari Nagar, New Delhi - 110 029, India
9. Correspondence to: Dr Neelam Pushker, Oculoplast and Paediatric Ophthalmology Services, Dr RP Centre for Ophthalmic Sciences, AIIMS, Ansari Nagar, New Delhi - 110 029, India; msbajaj32@hotmail.com
TTT for occult CNV: check 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 240 mW for the 1.2 mm spot. With these power levels 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 inadvertently lower than 800 mW for the 3 mm spot (or the power equivalent for other spot sizes) the treating physician would notice he has to compensate for the lower power by adjusting the instrument’s power level

We have used a diode laser (Iridex Corpora-

tion, Mountain View, CA, USA) with the recommended fibreoptic adapter since 1997 for the treatment of choroidal melanomas and have not observed without any apparent problems. Following the report by Reichel and coworkers, we started treating patients with occult CNV according to the recommended treatment parameters described above.

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 angiogram or OCT.

Lacking any possible explanation other than that the treatment method didn’t work, we finally asked a technician to check the laser. Immediately he noticed not only a visibly clear defect at the adapter of the fibreoptic but a mean power output from the 800 mW on the display to 560 mW at the end of the fibreoptic. Apparently the fibroptic 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 ‘visible’ grey to white 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 fibroptic) 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”) inefficiency of this possible beneficial treatment method.

A J Mueller, M Ulbig, A Kampik
Eye Clinic of the University, Mathildenstrasse 8, 80336 Munich, Germany

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 organisation to be named a recipient of the Nathan Davis International Award in Medicine and Public Health, awarded by the American Medical Association. This is the first time ever a non-US organisation has received 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 one 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 which can be made 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 (IFAB). 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 6910; fax: +44 (0)20 7608 3207; email: eyeresource@ucl.ac.uk; website: www.jech.co.uk). Annual subscription (4 issues) £25/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 Optical 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 Stevens, International Centre for Eye Health, 11–43 Bath Street, London EC1V 9EL, UK (tel: +44 (0)20 7608 6910; email: eyeresource@ucl.ac.uk).

Specific Eye Conditions (SPECS)

Specific Eye Conditions (SPECS) is a not for profit organisation which acts as an umbrella organisation for support groups of any conditions or syndromes 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 support groups’ websites. 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 this eventual cure for this hereditary disease, and through the BRPS welfare service, help members and their families copy 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, keratoprosthesis, 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-odonto-keratoprosthesis (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 Royal College of Surgeons, 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: glau soc@ukeire.freeserve.co.uk).