PostScript

LETTERS

Circumpapillary choroidal "haemorrhoid" in Klippel-Trenauney-Weber syndrome

Klippel-Trenauney-Weber syndrome is a neurocutaneous vascular disease characterised by deep venous dysplasia affecting the head and limbs.¹ Affected patients are born with bilateral facial port-wine stains, and develop progressive limb hypertrophy secondary to high tissue pressure from chronic venous and lymphatic outflow obstruction.¹ Reported ophthalmological signs include conjunctival and retinal varicosities, choroidal thickening, orbital varices and iris heterochromia.² This article describes treatment of a patient with Klippel-Trenauney-Weber syndrome and congenital glaucoma who developed circumpapillary choroidal varices in the right eye over a 15-year period of observation.

Case report

A 1-year-old girl had bilateral facial port-wine stains, lumbosacral and lower limb port-wine stains with associated limb hypertrophy, and congenital glaucoma in both eyes (fig 1A).

After surgery, intraocular pressure (IOP) was controlled by topical drugs. At age 4 years, visual acuity was 20/200 OD and 20/20 OS. Cup-to-disc ratio was 0.6 OD with no peripapillary atrophy and no associated choroidal varix (fig 1B), and 0.75 OS. By 12 years of age, incipient choroidal varices encircled the right optic disc (fig 1C). Magnetic resonance imaging with phlebography showed no abnormalities of the central nervous system.

The patient discontinued her drugs and was lost to follow-up until the age of 18 years. On re-examination, IOP was 42 mm Hg in the right eye and 32 mm Hg in the left eye. Corrected visual acuity values were 20/400 OD and 20/50 OS. Cycloplegic refraction was $-4.50+3.25 \times 92^\circ$ OD and $-2.50+0.50 \times 16^\circ$ OS. Retinal examinations showed peripapillary ectasia with circumpapillary choroidal varices bordering the staphylomatous area in the right eye (fig 1D). Fluorescein angiography showed uniform hypofluorescence of the superior varices with no leakage. Four months after Ahmed valve implantation and normalisation of IOP in the right eye, these circumpapillary varices showed no change in appearance.

Comment

Posterior choroidal outflow routes are common in highly myopic eyes.³ Using indocyanine green

videoangiography, Ohno-Matsui *et al*³ observed choroidal venous outflow through posterior routes in 61 of 255 (23.9%) highly myopic eyes versus only 1 of 42 (2.4%) control eyes. In all, 39 eyes had venous drainage into the optic nerve margin (known as chorio-vaginal veins of Coats),⁴ 24 eyes had macular vortex veins and 4 eyes had vortex veins that penetrated the sclera just within the edge of a peripapillary staphyloma, as in our patient. These posterior veins tended to be dilated and tortuous and showed delayed drainage, suggesting that they provided collateral venous outflow in the presence of choroidal circulatory stasis.³

Klippel-Trenauney-Weber syndrome is associated with orbital venous stasis and secondary glaucoma.¹ Our patient's choroidal varices demarcated an area of peripapillary ectasia, suggesting that a posterior pressure differential contributed to their development at this site. Increased vortex venous pressure or thrombosis due to a combination of orbital venous hypertension and raised IOP probably led to compensatory enlargement of pre-existing choroidal venous bypass channels. The evolution of this circumpapillary choroidal "haemorrhoid" is another ocular manifestation of the orbital venous stasis and raised IOP, which complicates the Klippel-Trenauney-Weber syndrome.

M C Brodsky

Departments of Ophthalmology and Pediatrics,
University of Arkansas for Medical Sciences, Little Rock, AR
Arkansas, USA

Correspondence to: Dr M C Brodsky, Arkansas
Children's Hospital, 800 Marshall, Little Rock, AR
72202, USA;
brodskymichaelc@uams.edu

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The enhanced S-cone syndrome in children

The enhanced S-cone syndrome (ESCS), a retinal degenerative disease often associated with *NR2E3* mutation,¹⁻⁴ is due to increased numbers of S-cones at the expense of other photoreceptors or miswiring distal to the photoreceptors.⁵ Adults complain of hemeralopia, and are diagnosed from their unique

Figure 1 Klippel-Trenauney-Weber syndrome. (A) Facial photograph showing bilateral port-wine stain. (B) Retinal photograph at 4 years of age, showing normal peripapillary choroid in the right eye. (C) Retinal photograph at 12 years of age, showing early formation of circumpapillary choroidal varices in the right eye. (D) Retinal photograph at 18 years of age, showing prominent circumpapillary choroidal varices. Informed consent was obtained for publication of this figure.

Figure 1 (A, case 1) In both eyes, the retinal pigment epithelium (RPE) had an unhealthy appearance, with scattered subretinal deposits most prominent in the fovea. No pigmentary deposits were seen. (B, mother of case 1) The appearance was classic for enhanced S-cone syndrome, with deep clumped retinal pigmentary deposits and RPE atrophy outside the vascular arcades of both eyes. Foveal schisis was seen in the left eye (not shown). (C, case 2) A prominent subretinal lesion was seen in a similar location in the posterior pole of both eyes (arrow). In addition, scattered small subretinal deposits and spots of pigments were present (arrowheads). (D, case 3) The RPE had an unhealthy appearance, with scattered small subretinal deposits and subretinal spots of pigment (arrowheads). One larger subretinal deposit was adjacent to the disc in the right eye (arrow).

retinal and electroretinogram (ERG) findings^{1–4}—characteristic deep clumped pigmentary deposition around the vascular arcades;^{1–4} varying degrees of retinoschisis;^{1–4} a similar, simplified and delayed ERG waveform response to flashes under photopic and scotopic conditions;^{2,3} and a delayed 30-Hz flicker ERG amplitude lower than that of the photopic a-wave.^{2,3} Paediatric ESCS and its differing clinical features is the subject of this report.

