LETTERS TO THE EDITOR

Spontaneous closure of a macular hole secondary to an accidental laser injury

Editor,—Early surgical intervention has been reported to achieve closure of laser induced macular holes.1 2 We report a case of spontaneous closure of a laser induced macular hole indicating that surgery should not be undertaken before a reasonable period of observation.

CASE REPORT
A 24 year old physics postgraduate student accidentally sustained an injury to his right eye while aligning an 806 nm titanium-sapphire laser. The laser parameters were pulse energy 2 mJ, pulse duration 100 femtoseconds, and repetition rate 10 Hz. The duration of exposure was limited by his blink reflex. He noted immediate impairment of central vision in this eye.

When examined by an ophthalmologist 2 days later, visual acuity was 6/18 in the right eye. Amsler testing demonstrated an absolute paracentral scotoma which was 1.5° in diameter and abutted fixation. A full thickness macular hole was present with loss of both neurosensory retina and retinal pigment epithelium (RPE). The hole was approximately 150 μm in diameter and located at the temporal margin of the foveola. There was no associated retinal oedema or haemorrhage. Fluorescein angiography showed a hyperfluorescent transmission defect.

At 4 weeks after injury, a cuff of subretinal fluid had developed around the macular hole (Fig 1). Visual acuity remained 6/18, but the size of the scotoma had correspondingly increased. The option of surgical intervention was considered, but a conservative approach was chosen at this stage.

The patient noticed a gradual improvement in his vision approximately 4 weeks later. At 12 weeks after injury, his visual acuity was 6/6. Amsler testing now demonstrated a relative paracentral scotoma which was 0.5° in diameter and located 3° from fixation. The macular hole was closed with residual RPE depigmentation at the site of the laser injury (Fig 2). There was no posterior vitreous detachment.

No further changes occurred during 6 months of follow up.

COMMENT
The mechanism of macular hole formation following accidental exposure to a Q switched laser is photomechanical tissue disruption (rather than photocoagulation). The natural history of these laser induced macular holes remains uncertain because this type of injury is uncommon. In a series of five cases, spontaneous closure was only observed in one eye that had complete retina at the time of injury.2 Two other cases of non-resolving laser induced macular holes have also been reported.1 3 This case report confirms that laser induced macular holes can close spontaneously with visual improvement. Furthermore, this event may be delayed for 8–12 weeks following the injury. The occurrence of spontaneous closure could possibly be influenced by macular hole size. The diameter of macular holes that have spontaneously resolved was 150 μm in this case and 180 μm in the previous report.1 While non-resolving macular holes have generally been larger (250–500 μm in diameter2 3), a 75 μm macular hole has been observed to enlarge without spontaneous closure.4 Spontaneous closure of small traumatic macular holes (0.1 disc diameter) has also been reported at 3–4 months after the injury.

There have been two recent reports of laser induced macular holes being successfully treated by early surgical intervention, performed at 3 weeks5 and 6 weeks6 after injury, respectively. In both reports, the macular hole was 300 μm in diameter. Surgery comprised pars plana vitrectomy, removal of the posterior cortical vitreous, and gas tamponade followed by face down posturing. Additional procedures comprised stripping of an early epiretinal membrane and adjuvant therapy with autologous thrombocyte concentrate.7 8 The rationale for surgical treatment was relief of tangential traction on the edges of the hole and reattachment of vitreous by tamponade, as for idiopathic macular holes.9

It is, however, important to recognise that laser induced macular holes can resolve spontaneously. Internal limiting membrane changes induced by laser injuries are capable of spontaneous regression, as demonstrated by reports of significant macular pucker improving spontaneously.10 Reparative events within the neurosensory retina and RPE may also influence macular hole closure, comprising fibroglial and retinal pigment epithelial hyperplasia.11 Surgical intervention for laser induced macular holes should therefore not be considered before a reasonable period of observation.

Failure of transpupillary thermotherapy (TTT) for choroidal melanoma: two cases with histopathological correlation

Editor,—We are concerned about the widespread use of transpupillary thermotherapy (TTT). Two patients referred for evaluation after TTT failed to destroy their tumours underwent ophthalmic oncology evaluation. Both patients were diagnosed as having recurrent choroidal melanoma, and opted for enucleation as definitive treatment. Clinical history and examination revealed evidence of a TTT laser effect with partial chorioretinal atrophy and temporary reductions in tumour height. Histopathology revealed attenuation of the retina and choroid above viable appearing melanoma. Despite temporary reductions in tumour height, resistant and/or untreated choroidal melanoma at the deep margins grew, resulting in TTT failure.

