

## LETTERS TO THE EDITOR

### Bilateral circumscribed haemangioma of the choroid not associated with systemic vascular syndrome

EDITOR.—Circumscribed choroidal haemangioma (CCH) is considered congenital, vascular, relatively rare hamartoma which typically occurs as a localised, monolateral lesion in patients without other vascular malformation. This tumour generally is discovered in adulthood and it is located in the macular area. CCH may be ophthalmoscopically confused with amelanotic melanoma, metastatic tumour, choroidal osteoma, disciform scar, serous detachment, and central serous chorioretinopathy, but may be differentially diagnosed with fluorescein angiography (FA), indocyanine green angiography (ICGA),<sup>1-3</sup> ultrasonography, and periodic observation.<sup>4</sup> The bilateral CCH localisation represents an extremely uncommon condition which, in literature, has been only reported in association with Sturge-Weber syndrome<sup>5,6</sup> or Klippel-Trenaunay-Weber syndrome.<sup>7</sup> To the best of our knowledge, this is the first documented case of bilateral CCHs in the absence of any other evidence of vascular systemic abnormalities.

#### CASE REPORT

A 81 year old white man was referred to our institution in June 1999 to undergo conservative therapy because of malignant choroidal melanoma of the left eye. He reported a 6 month history of bilateral, progressive reduction of the central vision, greater in his left eye. His best corrected visual acuity was 20/30 in the right eye and 20/40 in the left. Biomicroscopy of the anterior segment did not reveal any notable alterations with the exception of a bilateral nuclear cataract, more evident in the

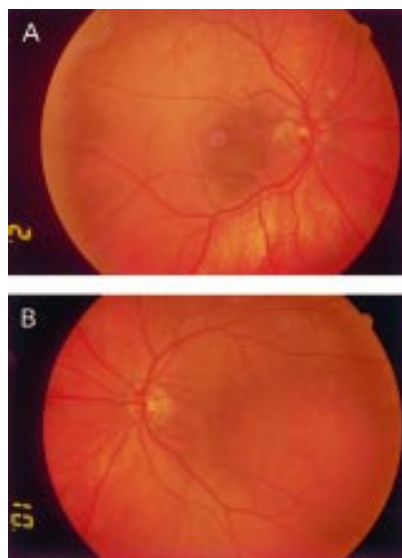


Figure 1 (A) Photograph of the right macular area reveals an irregular appearance of the retinal surface. (B) Photograph of the left temporal posterior pole shows a lesion, about 5 optic disc diameters in size and red-orange in colour.

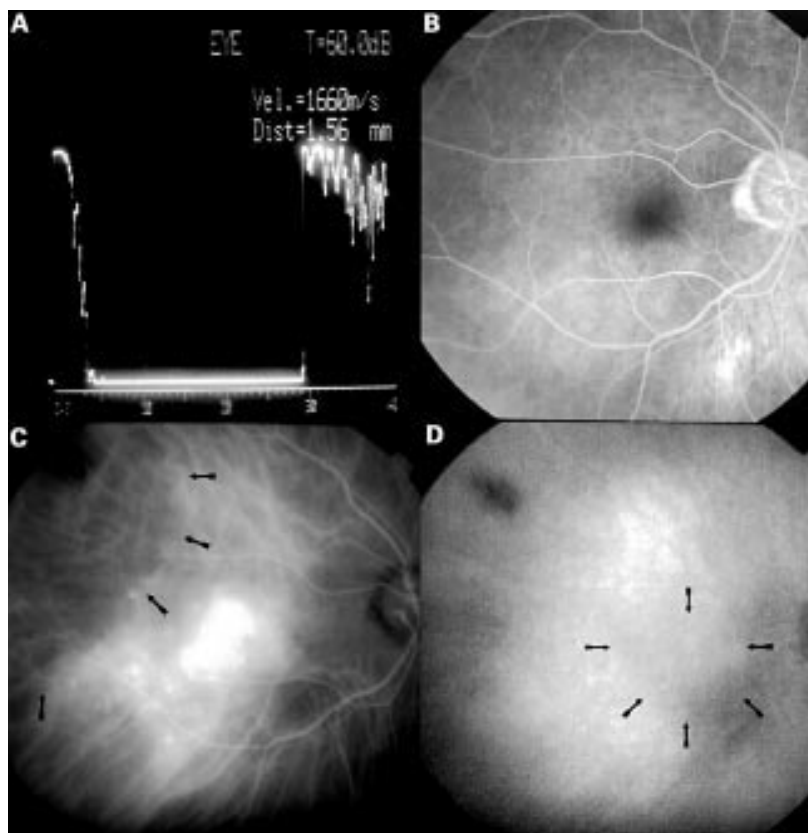


Figure 2 (Right eye). (A) Standardised A-scan ultrasonography at 1660 m/s shows the high internal reflectivity of the choroidal solid lesion at the level of the macular area. The maximum thickness of this small circumscribed lesion is 1.56 mm. (B) Late phase fluorescein angiogram reveals a hyperfluorescent area inferiorly located at the inferior posterior pole, secondary to a degenerative change of the retinal pigment epithelium. (C) Early indocyanine green photograph documents the filling of the choroidal macular haemangioma near to a sector of reduced choroidal perfusion (arrows). (D) Late indocyanine green angiogram shows an ill defined, relative macular hypofluorescence, corresponding to the previously described hyperfluorescent area, reliably the result of the clearing of the dye from the small haemangioma (arrows).

left eye. Intraocular pressure was 18 mm Hg in both eyes. Ophthalmoscopic examination of the left temporal posterior pole showed a lesion, about five optic disc diameters in size and red-orange in colour (Fig 1B), while, in the right macular area, an irregular appearance of the retinal surface was detected (Fig 1A). Bilateral B-scan echography confirmed the presence of a dome-shaped solid lesion, with regular profile and without choroidal cup, in the left eye, revealing a small solid lesion also in the right posterior choroid. Standardised A-scan ultrasonography documented that the maximum thickness of these solid lesions was 1.56 mm in the right eye (Fig 2A) and 3.32 mm in the left (Fig 3A). In the left eye the high and regular internal reflectivity of the lesion was consistent with the presence of a benign tumour, reliably of an angiomatous type. FA did not detail any significant abnormality in the right posterior pole (Fig 2B), showing an irregular fluorescence of the orange-coloured lesion previously described in the left eye (Fig 3B). ICGA confirmed the diagnosis of CCH of the left eye (Fig 3C, D) and documented an early hyperfluorescence, followed by a relative decrease in fluorescence ("washout"), corresponding to the echographic findings observed in the right macula (Fig 2C, D). The patient underwent chest x ray, abdominal and chest computed tomographies, total body scintigraphy, liver ultrasonography, blood, and urine analyses.

These investigations did not show any abnormality, reliably excluding the possible metastatic origin of the bilateral choroidal lesions. In the course of a 15 month follow up period, we periodically reassessed this patient, and did not diagnose any ocular or systemic modification.

#### COMMENT

Atypical CCH can cause differential diagnostic problems by its appearance at the time of presentation. Moreover, bilateral choroidal localisation of tumoral lesions raises the question about their primary or metastatic onset.<sup>8</sup> At our department we observed approximately one haemangioma of the choroid for every 15 malignant melanomas, referred to us yearly for conservative treatment. In spite of this relatively high frequency of haemangioma, this represents the first case in whom we diagnosed a bilateral circumscribed vascular hamartoma, which was not associated with any systemic syndrome. During the mid-term follow up (15 months) there were neither ocular nor systemic significant modifications. The echographic<sup>9</sup> and ICGA<sup>1-3,10</sup> features of these choroidal lesions, together with the lack of neoplasm or vascular abnormality in another part of the body, lead us to confirm the first documented diagnosis of bilateral CCHs. Last but not least, our findings demonstrate that FA and echography are not always capable of documenting the specific characteristics of small CCH; thus, when this kind of lesion is

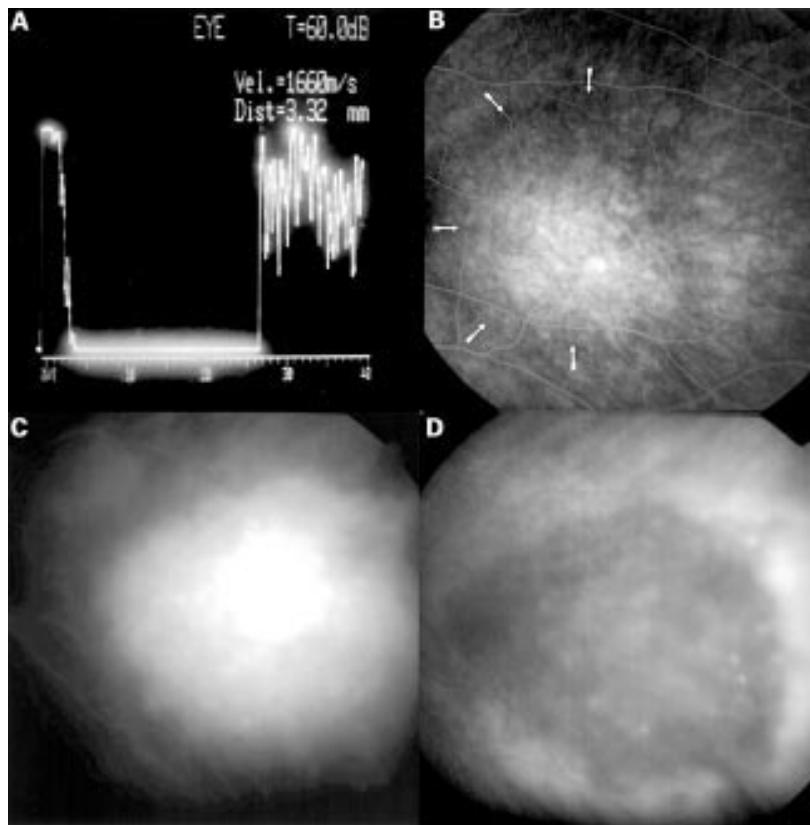


Figure 3 (Left eye). (A) Standardised A-scan ultrasonography at 1660 m/s demonstrates the temporal paramacular solid lesion of the choroid, with its high and regular internal reflectivity, consistent with the presence of an angiomatous benign lesion. The maximum thickness of this circumscribed choroidal haemangioma is 3.32 mm. (B) Late phase fluorescein angiogram shows an ill defined hyperfluorescent and hypofluorescent area in correspondence with choroidal haemangioma (arrows). (C) Early indocyanine green photograph reveals a rapid and complete fill up of the lesion. The haemangioma has a "mulberry appearance" at the stage of maximal fluorescence. (D) Late indocyanine green angiogram shows clearing of the dye from the tumour, associated with diffusion into the choroidal and subretinal space ("washout" phenomenon).