Case series

Three children were evaluated because of inward eye turn and poor night vision noted since approximately 2 years of age. Retinal examination (fig 1) and cycloplegic refractions were performed 40 min after cyclopentolate 1% drops. *NR2E3* was directly sequenced¹ from venous blood samples. ERGs, performed under chloral hydrate sedation and according to the recommendations of the International Society for Clinical Electrophysiology of Vision,³ were consistent with ESCS (fig 2). Family history was significant only for case 1.

Case 1 (a 3-year-old girl)

The patient's mother had a history of poor night vision for many years. The patient had central/steady/maintained vision in either eye, 18-prism diopters oesotropia at distance and near, and a cycloplegic refraction of +5.75–1.50×180 OD (right eye), +6.00–1.50×180 OS (left eye). Both eyes had an unhealthy retinal

pigment epithelium (RPE) appearance with subfoveal lesions OU (fig 1A). Wearing her full cycloplegic refraction, the patient had no oesotropia. Examination of her mother showed no strabismus, uncorrected visual acuity of 20/60 OD and 20/200 OS, deep clumped pigmentation outside the vascular arcades OU (fig 1B), foveal schisis OS, no significant cycloplegic refraction and an ERG diagnostic for ESCS (fig 2B). Both mother and daughter were homozygous for a previously reported *NR2E3* splice mutation (IVS1-2A→C).¹ The father (the mother's cousin) was confirmed as a carrier.

Case 2 (a 5-year-old boy)

The patient had a visual acuity of 20/80 OD and 20/40 OS, 20-prism diopters oesotropia at distance, 25-prism diopters oesotropia at near, and a cycloplegic refraction of +6.00–2.00×115 OD and +6.00–2.00×75 OS. There were multiple subretinal white deposits and an unhealthy appearance to the RPE (fig 1C). Wearing his full cycloplegic refraction, the patient had no oesotropia at distance and 20/30 vision in either eye. Direct sequencing of *NR2E3* was negative. Additional mutational analyses^{6,7} were not performed.

Case 3 (a 5-year-old boy)

The patient, not cooperative for visual acuity testing, had approximately 20-prism diopters oesotropia at near. Cycloplegic refraction was +7.25 OU. Retinal examination was significant

for subretinal white lesions (fig 1D). Wearing his full cycloplegic refraction, the patient had no oesotropia at distance and 20/30 vision OU. *NR2E3* sequencing showed homozygosity for a previously reported missense mutation (R311Q, CGG→CAG).¹

Discussion

The unique retinal phenotype that typically leads to the diagnosis of ESCS in adults was not observed in the children of this case series. The fact that the affected mother of case 1 exhibited the classic pattern of clumped pigmentation unique to ESCS led us to suspect the diagnosis in her 3-year-old daughter and raised our awareness for subsequent similar paediatric patients (cases 2 and 3). Murine models suggest that typical adult retinal phenotype develops over time.⁸ In one previously reported case, the characteristic retinal clumped pigmentation pattern developed between 9 and 11 years of age.⁴ The authors of that report also believed that significant hyperopia is a recurring feature of ESCS that may be missed without a cycloplegic refraction. Our case series suggests that night blindness, refractive accommodative oesotropia and subretinal lesions are presenting features of ESCS in young children.

Arif O Khan

Division of Pediatric Ophthalmology, King Khaled Eye Specialist Hospital, Riyadh, Saudi Arabia

Mohammed Aldahmesh, Brian Meyer

Aragene Project, King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia

Correspondence to: Dr A O Khan, Division of Pediatric Ophthalmology, King Khaled Eye Specialist Hospital, PO Box 7191, Riyadh 11462, Saudi Arabia; arif.khan@mssm.edu

This study was approved by the Human Ethics Committee and Institutional Review Board of the King Khaled Eye Specialist Hospital in Riyadh, Saudi Arabia.

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Figure 2 The electroretinograms (ERGs) of (A) case 1, (B) her mother, (C) case 2 and (D) case 3 were diagnostic for enhanced S-cone syndrome (ESCS)—a similar, simplified and delayed waveform response to flash under photopic and scotopic conditions; and a delayed 30-Hz flicker amplitude lower than that of the photopic a-wave. The left tracings of each column are for the left eye and right tracings for the right eye. Stimulus intensities are described in logarithmic (log) units relative to the standard stimulus (1.5–3 Candelas/m² at the surface of the Ganzfeld bowl). For each ERG in the first column (Rod Response), top tracings are for a minimal (0.25 log units) blue (430 nm) stimulus, middle tracings are for a standard (1.0 log unit) red (644 nm) stimulus, and bottom tracings are for a maximal (1.5 log units) white flash. Repeat recordings are seen in (A). In the second column (cone response), for the tracings in (A) and (C), the top tracings are for maximal flash with low background illumination (1 foot Lamberts), the middle tracings for standard flash with high background illumination (30 foot Lamberts), the second to last tracings are for maximal intensity flicker (30 Hz) with low background illumination, and the bottom tracings are for standard intensity flicker with low background illumination. Repeat recordings are seen for these tracings in (B) and (D), the top tracings are for maximal flash with low background illumination and the bottom tracings are for maximal intensity flicker with low background illumination; no repeats were done.