CASE REPORTS
Case 1
A 47 year old man developed a small (8 × 7 × 1.9 mm) macular choroidal melanoma. Before TTT, the tumour’s posterior margin was 2.25 mm from the foveola and the patient’s visual acuity was 20/20 left eye (with metamorphopsia).

Three months after TTT, the apical tumour height decreased to 1.1 mm but the posterior margin remained elevated and was “heavily” retreated. Three months later a third TTT was administered, resulting in “no visible tumour”. At 30 months a crescent of pigmentation was noted along the posterior margin of the TTT scar (Fig 1) and treated immediately with a fourth and ultimately with a fifth TTT (3 months later).

Sources of funding: None
Proprietary or financial interests: None

DOUGLAS K NEWMAN DECLAN W FLANAGAN
Department of Ophthalmology, Addenbrooke’s Hospital, Cambridge, UK

Correspondence to: Dr D K Newman, Department of Ophthalmology, Clinic 3 (Box 41), Addenbrooke’s Hospital, Hills Road, Cambridge CB2 2QQ, UK
Accepted for publication 6 March 2000


Failure of transpupillary thermotherapy (TTT) for choroidal melanoma: two cases with histopathological correlation

Case 1
A 47 year old man developed a small (8 × 7 × 1.9 mm) macular choroidal melanoma. Before TTT, the tumour’s posterior margin was 2.25 mm from the foveola and the patient’s visual acuity was 20/20 left eye (with metamorphopsia).

Three months after TTT, the apical tumour height decreased to 1.1 mm but the posterior margin remained elevated and was “heavily” retreated. Three months later a third TTT was administered, resulting in “no visible tumour”. At 30 months a crescent of pigmentation was noted along the posterior margin of the TTT scar (Fig 1) and treated immediately with a fourth and ultimately with a fifth TTT (3 months later).
Figure 2  Patient 2. Histopathological evaluation revealed tumour necrosis in the path of TTT as evidenced by attenuated retina (arrows). Again, a basal layer of intact choroidal melanoma can be seen at the tumour base and within the zone of treatment (arrows). The tumour mass is largely recurrence into the temporal quadrants.

COMMENT

Transpupillary thermotherapy involves aiming a large (for example, 2.5 mm) spot size diode laser at posterior choroidal melanomas to completely cover the tumour surface and a circumferential (1 mm) safety margin. Power is increased until the 1 minute application produces a light, white retinal “burn.” TTT is not consistent with clinical hyperthermia where tumour temperatures are measured and radiation is typically added.1,4

Korver and colleagues introduced the use of TTT for choroidal melanoma.3 Their histopathological evaluations demonstrated variable depths of TTT penetration.4 In order to address the possibility of untreated deep tumour, Oosterhuis advocates a “sandwich technique” adding plaque radiotherapy to treat the tumour’s base.3 Shields and Capone have advocated the use of TTT alone.6 Clinical and histopathological studies suggest that laser (argon, krypton) photocoagulation of choroidal melanoma is relatively ineffective.6 Laser treated melanomas typically demonstrate residual tumour which can grow over time. Radiation therapy also results in a tumour residua, but irradiated melanoma is considered sterilised (incapable of growth or metastasis).6,7 Surgeons also define successful TTT as cessation of growth or shrinkage, but like other forms of laser photocoagulation, the aim is to believe that residual heat treated tumour has been sterilised.1

Radiation has offered mean 5 year local control rates of 92.8%.8 TTT has thus far demonstrated similar control rates of 93%, but only with a mean 16 months’ follow up after treatment of small melanomas, and 94% after a mean 14 months (medium sized tumours).9,10 The ability of TTT to preserve vision has been poor. Because of aiming considerations, the perfect tumours for TTT are small, posterior, and melanotic. Case selection makes them relatively close to the optic nerve and/or fovea. This may explain how TTT has resulted in a loss of vision in 43% of patients with small melanomas and 41% in Shields’ series.3 TTT induced scotomas are typical. Traction maculopathy, haemorrhages, and optic nerve damage are common. Though these findings can also occur after ophthalmic radiotherapy they are rarely immediate.11

We present two cases where TTT resulted in inadequate treatment, leaving the ominous finding of malignant tissue at the tumour base adjacent to scleral emissary vessels. We feel that TTT should be scientifically compared with standard treatments before it is presented as standard therapy.

Supported (in part) by The EyeCare Foundation, Inc, New York City (http://www.eyecarefoundation.org).