suspected, ICGA represents the most important non-invasive tool for the diagnosis<sup>2</sup> to differentiate amelanotic choroidal melanoma, choroidal metastasis, and choroidal haemangioma.<sup>10</sup>

PERRI PAOLO  
INCORVAIA CARLO  
COSTAGLIOLA CIRO  
PARMEGGIANI FRANCESCO  
GIUSEPPE LAMBERTI  
PADUANO BEATRICE  
SEBASTIANI ADOLFO

Department of Ophthalmology, University of Ferrara,  
Ferrara, Italy

Correspondence to: Paolo Perri, MD, Sezione di Clinica Oculistica, Dipartimento di Discipline Medico-Chirurgiche della Comunicazione e del Comportamento, Università degli Studi di Ferrara, Corso Giovecca 203, 44100 Ferrara, Italy

sbd@dns.unife.it

Accepted for publication 5 March 2001

- Piccolino FC, Borgia L, Zinicola E. Indocyanine green angiography of circumscribed choroidal hemangiomas. *Retina* 1996;16:19-28.
- Arevalo JF, Shields CL, Shields JA *et al*. Circumscribed choroidal hemangioma: characteristic features with indocyanine green videoangiography. *Ophthalmology* 2000;107:344-50.
- Schalenbourg A, Piguet B, Zografos L. Indocyanine green angiographic findings in choroidal hemangiomas: a study of 75 cases. *Ophthalmologica* 2000;214:246-52.
- Nguyen AT, Anderson SF, Townsend JC. Circumscribed choroidal hemangioma. *J Am Optom Assoc* 1995;66:640-5.

- Scott IU, Alexandrakis G, Cordahi GJ *et al*. Diffuse and circumscribed choroidal hemangiomas in a patient with Sturge-Weber syndrome. *Arch Ophthalmol* 1999;117:406-7.
- Cheung D, Grey R, Rennie I. Circumscribed choroidal haemangioma in patient with Sturge-Weber syndrome. *Eye* 2000;14:238-40.
- Brod RD, Shields JA, Shields CL *et al*. Unusual retinal and renal vascular lesions in the Klippel-Trenaunay-Weber syndrome. *Retina* 1992;12:355-8.
- Perri P, Chiarelli M, Monari P, *et al*. Choroidal metastases. Echographic experience from 42 patients. *Acta Ophthalmol Suppl* 1992;204:96-8.
- Verbeek AM, Koutentakis P, Deutman AF. Circumscribed choroidal hemangioma diagnosed by ultrasonography. A retrospective analysis of 40 cases. *Int Ophthalmol* 1995-96;19:185-9.
- Shields CL, Shields JA, De Potter P. Patterns of indocyanine green videoangiography of choroidal tumours. *Br J Ophthalmol* 1995;79:237-45.

#### Tractional ciliary body detachment, choroidal effusion, and hypotony caused by severe anterior lens capsule contraction following cataract surgery

EDITOR.—Continuous curvilinear capsulotomy (CCC) first described by Gimble and Neuhann<sup>1</sup> has become the procedure of choice for cataract extraction by phacoemulsification. Untoward effects of capsulorhexis have not been frequently noted. Davidson first described capsular contraction syndrome as an exaggerated reduction in anterior capsulotomy and capsular bag diameter after cataract

surgery.<sup>2</sup> This specific clinical entity of "capsular contraction syndrome" is usually associated with a reduction in the capsular opening, malposition of the opening, reduction in the equatorial capsular diameter, and possibly intraocular lens (IOL) displacement.

Tractional ciliary body detachment and associated hypotony is an uncommon complication of severe anterior lens capsular contraction. Only three such cases have been reported in the literature.<sup>3,4</sup> We report a case of tractional ciliary body detachment caused by a severe anterior lens capsule fibrosis, in which Nd:YAG laser anterior capsulotomy was effective in relieving the traction caused by the capsular contraction. We illustrate the value of ultrasound biomicroscopy (UBM) in the diagnosis and management of such conditions.

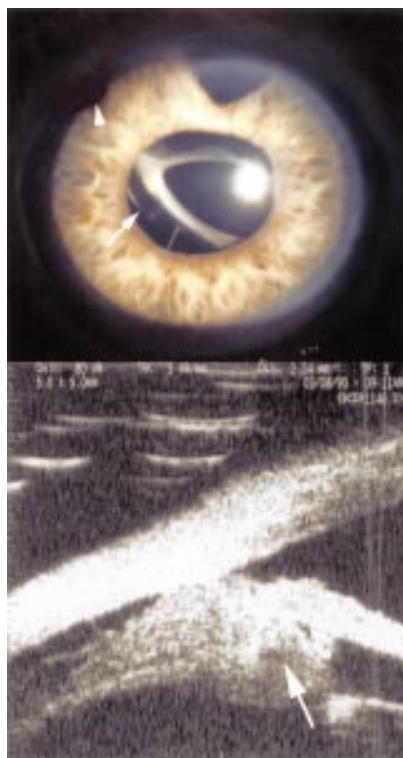
#### CASE REPORT

A 72 year old woman with primary open angle glaucoma and previous bilateral trabeculectomies (performed twice in the left eye) was followed up in our clinic since December 1999 for an ischaemic central vein occlusion in her right eye. She had a dense cataract in her left eye, which prevented the view of the fundus. The biometry of the left eye showed an axial length of 22.60 mm. Preoperatively intraocular pressures were 15 mm Hg in both eyes. She underwent an uncomplicated phacoemulsification through a superotemporal limbal wound. A capsulorhexis of about 5 mm was fashioned. A foldable three piece silicone IOL with poly(methylmethacrylate) (PMMA) haptics (Allergan SI40 NB) was implanted "in the bag." The lens had an optic diameter of 6.0 mm and a haptic diameter of 13.0 mm. In the immediate postoperative period she was noted to have a well centred IOL "in the bag" and fundus showed an inferior hemispherical vein occlusion involving the macula in the left eye. At this time she had a visual acuity of counting fingers at 2 metres in her right eye and 6/60 in her left eye.

Two and a half months following her cataract surgery she was referred by an optician with deterioration of vision in her left eye. Visual acuity was counting fingers at 2 metres in both eyes. Slit lamp biomicroscopy of the left eye showed a deep and quiet anterior chamber. Severe contraction of the CCC opening with eccentric displacement of the CCC orifice was noted and the IOL was displaced superiorly (Fig 1, above). Gonioscopy showed an open iridocorneal angle. There was no evidence of any iris changes or changes at the pupillary border, consistent with pseudoexfoliation in either eyes. Goldmann applanation tonometry revealed an intraocular pressure of 5 mm Hg in the left eye and 14 mm Hg in the right. Posterior segment evaluation of the left eye showed diffuse choroidal effusion. This was confirmed by B-scan ultrasonography, which showed total choroidal detachment. Ultrasound biomicroscopy (UBM, 50 MHz probe, Humphrey) showed a ciliary body detachment with central rotation of the ciliary body, as the underlying cause of the hypotony (Fig 1, below).

A neodymium: YAG (Nd:YAG) laser anterior capsulotomy was performed. Four relaxing radial anterior capsulotomy cuts were made at 2, 5, 8, and 10 o'clock. The Nd:YAG capsulotomy comprised 50 shots with a power of 1.4 mJ each. During the procedure the anterior capsule was noted to be thick. Immediate widening of the CCC orifice was noted following this procedure (Fig 2, above). The IOL also returned to a well centred position.





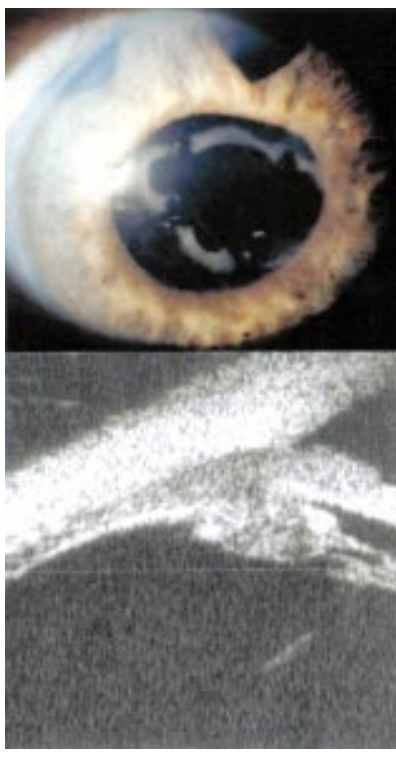
**Figure 1** (Above) Anterior segment photograph showing severe anterior capsular contraction with superior displacement of the IOL (arrow). Note the partly visible iridectomy (arrowhead). (Below) Ultrasound biomicroscopy showing ciliary body detachment with central rotation of the ciliary body (arrow).

Topical prednisolone acetate 1% (Predforte, Allergan, Westport, Ireland) four times a day was prescribed to the left eye. Three days after the anterior capsulotomy, the visual acuity remained at counting fingers at 2 metres in both eyes. The left eye showed a quite deep anterior chamber, well centred IOL and fundus showed resolution of the choroidal effusion, which was confirmed by B-scan ultrasonography. UBM examination showed reattachment of the ciliary body (Fig 2, below) and applanation tonometry showed an intraocular pressure of 14 mm Hg.

#### COMMENT

Capsulorhexis has become the preferred method of anterior capsulotomy, and untoward effects have not often been noted. Nevertheless, distinct complications of continuous tear capsulotomy are now recognised. This includes capsular bag hyperdistension, shrinkage of the anterior capsule opening with visual loss, and/or IOL decentration and lens epithelial hyperproliferation on the posterior lens capsule.

In 1993 Davidson first described the capsule contraction syndrome as a complication of continuous curvilinear capsulorhexis.<sup>2</sup> This syndrome is characterised by an exaggerated reduction in the equatorial diameter of the capsular bag, fibrosis of the anterior capsule, and shrinkage of its opening. It has been associated with various eye diseases including pseudoexfoliation,<sup>2,5</sup> pars planitis,<sup>2,6</sup> low grade vitritis,<sup>2</sup> high myopia,<sup>2,6</sup> retinitis pigmentosa,<sup>7</sup> and myotonic dystrophy.<sup>8</sup> It has also been seen in elderly patients. Commonly observed expressions of these diseases are weakened zonules or a chronic inflammation.



**Figure 2** (Above) Anterior segment photograph showing the radial capsulotomies and the widened anterior capsule. (Below) Post laser, ultrasound biomicroscopy showing reattached ciliary body.