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Retinal and subdural haemorrhages from minor falls?

Retinal and subdural haemorrhages with or without occult bone fractures in children aged <3 years is a characteristic presentation of the shaken baby syndrome (SBS) with or without blunt head impact.^{1–3} The signs may pose diagnostic dilemmas resulting from an inconsistent history given by the child's caretakers and the frequent absence of evidence of

external injury. Accidental blunt impact that leads to subdural haemorrhage is usually associated with significant trauma, skull fractures and only rare cases of retinal haemorrhage. There is abundant evidence that minor head trauma, in the absence of underlying medical conditions such as osteogenesis imperfecta type I,⁴ is only very rarely associated with severe intracranial injury or retinal haemorrhage, particularly the extensive multi-layered haemorrhages extending to the ora serrata, as seen in two thirds of the victims with SBS.^{1–3, 5}

A letter in the *British Journal of Ophthalmology* considers prior reports regarding Japanese children who sustained subdural and retinal haemorrhage after short falls.⁶ We believe that the statistical analysis and discussion

presented in the letter have inaccuracies that could lead to the incorrect conclusion that biological factors may explain the reported clinical findings which otherwise disagree with the findings in the world's literature on this topic.

Gardner suggests statistically significant discrepancies in age distribution between two Japanese cohorts with allegedly accidental head trauma^{7, 8} and Kivlin's American series of victims with shaken baby syndrome³ as one possible biological explanation for the unique nature of the Japanese cohorts, which he claims have statistically similar ages.⁶ One of the Japanese publications reports on 26 infants with retinal and subdural haemorrhages after fall backwards from sitting or standing on tatami mats.⁶ The other does not include the mechanism of injury or eye examinations.⁷

The degree of freedom (df) for two-sample independent t tests, assuming equality of variance, is $(n_1 - 1) + (n_2 - 1)$, where n_1 and n_2 are sample sizes of the two groups. When variances are unequal, Satterwaite adjustment is recommended.⁹ For data presented by Aoki, Ikeda and Kivlin, the sample sizes are 26, 14 and 102, respectively. When comparing Kivlin's cohort with Aoki's, df is 126 for equal variances and 65.3 for unequal variances. For t tests conducted by Gardner, df values were 13, 13, 25 and 39, which should have been 38, 114, 126 and 140 for equal variances, and 22.2, 20.2, 65.3 and 103 for unequal variances, for testing Aoki versus Ikeda, Ikeda versus Kivlin, Aoki versus Kivlin, and the combined Japanese studies versus Kivlin, respectively. As p values depend on df, the correct p values are 0.0247, <0.001, <0.001 and <0.001, respectively. Gardner's conclusion of similarity in age distribution between the two Japanese groups is therefore incorrect.

Classical p values represent the probability of making an incorrect rejection of the null hypothesis: the probability of saying that the mean ages of two groups are different when they are equivalent. p Value is not the probability of ruling in or out differences in group means or proportions (not being able to rule out a difference with a 20% probability).⁸

The two Japanese cohorts actually have significantly different ages, and both are different from Kivlin's sample. It is therefore unlikely that age is an explanatory factor for their unusual clinical findings. In addition, the mere act of falling over from a sitting or standing position is not developmentally possible in most victims of SBS, the incidence of which is highest in the first 6 months. Crying is a major factor in inciting SBS. The normal crying curve is similar to the SBS incidence curve.¹⁰

Thus, it is not surprising that Kivlin's patients are different from the Japanese samples. But why are the Japanese reports of subdural and retinal haemorrhage after minor trauma so very different from the bulk of the world's literature? Some of the Japanese patients were recruited before SBS had even been described or widely recognised in the world's literature. Gardner notes the admission in Aoki's paper that cases of abuse might have been included. At the time of Aoki's study, there were no child abuse teams or reporting laws in Japanese society.² Abuse could not have been adequately ruled out.

Anuradha Ganesh

Department of Ophthalmology, Sultan Qaboos University Hospital, Muscat, Oman

Derek Stephens

Population Health Sciences, The Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada

Jane D Kivlin

Department of Ophthalmology, Medical College of Wisconsin, Milwaukee, Wisconsin, USA

Alex V Levin

Departments of Paediatrics and Ophthalmology and Vision Science, The Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada

Correspondence to: Dr A V Levin, Department of Ophthalmology and Vision Sciences, The Hospital for Sick Children, 555 University Avenue, M158 Toronto, Ontario, Canada M5G 1X8; alex.levin@sickkids.ca

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Positive correlation between vitreous levels of advanced glycation end products and vascular endothelial growth factor in patients with diabetic retinopathy sufficiently treated with photocoagulation

We investigated whether vitreous levels of advanced glycation end products (AGEs) were positively correlated with vascular endothelial growth factor (VEGF) in patients with diabetic retinopathy patients sufficiently treated with retinal photocoagulation. Vitreous AGE and VEGF levels were significantly higher in patients with diabetes than in controls. Positive correlation between AGE and VEGF was found in patients with diabetic retinopathy sufficiently treated with retinal photocoagulation ($r = 0.44$, $p < 0.05$), but not in those who were insufficiently treated ($r = 0.26$, $p = 0.18$). The present observations

suggest that AGE may induce VEGF expression in an ischaemia-independent mechanism. AGE could be one of the important determinants of VEGF in diabetic retinopathy without obvious ischaemic regions.