PAUL T FINGER
ANDREW C LIPKA
JEFFREY L LIPKOWITZ
MARK JOFI
STEVEN A MCCORMICK
The New York Eye Cancer Centre, New York City, The Departments of Ophthalmology and Laboratory Medicine, The New York Eye and Ear Infrmary, New York City, and The Department of Ophthalmology, The New York University School of Medicine, New York City, New York, USA
Correspondence to: Paul T Finger, MD, FACS, Director, The New York Eye Cancer Centre, 5th Floor, 115 East 61st Street, New York, NY 10021, USA
pfinger@eyecancer.com
Accepted for publication 13 April 2000

Unusual presentation of diffuse melanoma of the iris

EDITOR—Diffuse melanoma of the iris is an unusual variant of anterior uveal melanoma. It is usually characterised by diffuse, circumferential neoplastic involvement of the iris, chamber angle and, sometimes, ciliary body.1 Patients usually present with ipsilateral raised intraocular pressure and heterochromia. There is often a delay in both the diagnosis and treatment of these tumours owing to their atypical presentation.2 A tendency for ciliary body involvement and extracocular extension may account for their generally poor prognosis.

We present an unusual case with diffuse melanoma of the iris diagnosed by high frequency ultrasonography and fine needle aspiration biopsy.

CASE REPORT

A 79 year old man with unilateral glaucoma on the left eye developed pain, red eye, and heterochromia during his follow up. He had an ocular history of glaucoma surgery (Baerveldt implant) 1 year before presentation, and recent cataract surgery on the left eye.

Because of uncontrolled glaucoma, heterochromia, and diffuse yellow-white deposits throughout the anterior chamber, cornea, with vitreous cells on left eye, he was referred for ophthalmic oncology evaluation. The examination of right eye was found to be normal. On examination of the left eye, he was noted to have a best corrected visual acuity of 20/250 and intraocular pressures of 46 mm Hg. Slit lamp examination of the left eye revealed yellow-white keratic precipitates on the cornea and 4+ cells in the anterior chamber (Fig 1A and B). The iris was significant for clumps of similarly coloured debris and neovascularisation (Fig 1A and B). Ophthalmoscopy revealed vitreous cells and the retina appeared normal. A transillumination defect (3 × 3 mm) was observed between 5 and 6 o’clock inferiorly in the pars plana. High frequency ultrasonography revealed deposits on the corneal endothelium, diffuse iris thickening, and a nodular thickening on the inferior quadrant of the ciliary body (Fig 1C). The diagnosis of the diffuse melanoma of iris was made by transcorneal fine needle biopsy of the anterior segment debris.

After a negative metastatic survey, the patient underwent enucleation with 50 Gy of postoperative radiation therapy. Histopathological evaluation of the enucleated eye confirmed the tumour to be a malignant melanoma with a diffuse involvement of the iris stroma (Fig 2A and B). Cytology revealed epithelioid malignant melanoma cells. Special stains of the harvested material was S100 positive (Fig 3A and B).

COMMENT

Diffuse melanoma of the iris is a rare entity among anterior uveal tumours.1 Classically, it is described as involvement of anterior uveal tissues in a complete ring, but it is used for any melanoma involving more than 6 clock hours of anterior uvea circumferentially.2 Jakobiec and associates reported that 13 of 183 (7%) patients with iris melanoma had diffuse melanoma; however, Jensen and associates reported 10 of 80 (12.5%) iris melanoma cases were diffuse melanoma.3 The ipsilateral glaucoma and heterochromia are the cardinal signs in this disease. The mechanism of glaucoma includes pigment dispersion, tumour invasion of the angle, angle closure, and iris and angle neovascularisation.4

Figure 1 Slit lamp examination of the left eye revealed yellow-white keratic precipitates on the cornea, 4+ cells in the anterior chamber (A); clumps of similarly coloured debris on iris with neovascularisation (B). On high frequency ultrasonography, deposits on the corneal endothelium, diffuse iris thickening, and a nodular thickening on the inferior quadrants of the ciliary body were observed (C).

Figure 2 Gross photograph of the eye showing diffuse involvement of iris with epithelioid tumour cells and small, amelanotic malignant melanoma of the inferior ciliary body (A). Tumour cells involved the chamber angle (B) (haematoxylin and eosin, x10).