In general, shrinkage of the anterior capsule according to Davidson<sup>2</sup> is produced by an imbalance between the centrifugal and centripetal forces on the capsular bag. Although the pathogenic mechanism responsible for excessive capsule fibrosis and contracture are not well understood, several histopathological studies have identified the cell types associated with pseudophakic fibrosis.<sup>8-10</sup> Frezzotti *et al*<sup>11</sup> attributed constriction of the anterior capsule opening to fibrogenic transformation of the subcapsular and equatorial lens epithelial cells (LECs). Nishi and Nishi<sup>7</sup> suggested that this fibrosis might be induced by interleukin 1 or 6 and other cytokines synthesised by residual LECs, which in turn affect the epithelial cells in an autocrine manner.

The following three main factors may account for anterior capsule contraction: (1) IOL material, (2) IOL design, and (3) CCC opening. The sphincter effect of an intact capsulorhexis seems to be important in creating significant capsule shrinkage. Some authors believe that the initial diameter of the CCC is an important factor in its pathogenesis. It is postulated that the more epithelium that is left the greater the potential for capsule contraction.<sup>12,13</sup> The IOL optic composition may influence the development of anterior capsule fibrosis. Davidson<sup>2</sup> suggested that one piece PMMA IOL with a large optic would help counterbalance the centripetal forces of capsular fibrosis. Werner *et al*<sup>14</sup> in their histopathological study comparing different IOL styles found that the rate of anterior capsule contraction was relatively high with plate-haptic silicone lenses. The lowest rate was noted with the three piece acrylic optic PMMA haptic IOLs. In their histopathological grading of anterior capsule contraction with IOL materials and designs, silicone optic-PMMA haptic IOL as used in this case

was rated third after plate haptic silicone lenses with large holes and small holes.

Anterior capsular shrinkage shifts the relative position of the lens equator, moving it to a more anterior location. This centripetal movement induces an inward pulling force on the zonular apparatus. Depending on the strength of this apparatus, a counteracting force might result. We feel that the smaller capsulorhexis size and the use of silicone IOL predisposed our patient to develop severe anterior lens capsule contraction. Severe anterior lens capsule contraction can exert continuous traction on the ciliary body resulting in a ciliary body detachment. In this case Nd:YAG radial anterior capsulotomy was helpful in relieving the phimosis and thereby removing the tractional force on the ciliary body.

The authors have no proprietary interest in any of the products described in this paper.

SATHISH SRINIVASAN  
JAN VAN DER HOEK  
FRANK GREEN  
HATEM R ATTA

Department of Ophthalmology, Aberdeen Royal  
Infirmary, Grampian University Hospitals,  
Aberdeen, UK

Correspondence to: Sathish Srinivasan, Tennent  
Institute of Ophthalmology, Gartnavel General  
Hospital, 1053, Great Western Road, Glasgow  
G12 0YN, UK

sathish@ukgateway.net

Accepted for publication 4 April 2001

- Gimble HV, Neuhann T. Development, advances, and methods of the continuous circular capsulorhexis technique. *J Cataract Refract Surg* 1990;16:31-7.
- Davidson JA. Capsule contraction syndrome. *J Cataract Refract Surg* 1993;19:582-9.
- Salzmann J, Khaw PT, Laidlaw A. Choroidal effusion and hypotony caused by severe anterior lens capsule contraction after cataract surgery. *Am J Ophthalmol* 2000;129:253-4.
- Lanzl IM, Kopp C. Ciliary body detachment caused by capsule contraction. *J Cataract Refract Surg* 1999;25:1412-14.
- Davidson JA. Structural features of intraocular lenses designed for use after capsulorhexis (letter). *J Cataract Refract Surg* 1993;19:112-16.
- Hansen SO, Crandall AS, Olson RJ. Progressive constriction of the anterior capsular opening following intact capsulorhexis. *J Cataract Refract Surg* 1993;19:77-82.
- Nishi O, Nishi K. Intraocular lens encapsulation by shrinkage of the capsulorhexis opening. *J Cataract Refract Surg* 1993;19:544-5.
- Pavilac MA, Foster CS, Kowal VO, *et al*. Peripseudophakic membrane; pathological features. *Arch Ophthalmol* 1993;111:240-4.
- Mietz H, Brunner R, Addicks K, *et al*. Fibrosis adjacent to the anterior lens capsule after extracapsular cataract extraction. *Int Ophthalmol* 1993;17:321-6.
- Ayaki M, Ohara K, Ibaraki N, *et al*. The outgrowth of lens epithelial cell on to the anterior capsule after intraocular lens implantation (letter). *Am J Ophthalmol* 1993;115:668-9.
- Frezzotti R, Caporossi A, Mastrangelo D, *et al*. Pathogenesis of posterior capsular opacification. Part II: Histopathological and in vitro culture findings. *J Cataract Refract Surg* 1990;16:353-60.
- Hayashi K, Hayashi H, Nakao F, *et al*. Reduction in the area of the anterior capsule opening after polymethylmethacrylate, silicone and soft acrylic intraocular lens implantation. *Am J Ophthalmol* 1997;123:441-7.
- Kimura W, Yamanishi S, Kimura T, *et al*. Measuring the anterior capsule opening after cataract surgery to assess capsule shrinkage. *J Cataract Refract Surg* 1998;24:1235-8.
- Werner L, Pandey SK, Gomez ME, *et al*. Anterior capsule opacification. A histopathological study comparing different IOL styles. *Ophthalmology* 2000;107:463-71.

### Angle closure in fellow eye with prophylactic pilocarpine treatment

EDITOR.—Prophylactic pilocarpine is often used in patients presenting with unilateral primary acute angle closure until definitive treatment with laser peripheral iridotomy can be performed.<sup>1</sup>

We present two cases of unilateral primary acute angle closure glaucoma treated with prophylactic pilocarpine that subsequently developed angle closure in the fellow eye within 24 hours of admission.

#### CASE REPORTS

##### Case 1

An 81 year old woman was referred from the orthopaedics department with increasing pain and redness in the right eye. Visual acuities were hand movements on the right and 6/24 improving to 6/9 with pinhole on the left. The right cornea was oedematous with intraocular pressures (IOP) of 56 mm Hg in the right and 17 mm Hg in the left. The iridocorneal angle was closed on the right eye, and narrow on gonioscopy (grade 1 inferiorly and closed superiorly) on the left, with bilateral moderate nucleosclerotic cataracts.

She was treated with intravenous Diamox 500 mg, topical levobunolol, 2% pilocarpine, and dexamethasone 0.1%. Review 1 hour later showed decreased oedema with IOP of right eye 24 mm Hg and left eye 15 mm Hg. Prophylactic 2% pilocarpine four times daily was started in the fellow eye and she was admitted to hospital. On review 8 hours after admission her IOP was 16 mm Hg in the right eye and 46 mm Hg in the left. The left cornea had minimal oedema and closed iridocorneal angle on gonioscopy.

A Nd:YAG laser peripheral iridotomy was performed in the left eye that night with subsequent resolution of the attack.

##### Case 2

A 46 year old hypermetropic woman (right eye +2.75DS/-0.5 × 160 left eye +4.5DS) with no significant ocular history presented to casualty with intermittent visual disturbance, followed by pain, redness, and decreased vision in the left eye. Visual acuity on presentation was right eye 6/9 and left eye 6/24. The left cornea was hazy with a shallow anterior chamber and IOP of 62 mm Hg. The right iridocorneal angle was narrow but open with pigmented grade 1 angle on gonioscopy. She was admitted and treated with topical apraclonidine, levobunolol, dexamethasone, and intravenous Diamox 500 mg. Pilocarpine 4% every 15 minutes for 1 hour was used in the left eye and a single dose of 4% pilocarpine was instilled in the right eye.

On review 2 hours after admission IOP was 45 mm Hg in the right eye and 26 mm Hg in the left. The right cornea remained clear, the anterior chamber appeared shallow, and repeat gonioscopy showed a closed iridocorneal angle on the right. The angle was opened by compression with a Zeiss gonioprism, and she underwent a Nd:YAG laser peripheral iridotomy initially in the right eye and subsequently in the left eye the following day.

#### COMMENT

The management of the fellow eye in acute glaucoma is controversial. Although Nd:YAG peripheral iridotomy has established itself as the treatment of choice,<sup>2,3</sup> the use of prophylactic pilocarpine until formal iridotomy can occur remains controversial. In a survey of the

members of the American Glaucoma Society pilocarpine was used as the treatment of the fellow eye when iridotomy was deferred by more than half the respondents, whereas close observation was the choice of a third.<sup>1</sup> Pilocarpine results in miosis thereby pulling the peripheral iris from the anterior chamber angle, relieving pupillary block and increasing aqueous outflow facility. Of more concern is the possibility of a paradoxical effect of pilocarpine by a dose dependent shallowing of the anterior chamber, potentially precipitating angle closure in compromised eyes.<sup>4,5</sup>

The above cases highlight concerns on the use of prophylactic pilocarpine (especially in higher concentrations) to the fellow eye. In these cases, prophylactic treatment with pilocarpine did not prevent and probably contributed to angle closure.

Early prophylactic peripheral iridotomy without pilocarpine treatment may be the treatment of choice.

Q MOHAMED  
D K FAHEY  
R M MANNERS  
Bristol Eye Hospital, Lower Maudlin Street, Bristol  
BS1 2LX, UK

Correspondence to: Mr Mohamed qureshm@yahoo.com

Accepted for publication 5 November 2000

- 1 Davidorf JM, Bajer ND, Derick R. Treatment of the fellow eye in acute angle-closure glaucoma: a case report and survey of the members of the American Glaucoma Society. *J Glaucoma* 1996;5:228-32.
- 2 Schwenn O, Sell F, Pfeiffer N, et al. Prophylactic Nd:YAG-laser iridotomy versus surgical iridectomy: a randomised, prospective study. *Ger J Ophthalmol* 1995;4:374-9.
- 3 Fleck BW, Wright E, Fairley EA. A randomised prospective comparison of operative peripheral iridectomy and Nd:YAG laser iridotomy treatment of acute angle closure glaucoma: 3 year visual acuity and intraocular pressure control outcome. *Br J Ophthalmol* 1997;81:884-8.
- 4 Abrahamson DH, Coleman DJ, Forbes M, et al. Pilocarpine: effect on the anterior chamber and lens thickness. *Arch Ophthalmol* 1972;87:615-20.
- 5 Abrahamson DH, Chang S, Coleman DJ, et al. Pilocarpine induced lens changes: an ultrasonic biometric evaluation of dose response. *Arch Ophthalmol* 1974;92:464.