Background

Vascular endothelial growth factor (VEGF) elicits retinal vascular hyperpermeability, thrombosis and angiogenesis, having a central role in the pathogenesis of diabetic retinopathy.¹ Furthermore, vitreous VEGF levels are increased in proliferative diabetic retinopathy, whereas the levels are decreased after treatment with panretinal photocoagulation (PRP).² These observations suggest that retinal ischaemia and resultant hypoxia could mainly contribute to VEGF induction in diabetic retinopathy.

Advanced glycation end products (AGEs), senescent macroprotein derivatives formed at an accelerated rate under diabetes, also stimulate VEGF expression in cell cultures and animal models.^{3,4} In addition, vitreous AGE levels are positively correlated with VEGF in patients with diabetic retinopathy, suggesting that AGEs may be a stimulant of VEGF *in vivo*.⁵ However, as AGEs predispose the retinal vessels to thrombogenesis,³ whether AGEs could induce VEGF expression in an ischaemia-independent manner remains unknown. Therefore, in this study, we determined the relationship between vitreous levels of AGEs and VEGF in patients with diabetic retinopathy who were sufficiently treated with PRP for controlling retinal ischaemia.

Figure 1 Vitreous levels of advanced glycation end products (AGEs; A) and vascular endothelial growth factor (VEGF; B) in controls without diabetes and in patients with diabetes, including the sufficiently treated group with panretinal photocoagulation (S-PRP) and the insufficiently treated group with no or focal photocoagulation (IS-RP). Data analysed by Mann-Whitney U test.

Figure 2 Correlation between the vitreous levels of advanced glycation end products (AGEs) and vascular endothelial growth factor (VEGF) in the sufficiently treated group with panretinal photocoagulation (S-PRP; A) and in the insufficiently treated group with no or focal photocoagulation (IS-RP; B). Spearman's correlation coefficient calculated by rank test.

Patients and methods

The study protocol was approved by our institutional ethics committee, and informed consent was obtained from all patients. Undiluted vitreous samples were collected during vitrectomy from patients with diabetes with a mean (standard deviation (SD)) age of 53 (12.6) years (45 samples from patients with proliferative diabetic retinopathy and 6 from those with diabetic macular oedema). Twenty eight samples from patients without diabetes with a mean (SD) age of 65.3 (6.7) years, having idiopathic macular hole or epiretinal membrane, served as controls. Vitreous levels of AGEs and VEGF were measured as described previously.² We classified patients with diabetes into two groups: a sufficiently treated group with PRP (S-PRP; $n = 23$) and an insufficiently treated group (no or focal retinal coagulation; IS-RP; $n = 28$), on the basis of the extent of retinal photocoagulation before vitrectomy as described previously.⁶ The data were analysed by the Mann-Whitney U test and Spearman's correlation coefficient by rank test.

Results

Vitreous levels of AGEs and VEGF were significantly higher in patients with diabetes than in controls (mean (SD) 0.13 (0.07) v 0.04 (0.03) U and 2.15 (2) v 0.12 (0.23) ng/ml, respectively; $p < 0.01$). As fig 1A and B shows, vitreous VEGF levels were higher in IS-RP than those in S-PRP (2.75 (2.3) v 1.4 (1.3) ng/ml, respectively; $p < 0.05$), whereas there was no significant difference of vitreous levels of AGEs between IS-RP and S-PRP (0.13 (0.07) v 0.13 (0.06) U, respectively). A positive correlation was found between AGEs and VEGF in S-PRP ($r = 0.44$, $p < 0.05$), but not in IS-RP ($r = 0.26$, $p = 0.18$; fig 2 A,B).

Comment

Our observations suggest that AGEs may induce VEGF expression in an ischaemia-independent mechanism. In this study, the

positive correlation between vitreous AGEs and VEGF levels disappeared when retinal ischaemia was not sufficiently controlled. Therefore, with the progress of diabetic retinopathy, retinal ischaemia and subsequent hypoxia may become a major determinant of VEGF. Our findings suggest that inhibition of AGE formation could prevent the development of early diabetic retinopathy by suppressing VEGF expression.

Masahiko Yokoi

Department of Ophthalmology and Visual Sciences,
Hokkaido University Graduate School of Medicine,
Hokkaido, Japan

Sho-ichi Yamagishi

Department of Internal Medicine, Division of
Cardiovascular Medicine, Kurume University School of
Medicine, Kurume, Japan

Masayoshi Takeuchi

Department of Biochemistry, Faculty of Pharmaceutical
Science, Hokuriku University, Kanazawa, Japan

Takanori Matsui, Yumiko Yoshida

Department of Internal Medicine, Division of
Cardiovascular Medicine, Kurume University School of
Medicine, Kurume, Japan

Kazuhiro Ohgami

Department of Ophthalmology and Visual Sciences,
Hokkaido University Graduate School of Medicine,
Hokkaido, Japan

Tamami Amano-Okamoto

Department of Ophthalmology, Nippon Telegraph and
Telephone East Corporation Sapporo Hospital, Sapporo,
Japan