Figure 3 Large epithelioid, discohesive, pleomorphic cells with granular cytoplasm and oval nuclei. Some cells contain melanin and have prominent nucleus (A) (haematoxylin and eosin, ×100). Positive dark staining characteristic of neural crest derived cells is noted in most of the cells (B) (S-100 stain, ×100).
The clinicians often pay more attention to the secondary glaucoma than to the heterogenous. So, there is usually a delay in diagnosis and often a history of previous glaucoma surgery in these patients. Conventional B scan ultrasonography is not so helpful for anterior uveal tumours. Ultrasound biomicroscopy offers a better diagnostic method to evaluate the lesions of iris, chamber angle, and ciliary body. Transillumination is another useful test to assess the ciliary body involvement, although transillumination defects have been variably reported, ranging from 4% to 87% of patients with diffuse uveal melanoma. The other diagnostic tool for iris, ciliary body aspiration biopsy with an accuracy rate of 90% in diagnosis and a low risk of tumour seeding.

Although our patient had a history of glaucoma and heterogenous, this case had an atypical presentation of uveal melanoma seeding in the anterior chamber and vitreous (a clinical picture similar to endophthalmitis). Clearly ultrasonographic biomicroscopy and fine needle aspiration biopsy were invaluable for the diagnosis and management of the case.

Enucleation is commonly performed for diffuse melanomas. But, despite surgery the prognosis for survival of these patients is typically worse than patients with nodular uveal melanomas of equivalent thickness. This may be due to the greater likelihood of epithelial cells, a higher rate of extracapsular extension, and/or their delays in diagnosis. Our patient is still alive with no evidence of metastasis and recurrence after 1 year.

HAKAN DEMIRCI
PAUL T FINGER
New York Ophthalmic Oncology Centre, New York City and the Department of Ophthalmology, New York Eye and Ear Infirmary, New York, USA

RUBINA COCKER
STEVEN A MCCORMICK
Department of Pathology and Laboratory Medicine, New York Eye and Ear Infirmary, New York, USA

Correspondence to: Paul T Finger, The New York Eye Cancer Centre, 5th Floor, 115 East 61st Street, New York, NY 10021, USA

Accepted for publication 13 April 2000


Promoter mutations of myocilin gene in Japanese patients with open angle glaucoma including normal tension glaucoma

EDITOR—Mutations causing primary open angle glaucoma (POAG) have been identified in the chromosome 1 open angle glaucoma gene (GLC1A), which encodes a 57 kD protein known as myocilin (MYOC). A number of mutations of the MYOC gene that are associated with glaucoma have been reported in different ethnic groups.1–3 The mutations occur in 2–4% of POAG patients, but mostly in the exons. Although five different such alleles have been identified among Japanese patients,4 they are rare and a promoter region has not received much attention. We conducted a study using the same methods as in Japanese patients with POAG and normal tension glaucoma (NTG) who had a family history of the disease in first and second degree relatives (p=0.30, 53), and in control subjects (n=63) who had no ophthalmological conditions.

The results of this screening for the Japanese patients with POAG disclosed no exon mutations. The introns at the exon/intron boundaries had no abnormalities. However, three abnormalities were found in the promoter region (Table 1). One was a polymorphism at –83 G→A (83 base pairs upstream from initiation codon), which had been reported previously in Westerners,4,5,6 and another was a new mutation of (GT) repeats at –339 to –314, which also seemed polymorphic. The last promoter mutation (–153 T→C) is newly observed, and was found in a subset of our patients. However, no significant difference was found in the first survey (Table 1).

The –153 T→C creates tandem repeats of [CAGCCCCAC]C. The CACC motif, transcription regulator in β-like globin genes, bridges the two repeats [CAGCCCCAC][CAGCCCC(T→C)]C. Thus, this mutation seems to affect the expression of the GLC1A gene. These results caused us to extend the examination in a second survey for the –153 T→C to other patients with POAG and NTG (n=53) and to new age matched control subjects (n=63). The result showed a significant difference between the patients and the control group (p<0.01, Fisher’s exact probability). The age matched second survey provided results similar to those of the first survey. Even when we combine the results of both, the difference was also evident (Table 1). No homozygosity for the –153 C was detected.

Thus, the –153 C mutation is very likely to be disease related. The mutation comprises nearly 20% of patients with POAG and NTG, but only 4.8% of the control subjects. An incidence as high as this has not been observed in any POAG related mutant reported previously.7 In fact, three control subjects carrying the –153C in the original survey were examined ophthalmologically, and to our surprise, two of them had POAG. These carriers in the control group, despite the absence of ophthalmological complaints, may have an insidious development of glaucoma.

Our preliminary study suggested that the promoter activity is different between the –153 T and C alleles, and it depends on the linkage with the number of GT dinucleotide repeats, about 160 nucleotides upstream from this mutation.