### Keratolysis in a patient with pemphigus vulgaris

EDITOR.—Pemphigus vulgaris is an autoimmune, blistering disease of the skin and mucous membranes.<sup>1</sup> The characteristic ocular finding is conjunctivitis, and corneal involvement is rare.<sup>2,3</sup> We present a case with pemphigus vulgaris with severe keratolysis that required a corneal transplantation.

#### CASE REPORT

A 41 year old man had suffered from pemphigus vulgaris for 2 years, and prednisolone 40 mg/day and cyclosporine 300 mg/day had been prescribed. He was admitted to the Hamamatsu University Hospital on 15 March 1999 with an acute exacerbation of the symptoms because of non-compliance with the corticosteroid therapy. He returned on 17 March 1999 because of increased discharge and visual loss in both eyes. His visual acuity was 20/20 right eye and 20/20 left eye, and his intraocular pressure was 24 mm Hg right eye and 20 mm Hg left eye. No remarkable findings were observed in both visual fields and optic discs. Slit lamp examination showed mild erosions of his eyelid and cornea. The treatment with prednisolone 40 mg/day and cyclosporine 300 mg/day was continued.



Figure 1 Photograph of the anterior segment of the right eye on 13 April 1999.

He returned on 9 April 1999 because of acute deterioration of vision in both eyes. His visual acuity was light perception in the right eye and counting fingers in the left. The right conjunctiva showed marked oedema and the anterior chamber was flat. Slit lamp examination showed that the lower two thirds of the right cornea had eroded leaving only Descemet's membrane and endothelium (Fig 1). The left conjunctiva showed mild oedema and slit lamp examination demonstrated anterior stromal opacities in the lower half of the cornea and bulla-like central corneal epithelial changes. Ofloxacin ointment was prescribed for both eyes.

The opacity of the right corneal stroma gradually increased, and scar-like tissue formed in the area of the erosion. Slit lamp examination showed that Descemet's membrane was touching the iris and lens. The corneal bullous degeneration in the left eye formed an erosion. After the corneal erosion and conjunctival oedema resolved, faint stromal opacities were observed in the region of the corneal lesion in the left eye.

Because of the overall improvement of the cornea of the right eye, an 11 mm right penetrating keratoplasty was performed on 22 September 1999. The dislocated lens was extracted and anterior vitrectomy was also performed. His visual acuity on 11 November 1999 was improved to 8/200 with +9.0 -2.5 × 65° D right eye, and 20/25 with -3.0 D -3.75 × 180° D left eye.

#### COMMENT

Corneal involvement is a rare complication in patients with pemphigus vulgaris. Severe corneal involvement has never been reported except in the case of a 56 year old man with severe ocular involvement including conjunctivitis, corneal ulceration, and perforation despite immunosuppressive therapy.<sup>4</sup> Although a causative organism was not isolated, the authors suggested that the complications were due to an infectious agent.

Two mechanisms have been suggested to cause the corneal erosion—bacteria or other pathogenic organisms that infect the cornea because of the epithelial defect and tear film disorder brought on by the corticosteroid and immunosuppressive therapy. Although the culture obtained from right ocular discharge before starting ofloxacin ointment showed a negative result, we could not deny the bacterial infection. We did not perform a bacterial or viral culture or polymerase chain reaction examinations using a corneal sample.

The second mechanism is an autoimmune mechanism against one of the intercellular adhesion molecule—for example, desmoglein (Dsg). The patient was diagnosed as pemphigus vulgaris by histological examination, direct immunofluorescent staining of the skin



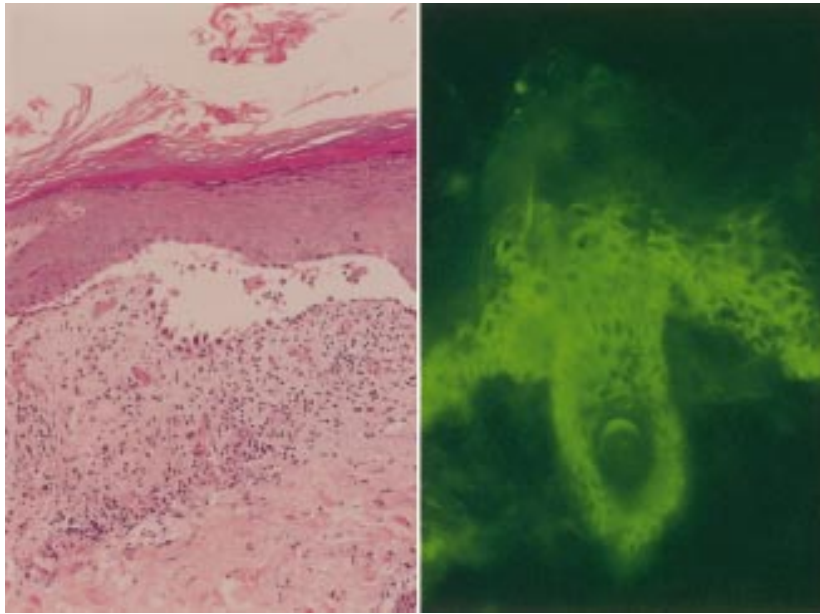


Figure 2 Histological examination by haematoxylin and eosin staining of lesional skin disclosed intraepidermal clefts which contained several acantholytic cells (left). The direct immunofluorescent staining of the skin showed intercellular deposition of immunoglobulin G (right).

showing intracellular deposition of immunoglobulin G and high titres of circulating anti-Dsg 3 and anti-Dsg 1 antibodies (Fig 2). Because the cornea usually does not have Dsg 3 but Dsg 2,<sup>5</sup> an autoimmune mechanism cannot be considered. However, prolonged epithelial defect by limbal damage may have resulted in the corneal erosion because of the expression of Dsg 3 by the epithelium of the corneal limbus. Although no infection was observed in both corneas, the association with an infectious mechanism may be involved in the pathogenesis of corneal erosion in our case.

MASAHIRO SUAMI  
MASARU KATO  
KENRO KOIDE  
YOSHIMASA USAMI  
NORIMASA HATA  
HIROYUKI MACHIDA  
YOSHIHIRO HOTTA

Department of Ophthalmology, Hamamatsu University,  
School of Medicine, Japan

KENTARO MATSUMOTO  
MASAHIRO TAKIGAWA  
Department of Dermatology

Correspondence to: Yoshihiro Hotta, MD, Department of Ophthalmology, Hamamatsu University School of Medicine, 3600 Handa-cho, Hamamatsu, 431-3192, Japan

hotta@hama-med.ac.jp.

Accepted for publication 16 April 2001

- Jordan RE. Pemphigus. In: Fitzpatrick TB, Eisen AZ, Wolff K, *et al*, eds. *Dermatology in general medicine*. New York: McGraw-Hill, 1999:571–9.
- Hodak E, Kremer I, David M, *et al*. Conjunctival involvement in pemphigus vulgaris: a clinical, histopathological and immunofluorescence study. *Br J Dermatol* 1990;123:614–20.
- Smith RJ, Manche EE, Mondino BJ. Ocular cicatricial pemphigoid and ocular manifestations of pemphigus vulgaris. In: Smolin G, ed. *International ophthalmology clinics, ocular manifestations of dermatologic disorders*. Philadelphia: Lippincott-Raven, 1997;37:63–75.
- Baykal HE, Pleyer U, Sonnichsen K, *et al*. Severe ocular involvement in pemphigus vulgaris. *Ophthalmology* 1995;92:854–7.
- Messent AJ, Blissett MJ, Smith GL, *et al*. Expression of a single pair of desmosomal glycoproteins renders the corneal epithelium unique amongst stratified epithelium. *Invest Ophthalmol Vis Sci* 2000;41:8–15.

#### Isolated episcleral plasmacytoma mimicking episcleritis in a patient with benign monoclonal gammopathy

EDITOR,—We present the unique case of a patient with an isolated plasmacytoma of the episclera mimicking a painful episcleritis. Plasmacytomas usually grow in the bone marrow probably because of their special homing receptors<sup>1</sup>—for example,  $\alpha_4\beta_1$  integrin.<sup>2</sup> Solitary plasmacytic tumours outside the bone marrow are rare. They mostly involve the oropharynx and the upper respiratory tract, but have also been encountered in the lids, the orbit, and the palpebral conjunctiva.<sup>3–5</sup> Only one case of a solitary epibulbar plasmacytoma with intraocular invasion has been reported yet.<sup>6</sup>

#### CASE REPORT

A 61 year old patient presented with an "inflammatory" episcleral nodule within the lower temporal quadrant and mild pain in his left eye (Fig 1), which had already lasted 5 months and had been diagnosed as episcleritis. There was no evidence of rheumatic disease; ANA and ANCA were negative. Neither dexamethasone eyedrops nor oral fluocortolone (60 mg) were helpful, thus an excisional biopsy was performed. The tumour seemed to be attached only to Tenon's capsule and could easily be removed.



Figure 1 Conjunctival and episcleral injection and flat subconjunctival tumour mass at the temporal part of the left eye.

Surprisingly, the histopathological examination revealed a monomorphous infiltrate of plasma cells with characteristic eccentric nuclei and basophilic cytoplasm (Fig 2). The cells stained positively with the plasma cell marker VS38 and showed a kappa light chain restriction. The proliferation rate was increased with an MIB1 positivity of 5%. Immunohistochemistry for CD20, IgA, IgD, and IgG was negative.

Three months later an IgA lambda monoclonal gammopathy with an IgA level of 5.6 g/l (normal 0.7–4.0 g/l) was found, but neither bone marrow biopsy nor bone scan showed any abnormalities. A local recurrence of the episcleral tumour with infiltration of the lateral rectus muscle 6 months after the initial diagnosis, was irradiated with 46 Gy over 2 months. The tumour resolved completely and did not recur. The IgA level of the serum ranged between 5.2 and 6.7 g/l over a period of almost 3 years.

#### COMMENT

Our case is unique in several respects. The isolated extramedullary plasmacytoma of our patient mimicked an episcleritis with mild pain and inflammatory reaction. As it turned out to be resistant to anti-inflammatory therapy a biopsy was performed which finally allowed for the correct diagnosis. Thus solitary plasmacytoma has to be included in the spectrum of ocular masquerade syndrome.<sup>7</sup>

Another interesting aspect is that our patient developed a monoclonal gammopathy, apparently not related to the isolated episcleral plasmacytoma. The latter showed a kappa light chain restriction, whereas in the serum the level of IgA lambda was increased. As a thorough general examination did not reveal any signs of systemic disease or isolated plasmacytoma elsewhere, the monoclonal component was attributed to a monoclonal gammopathy of unknown significance (MGUS) which is considered as a benign or premalignant disorder.