Shigeaki Ohno

Department of Ophthalmology and Visual Sciences,
Hokkaido University Graduate School of Medicine,
Hokkaido, Japan

Correspondence to: Dr Masahiko Yokoi, Department of
Ophthalmology, Teine-Keijinkai Hospital, Maeda 1-12,
Teine-ku, Sapporo 006-8555, Japan;
zoyokoi.tdr@keijinkai.or.jp

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Postoperative subconjunctival 5-fluorouracil in the management of recurring pterygium

The treatment of choice for pterygium is surgical excision. Recurrence is the most common undesirable treatment outcome. Surgery and other modalities of treatment including β -irradiation, topical thiotepa, intraoperative and postoperative use of mitomycin C, 5-fluorouracil (5-FU) and daunorubicin, have been described to reduce recurrence.¹⁻⁹ Multiple surgery is itself a risk factor for recurrence.⁹ We present a case in which the fourth surgery for recurrent pterygium resulted in further recurrence, which was thwarted by multiple intralesional injections of 5-FU.

Case report

A 34-year-old Afro-Caribbean woman was referred to us in October 2004 for the management of recurrent pterygium in the right eye. She had two previous surgeries, the first in 2002 with conjunctival autograft and the second in 2003 leaving behind bare sclera. A third attempt at removal in 2004 was aborted owing to excessive intraoperative bleeding.

Her unaided visual acuity was 6/9 right eye and 6/6 left eye. The right eye showed a highly vascularised, fleshy nasal pterygium measuring 11 × 8 mm. It had encroached 2.5 mm into the cornea (fig 1A). The recurrent pterygium in the right eye was excised for the third time in March 2005. On this occasion, mitomycin C (0.04%) was applied intraoperatively to the

scleral bed for 5 min and a double-layered amniotic membrane was grafted to cover the conjunctival defect. A recurrence at the original site was noted 2 months later (fig 1B), and in an attempt to arrest progression, topical 0.02% mitomycin C was given four times daily for 7 days (three cycles with an interval of 10 days between cycles). The recurrent pterygium, however, progressed to encroach on to the cornea (Fig 1C). At this point, subconjunctival injections of 5-FU into the advancing lesion, under topical anaesthesia, was started. A 26-gauge needle was used to deposit the injection in the core of the fibrovascular tissue away from the cornea. Over 5 months, she received 10 injections of 5-FU (5 mg in 0.2 ml/injection) given 1-2 weeks apart until the recurrent pterygium became less vascular and atrophic. No complications were noted. Now, 8 months after the last injection, there is no progression (fig 1D).

Comment

Pterygium recurrence is thought to be due to fibroblast proliferation and migration and hence use of 5FU, which inhibits fibroblastic activity, is believed to reduce recurrence rates. 5-FU is toxic only to proliferating cells and is considered to be safer than other agents.¹⁰ Postoperative use of 5-FU to halt the progression of recurrence has been described before, but involved a maximum of four injections with a maximum dose of 3 mg.¹¹ Our patient received 10 injections totalling 50 mg of 5-FU with no complications.

In cases with a high risk of recurrence, such as the one described, intralesional subconjunctival injection of 5-FU even at large doses seems to be safe, effective and well tolerated by the eye. Such an intervention should be considered as an option in the management of difficult cases of recurrent pterygium.

Figure 1 (A) Anterior segment photograph showing the fleshy recurrent pterygium before the third excision. (B) Photograph showing conjunctival recurrence of the pterygium 2 months after the third excision with intraoperative mitomycin C and amniotic membrane. (C) Photograph showing progression of recurrence and encroachment into the cornea. (D) Photograph showing appearance of the pterygium 8 months after the tenth 5-fluorouracil injection. Informed consent was obtained for publication of this figure.

Anupama Pherwani

Division of Ophthalmology and Visual Sciences,
University of Nottingham, Queens Medical Centre,
Nottingham, UK

Vipul Vakil

PBMA'S H V Desai Hospital, Pune, India

**Habibullah Eatamadi, Ravinder Singh,
Harminder S Dua**

Division of Ophthalmology and Visual Sciences,
University of Nottingham, Queens Medical Centre,
Nottingham, UK

Correspondence to: Professor H S Dua, Division of
Ophthalmology, B Floor, Eye ENT Centre, Queens
Medical Centre, University Hospital, Nottingham. NG7
2UH, UK; harminder.dua@nottingham.ac.uk

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A novel technique to treat traumatic corneal perforation in a case of presumed brittle cornea syndrome

The management of corneal perforation can be difficult. We describe a novel technique to manage corneal perforation in brittle cornea syndrome (BCS).

Case report

A 14-year-old daughter of consanguineous Pakistani parents presented with a history of a bottle cap having struck her left eye. She had a history of multiple trauma to both eyes since childhood.

At presentation, there was limbus-to-limbus corneal perforation in the left eye. The right eye

had a failed corneal graft (for extensive corneal opacities). An examination under general anaesthesia showed a collapsed left eye with rolled-in corneal edges, without any scleral injury. There was partial aniridia, aphakia and prolapsed vitreous, with no obvious retinal detachment. She was also noted to have hypermobility of the small joints of her hands, with bilateral camptodactyly of the fifth fingers and over-riding toes.