This –153 C allele may be found exclusively in Japanese patients and may be the major mutation associated with POAG and NTG in Japanese people. Clinical phenotypes differ among ethnic groups,8 which may be explained genetically.

The patent licence number of the glaucoma detection kit is 500223497.

This work was supported by a general research programme (C2-106161645) from the Ministry of Education, Science and Culture, Japan (Dr Suzuki) and New Frontier Project 2000, Japan (Dr Suzuki). We wish to thank Lynda Charters of Medical International for editing this manuscript.

RUYO SUZUKI
Department of Ophthalmology, Glaucoma Service, Yamaguchi University School of Medicine, 755-8505, Japan

YUKIO HATTORI KOZUE OKANO
Yamaguchi University School of Health Sciences

Correspondence to: Dr Ruyo Suzuki
suzuki@pc.cc.yamaguchi-u.ac.jp

Accepted for publication 13 April 2000


Table 1 Mutations of the promoter region

<table>
<thead>
<tr>
<th>Mutation</th>
<th>Patient group No (%)</th>
<th>Control group No (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>–83 G→A (GT)n</td>
<td>9/30 (30)</td>
<td>14/36 (39)</td>
</tr>
<tr>
<td>115C→T</td>
<td>13/15 (30)</td>
<td>22/33 (67)</td>
</tr>
<tr>
<td>183C→T</td>
<td>11/15 (30)</td>
<td>7/33 (21)</td>
</tr>
<tr>
<td>115C→T</td>
<td>3/33 (9.1)</td>
<td>3/33 (9.1)</td>
</tr>
<tr>
<td>115C→T</td>
<td>1/33 (3.0)</td>
<td>1/33 (3.0)</td>
</tr>
<tr>
<td>115C→T</td>
<td>3*38 (7.5)</td>
<td>3*38 (7.5)</td>
</tr>
<tr>
<td>115C→T</td>
<td>6/33 (4.8)</td>
<td>6/33 (4.8)</td>
</tr>
<tr>
<td>163/18 (19)</td>
<td>(age matched)</td>
<td>(age matched)</td>
</tr>
<tr>
<td>6/101 (5.9)</td>
<td>(p&lt;0.01)</td>
<td>(p&lt;0.01)</td>
</tr>
</tbody>
</table>

The maximal intraocular pressure in these patients was 35 mm Hg, and most intraocular pressures were between 15 and 22 mm Hg. *Three controls with the –153 C mutation later underwent ophthalmological examination of the optic disc and glaucomatous visual field defects. Two had a diagnosis of evident glaucoma and the third (a 22 year old man) was a glaucoma suspect.
Keratoconus associated with chromosome 13 ring abnormality

EDITOR,—We wish to report a patient with a ring abnormality of chromosome 13 who developed keratoconus. As far as we are aware such a patient has not previously been reported. This case may provide some further insight into the presumed genetic basis of keratoconus.

CASE REPORT
A 64 year old man was referred by her optometrist because of impaired distance vision present for several months which could not be satisfactorily corrected with spectacles. There was no history of familial ocular problems. The patient did not suffer from atopy.

Unaided visions were: right 6/9 part, left 6/24. The optimal spectacle correction and visual acuities were: right +1.00/−1.00 × 90 = 6/7.5, left +1.50/−3.00 × 110 = 6/18. With a pinhole the visual acuities improved to: right 6/5 part, left 6/6. The retinoscopy reflex in the left eye showed an “oil droplet” appearance with distortions, and slit lamp examination of this eye revealed a definite corneal cone. Conventional keratometry measurements were right 7.08 mm × 123/7.05 mm × 33 (47.62/47.87D), left 6.99 mm × 150/6.67 mm × 60 (48.25/50.62D). Videokeratography (TMS) demonstrated corneal topographies typical of keratoconus, more marked on the left side, with the cone apices inferior to the corneal centre. The condition was managed by the fitting of rigid gas permeable contact lenses.

The patient was born at full term weighing 2.2 kg. There was delay in achieving her early childhood development milestones and, as a result, chromosomal investigations were performed at the age of 8 years. These revealed a chromosome 13 ring abnormality (46X, r(13)). She showed mild learning difficulties, particularly of her reading and writing skills. She has, however, remained within mainstream education. During childhood she had persistent middle ear infections and required a hearing aid. Puberty was delayed with menarche occurring at age 15 years 2 months. At the age of 19 years, she has a height on the 95th centile, weight on the 75th centile, and occipitofrontal circumference on the 100th centile. She has mild dysmorphic features of epicantthic folds, depressed nasal bridge, and overfolded helices. She also has underdevelopment of the right breast and a hypoplastic toe nail on the right fifth toe.