Lymphocytes and plasma cells of the MALT, especially the GALT, are characterised by integrin  $\alpha_4\beta_7$ ,<sup>8</sup> instead of integrin  $\alpha_4\beta_1$ , which is displayed by plasma cells homing to the bone marrow.<sup>2</sup> According to this extramedullary plasmacytoma tend to occur more often in the MALT or GALT than in other locations except for the solitary plasmacytoma of the bone. Ninety per cent of the isolated plasmacytomas grow in the head and neck area, especially in the upper respiratory tract, but they are surprisingly rare in the gastrointestinal tract,<sup>9</sup> though 80% of all immunoglobulin producing cells of the body are located here.<sup>10</sup> The atypical location of the plasmacytoma presented here may be mediated through a specific repertoire of adhesion

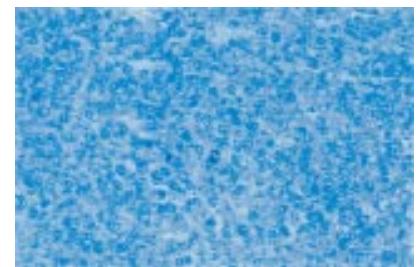


Figure 2 Monomorphous infiltrate of plasma cells with characteristic eccentric nuclei and basophilic cytoplasm (haematoxylin and eosin,  $\times 400$ ).

molecules. Since antibodies for detection of the above mentioned homing receptors in paraffin sections are not available until now, we were not able to find out whether special integrins or a total loss of them was responsible for the peculiar location of the tumour in our patient. It may only be speculated that the isolated plasmacytoma in our case arose from a monoclonal proliferation of plasma cells in an originally inflammatory infiltrate. Whether tissue specific immunoregulatory mechanisms involving accessory cells are also implicated in the localised episcleral tumour growth remain to be elucidated.

We thank Mrs Renate Buchen for technical assistance, Dr Sarah Coupland for providing the VS38 immunostaining, and Dr Flemming Staubach for reading the manuscript.

C AUW-HAEDRICH  
A SCHMITT-GRÄFF  
H WITSCHEL  
Universitäts-Augenklinik,  
Killianstrasse 5,  
D-79106, Freiburg,  
Germany

- 1 Urashima M, Chen BP, Chen S, *et al.* The development of a model for the homing of multiple myeloma cells to human bone marrow. *Blood* 1997;90:754–65.
- 2 Michigami T, Shimizu N, Williams PJ, *et al.* Cell-cell contact between marrow stromal cells and myeloma cells via VCAM-1 and alpha(4)beta(1)-integrin enhances production of osteoclast-stimulating activity. *Blood* 2000;96:1953–60.
- 3 Aboud N, Sullivan T, Whitehead K. Primary extramedullary plasmacytoma of the orbit. *Aust NZ J Ophthalmol* 1995;23:235–9.
- 4 Choi WJ, Tchah H, Kim YJ. Plasmacytoma presented as a lid mass—a case report. *Korean J Ophthalmol* 1991;5:92–5.
- 5 Cooper JH, Rootman J, Ramsey MS. Extramedullary plasmacytoma (amyloid tumour) of the caruncle. *Canad J Ophthalmol* 1989;24:166–8.
- 6 Zolog N, Georgescu L, Popescu E. Solitary epibulbar plasmacytoma with intraocular invasion. *Revista de Chirurgie, Oncologie, Radiologie, Orl, Oftalmologie, Stomatologie - Seria: Oftalmologie* 1980;24:297–9.
- 7 Hoang-Xuan T, Bodaghi B, Toubanc M, *et al.* Scleritis and mucosal-associated lymphoid tissue lymphoma: a new masquerade syndrome. *Ophthalmology* 1996;103:631–5.
- 8 Brandtzaeg P, Farstad IN, Johansen FE, *et al.* The B-cell system of human mucosae and exocrine glands. [Review] [350 refs] *Immunol Rev* 1999;171:45–87.
- 9 Dimopoulos MA, Kiamouris C, Mouloupoulos LA. Solitary plasmacytoma of bone and extramedullary plasmacytoma. *Hematology—Oncology Clinics of North America* 1999;13:1249–57.
- 10 Brandtzaeg P, Halstensen TS, Kett K, *et al.* Immunobiology and immunopathology of human gut mucosa: humoral immunity and intraepithelial lymphocytes. *Gastroenterology* 1989;97:1562–84.

### Crystalluria with sulphadiazine

EDITOR.—Toxoplasmosis is the commonest cause of posterior uveitis worldwide. Ocular toxoplasmosis may occur as part of the primary acquired infection or through reactivation of encysted organisms at the edge of an old chorioretinal scar.

Current indications for treatment include sight threatening lesions at or adjacent to macula or papillomacular bundle and disc or marked vitritis.

Treatment is commonly with a combination of the synergistic antagonists of folate metabolism, sulphadiazine, and pyrimethamine. Folic acid rescue is added to prevent bone marrow suppression. Steroids are frequently used in combination with antimicrobials in sight threatening inflammatory foci of infection.

We report a case of acute ureteric obstruction in a young female with her first presentation of recurrent ocular toxoplasmosis. We would like to bring to the attention of ophthalmologists the risk of crystalluria in patients being treated with sulphadiazine.

### CASE REPORT

A 22 year old, otherwise fit woman presented with floaters in the left eye. She had had poor vision since childhood when she had been diagnosed as “amblyopic” and undergone strabismus surgery for esotropia.

A pigmented and atrophic scar was present at the left macula, and involving the fovea. At the inferonasal edge of the scar was a raised creamy area of activity with overlying vitritis. A diagnosis of recurrent toxoplasmosis was made.

Despite the poor visual prognosis of this eye, the symptomatic nature of this lesion and the intensity of the inflammatory response prompted treatment. Pyrimethamine (75 mg immediately then 25 mg twice daily) and sulphadiazine (1 g four times daily) were started with folic acid (5 mg twice weekly). Topical dexamethasone, cyclopentolate, and oral prednisolone (60 mg reducing course) were added later.

Within 24 hours of starting treatment the patient felt unwell, with nausea, anorexia, and oligodipsia. She developed pink discoloration of the urine in which she noted sediment, and intense loin pain. Hospitalisation followed. Urinalysis demonstrated a pH of 5.0, urinary blood and protein. An intravenous urogram suggested an obstruction at the right vesicoureteric junction. Diagnostic retrograde ureteroscopy demonstrated crystalluria, and insertion of a temporary ureteric stent at this time, with administration of intravenous fluids, effected symptomatic relief. Sulphadiazine was suspended.

### COMMENT

The majority of reports of sulphadiazine crystalluria occur in patients with AIDS under treatment for toxoplasmosis encephalitis.<sup>1</sup>

These patients may have various factors predisposing them to the development of crystalluria such as poor fluid intake, fever, diarrhoea, hypoalbuminuria, and acidification of the urine. The associated polypharmacy of many AIDS patients may contribute to crystal or stone formation through the latter mechanism, or because of crystallisation of other drugs such as aciclovir, triamterene, primidone, or other sulphonamides.

Historically, sulphadiazine crystalluria has been reported in non-AIDS patients<sup>2</sup> and may cause renal impairment in 1–4% of HIV negative patients.<sup>1</sup> To our knowledge, however, this complication has not been reported in the ophthalmic literature. Ophthalmologists we surveyed were not aware of this potential complication, nor is it documented in the *British National Formulary*.

Although it occurred quickly in our patient, the complication usually occurs after a median of 10 days in HIV negative subjects at a cumulative sulphadiazine dose of 40 g.<sup>2</sup>

Microscopy of freshly voided urine commonly shows characteristic “sheaves of wheat” crystalluria and haematuria. Ultrasonography can reveal echogenic foci in the renal parenchyma as well as in the collecting systems, and hydronephrosis.<sup>3</sup> X Ray examination has a low diagnostic sensitivity.

Management can be conservative with prompt analgesia, intravenous fluids, plus or

minus diuretics, and alkalisation of urine with sodium bicarbonate to above a pH of 7.5. This usually achieves prompt dissolution of even large calculi.<sup>4</sup> It is not always necessary to stop sulphadiazine.

J M A SMITH  
A L L CURI  
C E PAVESIO

Moorfields Eye Hospital, City Road,  
London EC1V 2PD, UK

Correspondence to: Mr C E Pavesio

Accepted for publication 25 April 2001

- 1 Becker K, Jablonowski H, Haussinger D. Sulphadiazine associated nephrotoxicity in patients with the acquired immunodeficiency syndrome. *Medicine, Baltimore* 1996;75:185–94.
- 2 Keitzer WA, Campbell JA. Renal complications of sulphadiazine. *JAMA* 1943;119:701–3.
- 3 Kane D, Murphy JM, Keating S, *et al.* Renal ultrasonic findings in sulphadiazine induced renal failure. *Br J Radiol* 1996;69:925–8.
- 4 Diaz F, Collazos J, Mayo J, *et al.* Sulfadiazine-induced multiple urolithiasis and acute renal failure in a patient with AIDS and toxoplasma encephalitis. *Ann Pharmacother* 1996;30:41–2.

### Ocular involvement caused by the accumulation of porphyrins in a patient with congenital erythropoietic porphyria

EDITOR.—Congenital erythropoietic porphyria (CEP: MIM No 263700) is an extremely rare disorder inherited as an autosomal recessive trait, which is characterised by an 80–98% reduction in the activity of uroporphyrinogen III synthase (UROS: EC 4.2.1.75).<sup>1</sup> Clinically, CEP is characterised by severe cutaneous photosensitivity, chronic haemolysis, and massive porphyrinuria resulting from the accumulation in the bone marrow, peripheral blood, and other organs of large amounts of the non-physiological and pathogenic porphyrin isomers, uroporphyrin I and coproporphyrin I.<sup>2</sup> 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 manifestations, we reported a scleral change in the patient with CEP,<sup>3</sup> who had a remarkable increase of porphyrins in tear drops. Our case report strongly suggests that the accumulation of porphyrins in tear drops may directly cause the scleral changes in the patients with CEP.

### CASE REPORT

A 24 year old man presented typical manifestations of CEP such as skin ulcer and scarring. He was diagnosed with CEP in childhood, because of the elevation of porphyrins in urine. At the time of visit, slit lamp examination of bulbar conjunctiva revealed irregular hypertrophy between palpebral fissures in both eyes. A 3 × 4 mm area of scleral necrosis was observed at the limbus in the right eye (Fig 1). Hypertrophy of the temporal limbus and pigmentation of eyelids were also observed, but lid closure was normal. Corneal changes were not observed. Visual activity was right eye: 20/50, left eye: 20/20.

In order to cover the region of scleral necrosis, amniotic membrane grafting was performed, but postoperative wound healing was slow and the graft failed to be attached. Histological finding with a tissue taken during this operation showed an inflammatory infiltration of neutrophils and plasma cells in connective tissue under conjunctival layer (data not shown).