During primary repair, the cornea was noted to be soft, with cheese-wiring of 10/0 nylon sutures. At review on post-operative day 1, she had a flat anterior chamber, necessitating a second operation. During this operation, suture track leaks were observed with the use of fluorescein. These were successfully tamponaded with air. To allow sufficient duration of tamponade, a non-expansile (14%) perfluoropropane (C₃F₈) gas exchange was performed after transcorneal three port vitrectomy to gain maximal gas fill. Postoperatively, the cornea was Siedel negative. The patient was kept supine for 10 days, at the end of which the globe remained formed (fig 1).

A month later, the patient received a penetrating corneal injury to the right eye while not using her protective goggles. She underwent primary surgical repair similar to the left eye using C₃F₈ gas. The final visual acuity was hand movement by both eyes.

Discussion

The patient's history suggested an underlying connective tissue disorder affecting the eyes.

BCS is a generalised connective tissue disorder characterised by corneal rupture, after a minor trauma, or spontaneously.¹ Other features include keratoconus or keratoglobus, blue sclera, red hair, hyperelasticity of the skin without excessive fragility, and hypermobility of the joints.² BCS has been reported mainly in Middle Eastern consanguineous families, although no underlying genetic defect has been identified to date.³

A differential diagnosis is Ehlers-Danlos syndrome type VI, which is associated with kyphoscoliosis and thin sclera (with rupture after trivial trauma). It is characterised by the absence or mutation of the procollagen lysyl hydroxylase gene on chromosome 1, causing a deficiency of the enzyme lysyl-hydroxylase.⁴ This leads to a build-up of urinary hydroxylslypyridinoline. In contrast, BCS has normal total urinary pyridinoline ratios. The urinary test results of this patient showed a normal ratio of total lysyl-pyridinoline to total hydroxylslypyridinoline, suggesting a diagnosis of BCS.

Repair of corneal perforations using tissue adhesives and viscoelastic agents,⁵ and onlay epikeratoplasty with a donor corneoscleral button to repair a ruptured keratoglobus,⁶ has been reported previously. Air tamponade is also commonplace, but the intraocular gas tamponade we

used is a novel technique. Prolonged C₃F₈ gas contact with the corneal wound prevented aqueous egress, allowing sufficient wound integrity while keeping the globe formed. This is the first case report of the use of a non-expansile volume of C₃F₈ gas to repair the brittle cornea in BCS, which could be generally applied to fragile leaking corneas.

**Hussain Mohamed Hussin, Suman Biswas,
Mohamed Majid, Richard Haynes, Derek Tole**
Bristol Eye Hospital, Bristol, UK

Correspondence to: Mr H M Hussin, Bristol Eye Hospital,
Lower Maudlin Street, Bristol BS1 2LX; UK;
H.M.Hussin@bristol.ac.uk

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Sympathetic ophthalmia after ruthenium plaque brachytherapy

Sympathetic ophthalmia is a rare, bilateral inflammatory process with an incidence of 0.03/100 000 in the UK and Ireland.¹ It usually follows either penetrating eye injury or intraocular surgery. Although sympathetic ophthalmia has previously been described after irradiation of ocular melanoma,^{2,3} it has never been reported after simple ¹⁰⁶Ru plaque brachytherapy. We present a case which confirms that there is a risk of developing sympathetic ophthalmia after charged-particle therapy in the absence of a penetrating injury of the uveal tract.

Case report

A 41-year-old lady was referred by her optician for a slow-growing iris lesion. Fine needle aspiration biopsy confirmed the diagnosis of ciliary body malignant melanoma. Systemic investigations for metastatic disease were negative. The patient underwent routine surgery for the insertion and subsequent removal of a ¹⁰⁶Ru plaque. Postoperative recovery was uneventful.

At 6 months after surgery, the patient presented with a 1-week history of reduced vision in both eyes to 6/24 OD and 6/36 OS. This was accompanied by photophobia, soreness and redness of both eyes.

Figure 1 The left eye after the corneal perforation was repaired. Informed consent was received for publication of this figure.

Figure 1 Colour fundus photographs and fluorescein angiography showing yellowish sub retinal spots at the posterior pole along with neuro sensory detachments at the macula giving rise to retinal state. FFA shows early hypofluorescence followed by late staining of the yellow spots.

Examination showed moderate anterior uveitis with mutton fat keratic precipitates in the left eye. There was no vitritis. Both fundi showed macular neuroretinal detachments with faint yellowish subretinal spots. Fluorescein angiography showed multiple hypofluorescent spots in the fundus with neuroretinal detachments, which was also confirmed on optical coherence tomography (figs 1 and 2).

A diagnosis of sympathetic ophthalmia was made, and the patient was treated with intensive topical and systemic steroids. She responded well to treatment and was discharged on a tapering dose of systemic steroids. After 6 months, her vision had improved to 6/5 OU, with no evidence of recurrent inflammation.

Comment

The pathogenesis of sympathetic ophthalmia consists of an autoimmune hypersensitivity response directed against exposed uveal tissue in the traumatised (exciting) eye, which is followed by a similar response against the fellow (sympathising) eye. If left untreated, it follows a chronic, relapsing and progressive course. Various surgical causes previously reported include complicated cataract surgery,⁴ cyclocryotherapy,⁵ laser cyclophotocoagulation,⁶⁻⁸ proton beam and helium ion irradiation,^{2,3} and vitrectomy.^{9,10}

The disruption of uveal tissue that set off the chain of events in this case is thought to have resulted from the radioactive effect of the treatment. Fine needle aspiration biopsy is unlikely to have caused sympathetic ophthalmia, as the biopsy was taken through clear cornea under direct visualisation and avoiding choroidal tissue. Perforation at the time of suturing during surgery was not noted intraoperatively, and is unlikely given the very anterior location of the tumour, which made surgery technically easy at an area with relatively thick sclera.