Further cytogenetic analysis in 1999 demonstrated that the long arm subtelomere are absent from the ring. The karyotype is, therefore, 46,XX,r(13)(p11q34)ash r(13)(p11q34)(595A10-)

COMMENT
A number of cases of ring 13 have been reported with the same breakpoints of p11 and q34.1 While microcephaly, mild dysmorphism, mental retardation, and foot anomalies have been described, there have been no reports of an association with keratoconus.

The aetiology of keratoconus remains unclear. The thinning of the corneal stroma and the resulting ectasia are presumed to be due to an abnormality of the corneal collagen or extracellular matrix. Although many cases occur sporadically, twin and family studies suggest that there is, at least in part, a genetic basis to the condition.2 Candidate genes include those that code for the components of collagen. In the case described above, the ring (13) has occurred following a deletion of the end of the long (q) arm of the chromosome. The association with keratoconus raises the possibility that a deleted gene may have a role in the maintenance of corneal integrity. It is interesting that the genes COL4A1 and COL4A2 which code for the α1 and α2 chains, respectively, of collagen IV are both located at the end of the long arm of chromosome 13 (13q33-q34).1

C J HEAVEN
Royal Albert Edward Infirmary, Wigan WN1 2NN

F LALLOO
E MCHALE
St Mary’s Hospital, Manchester M13 9JH, UK

COMMENT
Vitamin A deficiency is a major cause of ocular morbidity especially in underdeveloped countries. In the West sporadic cases have been reported usually associated with malabsorption syndromes, small intestinal bypass surgery, or abnormal metabolism. We report a case of an ophthalmological diagnosis of vitamin A deficiency secondary to coeliac disease. To our knowledge keratomalacia in association with coeliac disease has not been described previously.

CASE REPORT
A 64 year old man presented with a 6 week history of subjective redness of his right eye associated with blurring of vision. His left eye was asymptomatic and he had no ocular history of note. He had a history of diet controlled coeliac disease proved by jejunal biopsy. Several weeks earlier he had complained of persistent diarrhoea despite adherence to his gluten-free diet.

On examination visual acuity was counting fingers on the right and 6/6 on the left. The left eye was normal except for multiple fluorescent staining scattered fine superficial punctate erosions. The right eye was diffusely injected and the cornea showed filamentary changes with multiple underlying punctate staining epithelial defects. There were no other pathological features.

A provisional diagnosis of filamental keratitis was made and he was treated with topical acetyl cysteine to the right eye and topical lubricants to the left eye. Two weeks later he reported a marked deterioration in symptoms. Visual acuity remained unchanged. Corneal examination revealed a large central full thickness epithelial defect. Regular topical lubricants were applied and a botulinum toxin injection was administered. Full physical examination at this stage revealed a thin man but no other relevant findings.

After 1 week there was complete failure of re-epithelialisation (Fig 1). The suspicion of a keratomalacia secondary to vitamin A deficiency was raised and an intramuscular injection of 100 000 units of vitamin A was immediately administered. Subsequent serum vitamin A levels were 13 (normal 330–1100). Six days later there was a dramatic symptomatic improvement. Visual acuity had improved to 6/18. The cornea was almost completely healed with only a few areas of superficial epithelial defect remaining. The patient was referred back to the gastroenterologists who investigated his continuing malabsorption syndrome and admitted standard dietary supplementation including regular vitamin A injections.

Ophthalmology review occurred 1 month later when full corneal healing was noted. The visual acuity had improved to 6/12 and since then he has had no further ocular problems.

REFERENCE
CASE REPORT

A 35 year old woman was referred for ophthalmological examination with distortion of vision in her left eye. She noticed this in her left eye vision 2 weeks before an episode of pre-eclampsia which led to a stillbirth at 26 weeks of pregnancy. One week before her ophthalmic presentation she was diagnosed as having the antiphospholipid syndrome, and treated with aspirin 75 mg a day.

The presence of antiphospholipid antibody is associated with choroidal disturbance in more than 30% of the patients with ocular changes. Our patient had two risk factors for choroidal ischaemia: pre-eclampsia and antiphospholipid antibodies. We believe that this association led to damage to choriocapillaris-Bruch’s membrane-RPE complex and secondary choroidal neovascular membrane formation.