To confirm whether this scleral necrosis is caused by the direct effect of the accumulation



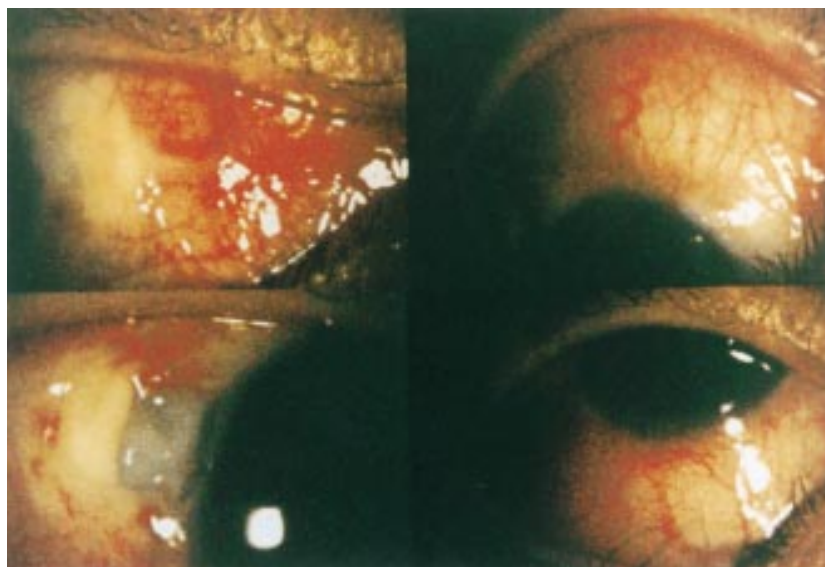


Figure 1 Four direction images of right eye. Irregular hypertrophy at the temporal limbus and scleral necrosis at the limbus were observed.

of porphyrins in tear drops, analysis of tear drop porphyrins was performed after obtaining informed consent. In normal control, no porphyrin isomers were observed, whereas in this patient, remarkable elevations of type I porphyrins and protoporphyrin were observed (Fig 2).

Furthermore, sequence analysis of *UROS* was performed and an A to G transition of nucleotide 184 that predicted a threonine to alanine substitution at residue 62 (T62A), and a C to T transition of nucleotide 745 that predicted a glutamine to premature stop codon (Q249X). These mutations have been previously reported by Xu *et al.*<sup>4</sup>

#### COMMENT

This patient was confirmed to have compound heterozygous mutations, T62A/Q249X. These mutations had been described by Xu *et al* in a Japanese patient with CEP.<sup>4</sup> They performed in vivo expression study for

each mutation, and confirmed that each of them had no residual activity. We can expect that both mutations in this case are "disease causative."

Scleral changes at the body surface lesions in CEP are mainly caused by the accumulation of porphyrins.<sup>4</sup> Here we proved the accumulation of porphyrins in tear drops with a single case of CEP. Additional cases are needed to confirm the presence of porphyrins in tear drops although they are asymptomatic for eye involvement. Since our finding demonstrates the likelihood that accumulated porphyrins in tear drops directly exerted a toxic effect in scleral lesions, the protection of sunlight by ultraviolet cut glasses is strongly recommended for prevention against the initiation and progression of scleral lesions in the patients with CEP.

K KURIHARA

Imaizumi Eye Hospital, Koriyama, Japan

N TAKAMURA

Department of International Health and Radiation Research, Atomic Bomb Disease Institute, Nagasaki University School of Medicine, Nagasaki, Japan

S IMAIZUMI

Imaizumi Eye Hospital, Koriyama, Japan

S YAMASHITA

Department of International Health and Radiation Research, Atomic Bomb Disease Institute, Nagasaki University School of Medicine, Nagasaki, Japan

M KONDO

Department of Nutrition and Biochemistry, National Institute of Public Health, Tokyo, Japan

Correspondence to: Noboru Takamura, MD, Department of International Health and Radiation Research, Atomic Bomb Disease Institute, Nagasaki University School of Medicine, 1-12-4 Sakamoto, Nagasaki 852-8523, Japan

takamura@net.nagasaki-u.ac.jp

Accepted for publication 26 April 2001

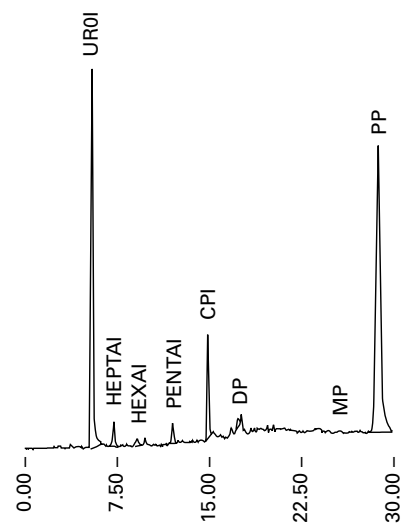


Figure 2 Tear drop porphyrin analysis by high performance liquid chromatography (HPLC). In a normal sample, no porphyrin isomers were observed (data not shown), whereas in a patient sample remarkable elevation of uroporphyrin I + III (UR0I + III), coproporphyrin I (CPI), and protoporphyrin IX (PP) were observed (8.48, 1.46, and 22.96  $\mu\text{g/g}$  creatinine, respectively).

4 Xu W, Warner CA, Desnick RJ. Congenital erythropoietic porphyria: identification and expression of 10 mutations in the uroporphyrinogen III synthase gene. *J Clin Invest* 1995;95:905-12.

#### Bilateral facial nerve palsy associated with p-ANCA positive vasculitis in a patient with rheumatoid arthritis

EDITOR,—Rheumatoid arthritis is a chronic, generalised, symmetrical, inflammatory polyarthritis. Extra-articular associations may involve the eyes, heart, lung, skin, and more rarely, the central and peripheral nervous system. We describe a case of bilateral facial paresis associated with a p-ANCA positive vasculitis in a patient with rheumatoid arthritis.

#### CASE REPORT

A 67 year old woman presented with 2 days of left sided facial weakness. She was known to suffer from rheumatoid arthritis, and displayed the characteristic hand and finger deformities of this condition. Additional features of vitiligo, hypothyroidism, and splenomegaly were present. Her medication consisted of methotrexate 5 mg weekly, thyroxine 100  $\mu\text{g}$  once daily, and folic acid 5 mg once daily. Examination revealed isolated left sided lower motor neuron facial nerve paresis, and a left Bell's palsy was diagnosed. One week later, she returned with right sided facial weakness. No improvement on the left side had occurred and bilateral lower lid paralytic ectropion was evident. A provisional diagnosis of rheumatoid associated mononeuritis multiplex was made, and a rheumatology consultation was obtained. Haematological investigations revealed a positive rheumatoid factor (RF) and p-ANCA, and a raised plasma viscosity of 1.80. Other autoimmune studies including ANA, anti-Ro and La antibodies, and c-ANCA were negative, and renal function was normal. Chest radiography and magnetic resonance imaging of the brain were unremarkable.

Three pulses of intravenous methylprednisolone 500 mg were given over 3 days, with commencement of oral prednisolone 1 mg/kg. Despite intensive topical lubrication, developing exposure keratopathy necessitated the surgical correction of the bilateral paralytic ectropion. The oral prednisolone was rapidly tapered down to 5 mg/day, and then discontinued after 3 months. p-ANCA levels subsequently became undetectable.

Full orbicularis function gradually recovered, but only partial recovery of the lower facial muscles occurred. Renal function remained normal throughout and there was no significant exacerbation of the polyarthritis.

#### COMMENT

Facial nerve weakness may be the result of a number of underlying disorders including vasculitis. The development of bilateral signs in rapid succession, in association with rheumatoid arthritis, highlighted a potential vasculitic process in this case. Other causes of bilateral weakness such as pontine disease—for example, demyelination, or primary muscular disorders—for example, myasthenia gravis, and post-infective polyneuropathy were excluded on clinical grounds and after investigation.

Rheumatoid factor consists of IgM antibodies against the patients' own IgG, and is an important diagnostic feature in rheumatoid arthritis. However, RF may also be seen in

- Sassa S, Kappas A. Molecular aspects of the inherited porphyrias. *J Intern Med* 2000;247:169-78.
- Deybach JC, Grandchamp B, Grelier M, *et al*. Prenatal exclusion of congenital erythropoietic porphyria (Günther's disease) in a fetus at risk. *Hum Genet* 1980;53:217-21.
- Tanigawa K, Takamura N, Nakata K, *et al*. Ocular complication in congenital erythropoietic porphyria. *Ophthalmologica* 1996;210:183-5.

polyarteritis nodosa, scleroderma, Wegener's granulomatosis, systemic lupus erythematosus, and sarcoidosis. No clinical or other investigative features of these conditions were demonstrated in the case described here, and the patient displayed typical erosive joint features of rheumatoid arthritis. RF may lead to immune complex (IC) mediated vasculitis due to IC formation and deposition in the joints and vessels causing endothelial damage, perivascular cellular infiltration, and thrombus formation.<sup>1</sup>

Another mechanism of a vasculitic process is through leucocyte mediated cytotoxicity caused by ANCA. ANCA may promote neutrophil activation and endothelial injury,<sup>2-4</sup> by targeting the neutrophil granule enzymes protease 3 (c-ANCA) and myeloperoxidase (p-ANCA). ANCA are useful diagnostic serological markers in a number of vasculitic conditions such as Wegener's granulomatosis, microscopic polyangiitis, and Churg-Strauss syndrome. They may be found less commonly in rheumatoid arthritis, systemic lupus erythematosus,<sup>5</sup> inflammatory bowel disease, and autoimmune hepatobiliary diseases.<sup>6</sup> In one study, the incidence of p-ANCA in patients with rheumatoid arthritis was 21%, and was strongly associated with nephropathy, more severe disease, and increased inflammation.<sup>7</sup>

In this case, other conditions more commonly associated with positive ANCA titres were excluded on clinical grounds and following investigation. Magnetic resonance imaging is sensitive for cerebral vasculitis,<sup>8</sup> and excluded CNS involvement.

The optimum treatment of ANCA associated vasculitis is generally considered to consist of a combination of corticosteroids and other immunosuppressive agents. Methotrexate, cyclosporin, azathioprine, or cyclophosphamide may be used although the most effective treatment protocols are yet to be determined. Evidence of renal or CNS involvement should prompt aggressive therapy because of potentially life threatening complications. In this case, therapy consisted of pulsed intravenous methylprednisolone in the initial phase, followed by oral prednisolone. Additional immunosuppression was not required as widespread evidence of disease activity was absent. Gradual improvement of the facial paresis occurred and vigorous treatment of the exposure keratopathy prevented visual loss in this case.