This case shows a rare delayed complication of Ruthenium brachytherapy that has never been reported previously. The most likely differential diagnosis is Vogt Koyanagi Harada syndrome, which may present in a similar manner.

Figure 2 Sequential OCT scans of the right (top) and left (bottom) eyes showing extensive neurosensory retinal detachments and the resolution of SRF over a 3 week period of treatment with steroids.

However, Vogt Koyanagi Harada syndrome follows a relapsing remitting course, often with systemic symptoms despite treatment with immune suppression, unlike sympathetic ophthalmia, which is a potentially curable disease if managed properly in acute stages. An absence of recurrence of disease process on stoppage of therapy, as well as the clinical history of our patient, makes the diagnosis of sympathetic ophthalmia more likely.

Nadeem Ahmad

Ophthalmology Department, Royal Hallamshire Hospital, Sheffield, UK

Terrence K Soong, Sachin Salvi, Paul A Rudle, Ian G Rennie

Royal Hallamshire Hospital, Sheffield, UK

Correspondence to: Mr N Ahmad, Ophthalmology Department, A Floor, Royal Hallamshire Hospital, Glossop Road, Sheffield S10 2JF, UK; ophthdoc@tesco.net

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Frequency of non-arteritic anterior ischaemic optic neuropathy in adult Chinese: The Beijing Eye Study

Non-arteritic anterior ischaemic optic neuropathy (NAION) is an acute optic neuropathy occurring predominantly in small optic nerve heads in elderly patients.^{1–3} It has been debated which factors, other than old age and a small optic disc size, predispose to the disease. Data

on the prevalence of NAION in the general population has so far been scarce.^{4,5} They have been completely missing for the Chinese. Therefore, the aim of this study was to evaluate the prevalence of optic nerve damage with the features of a preceding NAION in the Beijing Eye Study.

The Beijing Eye Study is a population-based cohort study in Northern China.⁶ The Medical Ethics Committee of the Beijing Tongren Hospital approved the study protocol and all participants gave their informed consent, according to the Declaration of Helsinki. Of 5324 individuals aged ≥ 40 years residing in the study area, 4439 individuals (2505 women) participated in the eye examination (response rate, 83.4%). This study included 4027 (90.7%) subjects for whom readable optic disc photographs were available. The mean (standard deviation (SD)) age was 55.2 (10) (median, 55; range, 40–101) years. The participants underwent an ophthalmic examination including photographs of the optic disc and macula (Fundus camera CR6-45NM, Canon, Lake Success, New York, USA) and frequency doubling perimetry (screening program C-20-1; Zeiss-Humphrey, Dublin, California, USA) as described in detail previously.⁶ For all eyes with visual acuity < 0.6 and for all eyes with any visual field loss, the photographs of the macula and optic disc were assessed twice by a panel that included several ophthalmologists (YW, LX, JBJ). The diagnostic criteria for NAION were a small optic disc with a cup/disc diameter ratio of ≤ 0.4 , segmental pallor, segmental loss of the retinal nerve fibre layer and segmental visual field loss.^{1–3,7}

Of the 8876 eyes included in the study, only one eye fulfilled the definition of NAION. The age of the male subject with suspected previous NAION was 71 years, his vision was 0.30, and he showed visual field defects in the inferior hemisphere. His optic disc, with a size of 2.0 mm², did not have cupping and exhibited a pale neuroretinal rim in its superior half. The visibility of the retinal nerve fibre layer was markedly reduced in the temporal superior region, and the temporal superior artery was markedly thinner than the temporal inferior artery. In a mathematical sense, the calculated mean (SD) prevalence of NAION in the whole population was 0.02 (1.6%) (95% confidence interval -0.02 to -0.07), or about 1 in 4500 subjects.

Comment

The prevalence rate of 1 in about 4500 Chinese with an age of ≥ 40 years may be at the lower end of the frequency range reported and calculated from previous studies on Caucasian populations in which about 2.3–10.3 patients per 100 000 inhabitants > 50 years were affected with NAION in the US per year.^{4,5} Despite its marked statistical limitation due to the low prevalence rate of NAION, this study may, therefore, support the finding from previous investigations that whites may be affected by NAION more commonly than population groups of another ethnic background such as Chinese.^{4,5} One may consider that the inter-ethnic differences in optic disc size, with the smallest optic discs found in Caucasians, medium-sized optic discs in Asians and largest discs in Afro-Americans, might be responsible for the interethnic differences in the frequency of NAION, which occurs predominantly in small optic nerve heads. The major limitation of this study is the low prevalence rate of NAION so that the prevalence rate for NAION as calculated in the present investigation may have to be

confirmed in even larger population-based studies with > 10 000 subjects included. One may conclude that NAION-associated optic nerve damage is present in 1 out of about 4500 adult Chinese. The figure will be around 100 000 patients with NAION-induced optic nerve damage in the whole of China.