Figure 1 By observing from superior side, we could diagnose the absence of adhesion of the proliferative tissue to the retina. S = superior side, N = nasal side, A = anterior side; OD = optic disc, PF = proliferative tissue.
postoperative inflammation. Eissnig's pearl type emerged 6 months after cataract surgery, requiring posterior capsulotomy by YAG laser. In 1994, band keratopathy appeared and progressed gradually as a result of chronic uveitis of Behçet's disease. By November 1999, although his corrected visual acuity was still 10/20, ophthalmoscopic evaluation of the vitreous body and the fundus became impossible because of band keratopathy and severe after cataract. Because of the chronic uveitis, this patient could not receive a penetrating keratoplasty operation or excimer laser treatment for band keratopathy. Thus, three dimensional ultrasonography was performed using a 3D i-Scan ultrasonograph system (Ophthalmic Technologies Inc, Downsview, Ontario, Canada) to measure the degree of vitreous opacification and to detect the presence of proliferative tissues in the vitreous body. As shown in Figures 1 and 2, we could diagnose the absence of adhesion of the proliferative tissue to the retina by observing from both superior side and nasal side. Because this examination excluded the possibility of retinal traction by proliferative tissues and retinal detachment, only periodic check ups have been conducted.

COMMENT
Two dimensional ultrasonography has traditionally been used to examine retinal or vitreous diseases with invisible fundus. Three dimensional ultrasonography has an advantage over two dimensional ultrasonography in that cross sections of the eye can be observed and the size of the space occupied by the lesion can be measured. Two dimensional ultrasonography, however, is superior to three dimensional ultrasonography for observing the dynamic changes of the membranous tissue associated with eye movement. We report here of a case in which two dimensional ultrasonography could not detect the adhesion of the proliferative tissue to the retina. This case was successfully examined by three dimensional ultrasonography. By observing many cross sections, we could diagnose the absence of adhesion of the proliferative tissue to the retina. Three dimensional ultrasonography was essential in determining the therapeutic approach for this patient. Further improvement of the technique using three dimensional ultrasonography may expand the possible application of this technique to patients with other invisible fundus as well.

KAZUKO ENDO
Division of Ophthalmology, Tokyo University Branch Hospital, Tokyo, Japan

SATOSHI KATO
HARUMI FUKUSHIMA
KENJI INOUE
JIRO NUMAGA
HIDETOSHI KAWASHIMA
Division of Ophthalmology, Tokyo University Branch Hospital, Tokyo, Japan

Correspondence to: Satoshi Kato, MD, Division of Ophthalmology, Tokyo University Branch Hospital, 3-28-6 Meijirodai, Bunkyo-ku, Tokyo 112-8688 Japan katou-s@ka2.so-net.ne.jp
Accepted for publication 18 April 2000

Late complications after pterygium excision with high dose mitomycin C instillation

EDITOR,—To prevent recurrence of pterygium after excision, instillation of 0.04% mitomycin C has been used in Japan and northern America. However, early (less than 14 months) development of serious complications including scleral ulceration has been reported. 1–3 Fujitani et al have reported that corneal perforation developed 33 months after therapy. In the present study we report on late complications of mitomycin C treatment.

CASE REPORT
Four patients were included in this study (Table 1). All patients underwent pterygium excision and postoperative topical instillation of 0.04% mitomycin C four times a day for 2–3 weeks. The patients complained of ocular pain or irritation 18–25 years after treatment. Scleral ulceration with calcified plaque was found. After plaques were removed, uveal tissue bulged, and scleral patch grafts were successfully performed.

Table 1 Characteristics of patients

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Sex</td>
<td>F</td>
</tr>
<tr>
<td>Eye</td>
<td>R</td>
</tr>
<tr>
<td>Age at pterygium excision (years)</td>
<td>60</td>
</tr>
<tr>
<td>Mitomycin C, 0.04%</td>
<td>+</td>
</tr>
<tr>
<td>four times a day</td>
<td>+</td>
</tr>
<tr>
<td>duration (weeks)</td>
<td>2</td>
</tr>
<tr>
<td>Age at ocular irritation or pain (years)</td>
<td>78</td>
</tr>
<tr>
<td>Duration between mitomycin C and complaint (years)</td>
<td>18</td>
</tr>
<tr>
<td>Visual acuity at complaint</td>
<td>20/20</td>
</tr>
<tr>
<td>Scleral ulceration</td>
<td>+</td>
</tr>
<tr>
<td>Calculated plaque</td>
<td>+</td>
</tr>
<tr>
<td>Bacterial culture</td>
<td>–</td>
</tr>
<tr>
<td>Rheumatoid factor</td>
<td>–</td>
</tr>
<tr>
<td>Bulging uveal tissue after removal of plaque</td>
<td>+</td>
</tr>
<tr>
<td>Scleral patch graft</td>
<td>+</td>
</tr>
<tr>
<td>Further therapy</td>
<td>PE</td>
</tr>
<tr>
<td>Follow up (years)</td>
<td>5</td>
</tr>
<tr>
<td>Visual acuity at last visit</td>
<td>20/20</td>
</tr>
<tr>
<td>Good outcome</td>
<td>+</td>
</tr>
</tbody>
</table>