Bilateral facial nerve palsy is rarely seen in vasculitic conditions. Isolated reports of bilateral facial nerve paralysis associated with Sjögren's syndrome<sup>9</sup> and polyarteritis nodosa<sup>10</sup> exist.

Rheumatoid arthritis is a common condition, and life threatening complications, although rare, are well recognised. Initial presentation may be to the ophthalmologist and awareness of such situations, will improve the prognosis for these patients.

OWEN G STEWART  
IAN G SIMMONS  
MIKE F R MARTIN  
ANDREW J MORRELL

Department of Ophthalmology, Leeds General Infirmary, Clarendon Wing, Leeds LS2 9NS, UK

Correspondence to: Mr Stewart  
owenstewart@fsmail.net

Accepted for publication 6 June 2001

1 Vollertson RS, Conn DL. Vasculitis associated with rheumatoid arthritis. *Rheum Dis Clin N Am* 1990;16:445-6.

- Ewert BH, Jennette JC, Falk RJ. Anti-myeloperoxidase antibodies stimulate neutrophils to damage human endothelial cells. *Kidney Int* 1992;41:373-83.
- Palay DA, Stulting RD, Waring GO III, et al. Penetrating keratoplasty in patients with rheumatoid arthritis. *Ophthalmology* 1992;99:622-7.
- Savage CO, Pottinger BE, Gaskin G, et al. Anti-myeloperoxidase and proteinase 3 in systemic vasculitis stimulate neutrophil cytotoxicity toward cultured endothelial cells. *Am J Pathol* 1992;14:335-42.
- Forde AM, Feighery C, Jackson J. Antimonocyte antibodies in granulomatous disease. *Clin Immunol Immunopathol* 1996;81:88-95.
- Zhao MH, Short AK, Lockwood CM. Antineutrophil cytoplasm autoantibodies and vasculitis. *Curr Opin Haematol* 1995;2:96-102.
- Mustila A, Korpela M, Mustonen J, et al. Perinuclear antineutrophil cytoplasmic antibody in rheumatoid arthritis: a marker of severe disease with associated nephropathy. *Arthritis Rheum* 1997;40:710-7.
- Pomper MG, Miller TJ, Stone JH, et al. CNS vasculitis in autoimmune disease: MR imaging findings and correlation with angiography. *Am J Neuroradiol* 1999;20:75-85.
- Uchihara T, Yoshida S, Tsukagoshi H. Bilateral facial paresis with Sjögren's syndrome. *J Neurol* 1989;236:186.
- Dudley JP, Goodman M. Periarthritis nodosa and bilateral facial paralysis. *Arch Otolaryngol* 1969;90:139-46.

### Bilateral conjunctival lesions in Melkersson-Rosenthal syndrome

EDITOR.—The Melkersson syndrome is a rare granulomatous disease of unknown origin. The typical clinical picture consists of recurrent facial oedema associated with peripheral facial palsy and was first described by Melkersson in 1928.<sup>1</sup> Three years later a fissured tongue called lingua plicata was added to the classic features by Rosenthal.<sup>2</sup> This clinical triad in patients with granulomatous cheilitis, facial palsy, and fissured tongue was first called Melkersson-Rosenthal syndrome (MRS) by Lüscher in 1949.<sup>3</sup>

We report on a patient with the typical clinical signs who had chronic bilateral conjunctival lesions. To our knowledge an association of conjunctival lesions with MRS has not been described previously.

#### CASE REPORT

A 64 year old man presented with a fissured tongue, recurrent painless facial oedema, especially of the eyelids, and facial flush for 6 years. A review of the other systemic diseases was unremarkable. He required blepharoplasty for the correction of lid malformation. The histopathological findings of the skin biopsy confirmed the clinical suspicion of MRS by the typical granulomatous infiltration (Fig 1A).

Furthermore, he complained bilateral conjunctival swelling had been present for 6 months. Visual acuity was 20/30. Slit lamp examination revealed a bilateral fleshy mass extending from the upper fornices to the limbus and conjunctival hyperaemia (Fig 1B). Motility of the eyeball was normal and an exophthalmus has not been present. In the magnetic resonance image (MRI) of the orbit a bilateral enlargement of lacrimal glands and a swelling of the lateral rectus and superior rectus muscle of the right eye were observed. Staging examinations for lymphoma or other malignancies were uneventful. Since differential diagnosis included a bilateral orbital lymphoma a conjunctival biopsy was performed. The histopathological examination of the conjunctival specimen by light microscopy revealed a subepithelial process. An infiltrate of small lymphocytes without any differentiation and with septate orientation was found

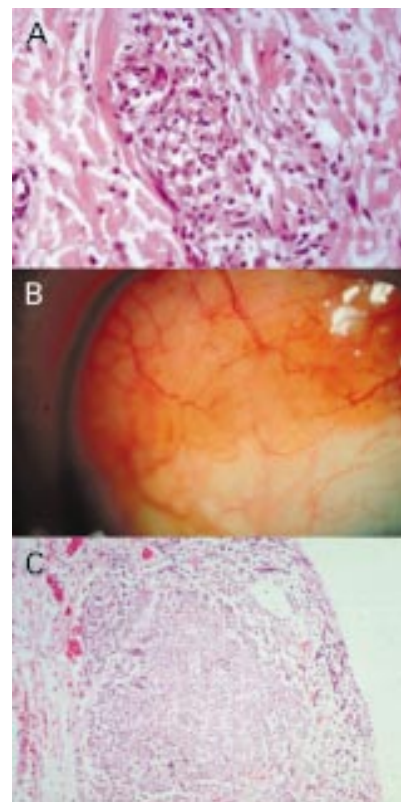


Figure 1 (A) Histopathological examination of skin biopsy with epithelioid infiltration (haematoxylin and eosin, original magnification  $\times 400$ ); (B) biomicroscopic view right eye shows a fleshy mass in the superior fornix; (C) histopathological examination of conjunctival masses shows an infiltration of small lymphocytic cells with septate orientation (haematoxylin and eosin, original magnification  $\times 200$ ).

(Fig 1C). By immunohistochemical examination no monoclonal pattern was determined, therefore, excluding a lymphoma.

Consequently, the patient was treated with clofazimine 100 mg daily. No progression in clinical findings was seen afterwards while he was on a maintenance dosage of the drug.

#### COMMENT

Disymptomatic or monosymptomatic clinical courses are frequently observed in MRS. As the symptoms rarely appear simultaneously MRS often can be diagnosed only by longitudinal follow up series.<sup>4</sup> Males and females are equally affected.<sup>5</sup> Symptoms usually manifest during adolescence and have rarely been seen in childhood or individuals older than 50 years.<sup>6</sup> The pathogenesis of MRS still remains obscure. Several predisposing factors have been considered such as heredity, infection, allergy, or derangement of cranial autonomic vasomotor innervation.<sup>1,7</sup> Cranial nerve dysfunction (that is, trigeminal nerve), parasympathetic (flush, pain), and ocular involvement have been associated with MRS. Summarised ocular involvement includes granulomatous blepharitis, exophthalmus with lagophthalmus, and burning sensations, which may be related to exposure keratitis. In rare cases, palsies of the medial rectus muscle, papilloedema, and retrobulbar neuritis have been described.<sup>4-6,8,9</sup>

Conjunctival involvement has not been reported as yet. By conjunctival biopsy taken from our patient we have shown that conjunctival lesions may be present in MRS.



A satisfactory conservative therapy has not been established so far. The results of various modes of symptomatic treatment, including systemic or topical glucocorticosteroids, are questionable.<sup>10</sup> They may reduce the patients' complaints, at least temporarily. Another treatment consists of clofazimine, which is an oral phenazine. This drug had been useful in other conditions with granulomatous inflammation.<sup>9</sup> Finally, a surgical excision of the masses had been suggested for granulomatous cheilitis or blepharitis, in order to improve the motility of the eyeball when exophthalmus occurred. Conjunctival biopsy with histopathological and immunohistochemical examination may be helpful to differentiate it from other lymphoid lesions.

CARSTEN HEINZ  
INGA WEINMANN

Department of Ophthalmology, University Essen,  
Germany

ARND HEILIGENHAUS

Department of Ophthalmology, St Franziskus Hospital,  
Muenster, Germany

PETER ALTMAYER

Department of Dermatology, University of Bochum,  
Germany

KLAUS-PETER STEUHL

Department of Ophthalmology, University Essen,  
Germany

Correspondence to: Carsten Heinz, MD, Department of Ophthalmology, University of Essen, Hufelandstrasse-55, 45122, Essen, Germany  
Carsten.Heinz@uni-essen.de

Accepted for publication 24 April 2001

- Melkersson E. Case of recurrent facial paralysis with angioneurotic edema. *Hygæa* 1928;**90**:737-41.
- Rosenthal C. Klinisch-erbbiologischer Beitrag zur Konstitutionspathologie; Auftreten von (rezidivierender familiärer) Facialislähmung, angioneurotischem Gesichtsoedem und Lingua plicata in Arthritis-Familien. *Ztschr Neurol Psychiatry* 1931;**131**:475-501.
- Lüscher E. Syndrom von Melkersson-Rosenthal. *Schweiz Med Wochenschr* 1949;**79**:1-3.
- Yeatts RP, White WL. Granulomatous blepharitis as a sign of Melkersson-Rosenthal syndrome. *Ophthalmology* 1997;**104**:1185-9: discussion 9-90.
- Greene RM, Rogers RS. Melkersson-Rosenthal syndrome: a review of 36 patients [see comments]. *J Am Acad Dermatol* 1989;**21**:1263-70.
- Gottwald W. Melkersson-Rosenthal Syndrom. Teil 1. Klinisches Bild, Diagnose. *Fortschr Med* 1981;**99**:249-52.
- Sussman GL, Yang WH, Steinberg S. Melkersson-Rosenthal syndrome: clinical, pathologic, and therapeutic considerations. *Ann Allergy* 1992;**69**:187-94.
- Hallett J, Mitchell B. Melkersson-Rosenthal syndrome. *Am J Ophthalmol* 1968;**65**:542-4.
- Podmore P, Burrows D. Clofazimine—an effective treatment for Melkersson-Rosenthal syndrome or Miescher's cheilitis. *Clin Exp Dermatol* 1986;**11**:173-8.
- Kesler A, Vainstein G, Gadoth N. Melkersson-Rosenthal syndrome treated by methylprednisolone. *Neurology* 1998;**51**:1440-1.