+ = yes; − = negative; PE = phacoemulsification of cataract and intraocular lens implantation.


Figure 1 Case 1. Postoperatively, a rough surfaced hard plaque is seen at the nasal side of the right eye. The conjunctival epithelium is defective, and the sclera is thin at the site of the plaque (A). Postoperatively, the conjunctiva covers the graft in the right eye (B).

Case 1
A 78 year old woman complained of ocular irritation in the right eye in January 1995. The patient had undergone excision of pterygium in the right eye, and topical instillation of 0.04% mitomycin C four times a day for 2 weeks was administered in 1977 at another eye clinic. Our examination disclosed a visual acuity of right eye 20/20 with correction. Her intraocular pressures were 12 mm Hg in both eyes. A rough surfaced whitish hard plaque, 6 x 4 mm, was seen at the nasal side of the right eye (Fig 1A). The conjunctival epithelium was defective and the sclera was thin at the site of the plaque. Wheel-like lenticular opacities were seen bilaterally. Both eyes appeared normal otherwise. Bacterial culture from a scraping sample of the plaque was negative. Laboratory test results including rheumatoid factor were negative or within normal range. On 2 February 1995 the patient underwent excision of the plaque. After the plaque (which was firmly adherent to the underlying sclera) was excised the uveal tissue bulged. A patch graft, 7 x 5 mm, of full thickness sclera, was obtained from an eyebank and preserved in 99% ethanol at -20°C.
rinsed in 0.9% NaCl solution just before use, and secured with 10-0 nylon sutures. Conjunctiva was pulled down over the graft and was sutured with 8-0 polyglactin. The removed plaque stained with alizarin red, suggesting calcification. Thereafter, the patient had no complaints of irritation. Five years later the patient had good visual acuity in both eyes. The scleral graft was covered with conjunctiva in the right eye (Fig 1B).

COMMENT

In our patients, ocular irritation, or pain associated with scleral ulceration with calcified plaque occurred more than 10 years after treatment. To our knowledge, calcified plaque development after simple excision of pterygium is rare. Scleral ulceration with calcified plaque in our patients was quite similar to that reported by Fujitani et al.\(^4\) It is possible that scleral lesions in our patients may be secondary to the topical use of 0.04% mitomycin C. To avoid complications, mitomycin C at a lower concentration should be applied for a shorter period of time, as previously described.\(^3\) Recently, mitomycin C has been used as adjunct in trabeculectomy. Eyes treated with mitomycin should be carefully observed for longer than 20 years. We believed that scleral ulceration with calcified plaque following topical mitomycin C instillation could be treated with scleral patch grafting.

SEJI HAYASAKA
YOSHIO IWASA
YASUNORI NAGAKI
CHIHARU KADOI
MASAYUKI MATSUMOTO
YORIKO HAYASAKA
Department of Ophthalmology, Toyama Medical and Pharmaceutical University, Toyama, Japan

Correspondence to: Dr Seiji Hayasaka, Department of Ophthalmology, Toyama Medical and Pharmaceutical University, 2630 Sugitani, Toyama, 930-0194 Japan
ophthal@ms.toyama-mpu.ac.jp
Accepted for publication 18 April 2000


Contributors please note:

Communications from all countries except the UK and Republic of Ireland should be sent to Professor C Hoyt, Editor, British Journal of Ophthalmology, University of California, Department of Ophthalmology, 10 Kirkham Street, K 301, San Francisco, CA 94143-0730, USA (tel: 001 415 502-6871; fax: 001 415 514-1521).

Manuscripts from the UK and the Republic of Ireland should be sent to Professor Andrew Dick, UK Editor, British Journal of Ophthalmology, Division of Ophthalmology, University of Bristol, Lower Maudlin Street, Bristol BS1 2LX (tel: +44 (0) 0117 929-4496; fax: +44 (0)117 929-4607).