#### Choroidal detachment following extracapsular cataract extraction in a patient treated with latanoprost

EDITOR.—Adverse reactions associated with the topical administration of the synthetic prostaglandin F<sub>2α</sub> analogue latanoprost have been described.<sup>1</sup> We would like to report a case of choroidal detachment following extracapsular cataract extraction in a patient treated with topical latanoprost.

#### CASE REPORT

A 78 year old man initially presented with primary open angle glaucoma in 1981. This was well controlled on timoptol and ophthalmic

follow up was uneventful except for the development of left age related maculopathy in 1995 reducing the vision to 6/9. In November 1999 the intraocular pressure (IOP) became uncontrolled and a left sided cataract noted. Latanoprost was substituted with subsequent control of the IOP.

He underwent an uneventful left extracapsular cataract extraction by a traditional, non-phacoemulsification technique at another facility in January 2000 (the operating surgeon did not perform phacoemulsification on any cataract patient). Postoperative drops were betamethasone, chloramphenicol, and latanoprost. Immediately postoperatively he experienced nocturnal eye pain and subsequent photophobia. He also noticed a shadow in his left vision. Two weeks postoperatively he still had persistent eye pain and the IOP was recorded as 25 mm Hg. Acetazolamide (orally) and Timolol LA (MSD) were added to the above medications. Three days later examination revealed a visual acuity of 6/24 and IOP 16 mm Hg. Funduscopy showed the presence of a large temporal choroidal effusion.

An opinion was requested and we first saw the patient 3 days later. Visual acuity was 6/60 at best, and examination revealed corneal folds, a marked anterior uveitis with 3+ cells, and a 360 degree choroidal detachment most marked temporally. The IOP measured 10 mm Hg. The latanoprost, chloramphenicol, and acetazolamide were stopped, the Timolol LA continued and dexamethasone 0.1% 2 hourly and cyclopentolate 1% twice daily commenced. Three days later the choroidal detachment had absorbed completely and there were no signs of uveitis. The IOP was 22 mm Hg and the visual acuity had improved to 6/12 at best.

#### COMMENT

The development of choroidal detachment in a patient with primary open angle glaucoma following cataract extraction has been described.<sup>2</sup> However, this patient had previously had a trabeculectomy, undergone phacoemulsification, and had severe hypotony postoperatively. In another report choroidal effusion and hypotony were noted in a patient who 8 months before commencing latanoprost had undergone a combined cataract extraction and trabeculectomy.<sup>1</sup> It is likely that, in our case, the choroidal detachment was present from a short time following surgery in view of the subjective shadow in the patient's vision. It would appear that the detachment developed and persisted in the presence of an elevated IOP. Withdrawal of the latanoprost led to complete resolution of the choroidal detachment but the IOP remained elevated. Uveal effusion has been noted following phacoemulsification without concurrent use of latanoprost. However, in this study all effusions were small and correlated with the presence of hypotony following surgery.<sup>3</sup>

Latanoprost would appear to lower IOP by increasing uveoscleral outflow<sup>4</sup> and it has been suggested that the increased outflow facility while on latanoprost may contribute to hypotony and the development of choroidal effusions.<sup>1,2</sup> Although our patient may have had an episode of hypotony immediately following his surgery, IOP measurements did not suggest this. The possibility of latanoprost initiating or potentiating choroidal detachment in the absence of hypotony following cataract extraction should therefore be considered. This hypothesis is supported by the

presence of significant uveitis in this case some time following the surgery.

To our knowledge there have been no studies examining the incidence and severity of uveitis following cataract surgery where latanoprost has been continued. This case emphasises the possibility that idiosyncratic reactions can occur in patients undergoing surgery while continuing to use antiglaucoma medications which may potentiate the inflammatory response. Such patients may require more frequent review and should be warned to attend urgently if unexpected symptoms occur in the early postoperative period. Surgeons who perform cataract surgery on eyes in which the breakdown of the blood-aqueous barrier is expected to be greater than that produced by routine phacoemulsification surgery should consider substituting another IOP lowering agent for latanoprost in the immediate preoperative and postoperative period.

RAJEN GUPTA

STEPHEN A VERNON

Eye and ENT Centre, Queen's Medical Centre,  
Nottingham NG7 2UH, UK

Correspondence to: Mr Vernon

Accepted for publication 11 June 2001

- Rowe JA, Hattenhauer MG, Herman DC. Adverse side effects associated with latanoprost. *Am J Ophthalmol* 1997;**125**:683-5.
- Wu G. Severe hypotony following cataract extraction in a patient on latanoprost. *Eye* 2000;**14**:915-16.
- Sabti K, Lindley SK, Mansour M, et al. Uveal effusion after cataract surgery: an echographic study. *Ophthalmology* 2001;**108**:100-3.
- Patel SS, Spencer CM. Latanoprost: a review of its pharmacological properties, clinical efficacy and tolerability in the management of primary open angle glaucoma and ocular hypertension. *Drug Ageing* 1996;**9**:363-78.

## MAILBOX

#### TTT and CNV

EDITOR.—We thank Ergun and Stur<sup>1</sup> for their interest in our paper and agree with their comments that it is not possible to directly compare a pilot study with the results of a randomised controlled study. We also pointed out in our conclusion that studies such as this one cannot prove efficacy of a treatment but can only indicate fruitful areas of further research. We also pointed out that the angiographic follow up data were not complete, as once membrane closure was obtained the patients were followed up clinically.

The issue of the laser spot size in transpupillary thermotherapy (TTT) is confusing; however, it is known that more irradiance (W/cm<sup>2</sup>) is needed for smaller laser spots because heat conduction from choroidal blood flow cools smaller spots more efficiently than larger spots.<sup>2</sup> This physiological phenomenon was established in experiments,<sup>3</sup> theoretical,<sup>4</sup> and clinical<sup>5</sup> studies. Furthermore, it is true that overlapping zones occur when multiple spots are used for very large treatment areas. None the less, these zones experience the same temperature rise as every other treated area and no clinical abnormalities have been noted in the small overlapping zones. Although TTT is mainly used for occult membranes our results indicate that it may have a place in classic

membranes and in this study stabilisation of vision was obtained in the majority of these patients and in a minority an improved vision was noted.

R NEWSOM  
King's College Hospital,  
London SE5 9RS, UK

- 1 Ergun E, Stur M. TTT in CNV (mailbox). *Br J Ophthalmol* 2001;**85**:1013.
- 2 Wolbarsht ML. *Safety with lasers and other optical sources: a comprehensive handbook*. New York: Plenum Press 1980:130-1.
- 3 Mainster MA, Reichel E. Transpupillary thermotherapy for age-related macular degeneration: long-pulse photocoagulation, apoptosis, and heat shock proteins. *Ophthalmic Surg Lasers* 2000;**31**:359-73.
- 4 Mainster MA, White TJ, et al. Spectral dependence of retinal damage produced by intense light sources. *J Opt Soc Am* 1970;**60**:848-55.
- 5 Reichel E, Berrocal AM, et al. Transpupillary thermotherapy of occult subfoveal choroidal neovascularization in patients with age-related macular degeneration. *Ophthalmology* 1999;**106**:1908-14.

---

## NOTICES

---

### Affordable eye care

The latest issue of *Community Eye Health* (37) discusses affordable eye care. For further information please contact *Community Eye Health*, International Centre for Eye Health, Institute of Ophthalmology, 11-43 Bath Street, London EC1V 9EL. (Tel: (+44) (0) 20-7608 6909/6910/6923; fax: (+44) (0) 7250 3207; email: [eyesource@ucl.ac.uk](mailto:eyesource@ucl.ac.uk)) Annual subscription £25. 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: [eyesource@ucl.ac.uk](mailto:eyesource@ucl.ac.uk)).

### 22nd Annual Meeting of the Glaucoma Society (UK & Eire)

The 22nd Annual Meeting of the Glaucoma Society (UK & Eire) will take place on 22 November 2001 at the Central Conference Centre, 90 Central Street, London EC1V 8AQ.

The Allergan Guest Lecture will be delivered by Professor Jost Jonas of the University of Erlangen, Germany on the subject of the optic disc.

Further details: Mrs Janet Flowers, Administrator, 29 Quarry Hill, Grays, Essex, RM17 5BT (tel/fax: 01375 383172; email: [glaucomasocuk@talk21.com](mailto:glaucomasocuk@talk21.com); website: [www.iga.org.uk](http://www.iga.org.uk)).

### 41st St Andrew's Day Festival Symposium on Therapeutics

The 41st St Andrew's Day Festival Symposium on Therapeutics will be held on 6-7 December 2001 at the Royal College of Physicians of Edinburgh. Further details: Ms Eileen Strawn, Symposium Co-ordinator (tel: 0131 225 7324; fax: 0131-220 4393; email: [e.strawn@rcpe.ac.uk](mailto:e.strawn@rcpe.ac.uk); website: [www.rcpe.ac.uk](http://www.rcpe.ac.uk)).

### 4th International Conference on the Adjuvant Therapy of Malignant Melanoma

The 4th International Conference on the adjuvant therapy of malignant melanoma will be held at The Royal College of Physicians, London on 15-16 March 2002. Further details: Conference Secretariat, CCI Ltd, 2 Palmerston Court, Palmerston Way, London SW8 4AJ, UK (tel: + 44 (0) 20 7720 0600; fax: + 44 (0) 20 7720 7177; email: [melanoma@confcomm.co.uk](mailto:melanoma@confcomm.co.uk); website: [www.confcomm.co.uk/Melanoma](http://www.confcomm.co.uk/Melanoma)).

### XXIXth International Congress of Ophthalmology

The XXIXth International Congress of Ophthalmology will be held on 21-25 April 2002 in Sydney, Australia. Further details: Congress Secretariat, C/- ICMS Australia Pty Ltd, GPO Box 2609, Sydney, NSW 2001, Australia (tel: +61 2 9241 1478; fax: +61 2 9251 3552; email: [ophthal@icmsaust.com.au](mailto:ophthal@icmsaust.com.au); website: [www.opthalmology.aust.com](http://www.opthalmology.aust.com)).

### International Society for Behçet's Disease

The International Society for Behçet's Disease was inaugurated at the 9th International Congress on Behçet's Disease. Professor Shigeaki Ohno represents the ophthalmology division (Department of Ophthalmology and Visual Sciences, Hokkaido University Graduate School of Medicine, Sapporo, Japan: tel: +81-11-716-1161 (ext 5944); fax +81-11-736-0952; email: [sohno@med.hokudai.ac.jp](mailto:sohno@med.hokudai.ac.jp)). The 10th International Congress on Behçet's Disease will be held in Berlin 27-29 June 2002. Further details: Professor Ch Zouboulis (email: [zoubbere@zedat.fu-berlin.de](mailto:zoubbere@zedat.fu-berlin.de)).