Yaxing Wang, Liang Xu

Beijing Institute of Ophthalmology, Beijing Tongren Hospital, Capital University of Medical Science, Beijing, China

Just B Jonas

Department of Ophthalmology, Faculty of Clinical Medicine, Mannheim, University of Heidelberg, Mannheim, Germany

Correspondence to: Professor J B Jonas, Beijing Institute of Ophthalmology, Beijing Fongren Hospital, Capital University of Medical Science, 17 Hougou Street, Chong Wen Men, 100005 Beijing, China; jost.jonas@augen.ma.uni-heidelberg.de

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Frequency of spontaneous pulsations of the central retinal vein

The central retinal vein is the only structure in the body which can be examined non-invasively, runs through the cerebrospinal fluid space, and has a shape that depends on the relationship between its internal pressure and the pressure in the space surrounding it. Estimation of central retinal vein pressure is, therefore, helpful in the assessment of cerebrospinal fluid pressure—that is, the intracranial pressure.^{1–4} Central retinal vein pressure may be assessed by determining the external pressure at which the central retinal vein starts to pulsate. This method of assessment is similar to Riva-Rocci's method of indirect measurement of arterial blood pressure. For the central retinal vein, the external pressure is the intraocular pressure. The purpose of the present study was to find out the proportion percentage of subjects in whom the central retinal vein shows spontaneous pulsations, indicating that the pressure in the vein is lower than the intraocular pressure. The assessment of spontaneous retinal venous

pulsations may be very useful for the ophthalmic assessment whether the intracranial pressure is normal, or if spontaneous vein pulsation cannot be detected, whether the intracranial pressure is likely to be elevated.¹⁻⁴

Case report

Our clinical observational case series included 199 patients (384 eyes; mean (standard deviation (SD)) age, 63.9 (12.3) years; range, 7–90 years) attending the hospital because of cataract ($n = 66$), age-related macular degeneration ($n = 37$) or other diseases ($n = 96$) not affecting the optic nerve or primarily the inner retina. Intraocular pressure ranged between 10 and 21 mm Hg. The mean (SD) refractive error was -0.15 (3.04) D (range, -15.5 to $+6.50$ D). Using tropicamide and phenylephrine 5% eye drops, the pupil was dilated. The optic disc was examined using a slit lamp and a hand-held 78-D ophthalmoscopic lens for at least 30 s. Any small pulsatile synchronous movement of the central retinal vein or its major branches inside the optic disc was noted as spontaneous pulsations. The non-contact examination was part of a routine ophthalmoscopic examination of the fundus of the patients. The medical ethics committee approved the study protocol, fulfilling the criteria of the Declaration of Helsinki.

Spontaneous central retinal vein pulsations were detected in 343 (89.3%; 95% confidence interval (CI), 7.6 to 13.8) eyes of 186 (93.5%; 95% CI, 3.1 to 10) patients. The presence of a spontaneous central retinal vein pulsation was statistically independent of age ($p = 0.57$; 95% CI, 0.98 to 1.04) and gender ($p = 0.78$; odds ratio (OR): 1.19; 95% CI, 0.39 to 3.68). Frequency of detected spontaneous central retinal vein pulsations was significantly associated with hyperopic refractive error ($p = 0.017$; 95% CI, 1.08 to 2.19).

Comment

Confirming the findings of previous studies,^{5,6} the results of the present study (relatively high frequency of ophthalmoscopically detected spontaneous pulsations of the central retinal vein), suggest that about 10% of otherwise normal people do not have ophthalmoscopically detectable spontaneous central retinal vein pulsations. Our results as well as the previous findings may be important for several reasons: in a patient with an increased intracranial pressure, the retrobulbar cerebrospinal fluid pressure rises, eventually equalling the intraocular pressure. When this occurs, there is no longer a fluctuating intravascular pressure gradient between the intraocular retinal veins and the retrolaminar retinal vein. The venous blood flow becomes constant, and spontaneous central retinal vein pulsations cease.⁴ Based on the results of previous studies and the present investigation a lack of a spontaneous central retinal vein pulsation in a patient with a presumed increase in intracranial pressure may suggest with a probability of 10% a normal finding and with a probability of about 90% an abnormal situation. To cite an example, by Levine searched for spontaneous retinal venous pulsations in 218 subjects in a previous investigation.⁶ Spontaneous venous pulsations were present in 87.6% of 146 unselected subjects 20–90 years of age, and were absent in 100% of 33 patients with raised intracranial pressure without papilloedema and in 10 patients with papilloedema. Lumbar puncture in nine patients with raised intracranial pressure established the upper level at which spontaneous pulsations

disappear at 190 mm H₂O, and no pressure above 180 mm H₂O was found in 29 patients with venous pulsations present before lumbar puncture. Some normal subjects with no pulsations showed definite pulsations on subsequent examinations. Levine's findings show that presence of spontaneous venous pulsations is a reliable indicator of an intracranial pressure below 180–190 mm H₂O. They suggest, like the results of the present investigation, that pulsations may be absent in normal subjects and absence of pulsations is, therefore, not a reliable guide to raised intracranial pressure.

In conclusion, ophthalmoscopic assessment of spontaneous pulsation of the central retinal vein is useful for the estimation of increased intracranial pressure; in a similar manner, it may be useful for the diagnosis of glaucomatous optic neuropathy and retinal vein occlusions, in which increased central retinal vein pressure has been reported.⁷

Bjoern Harder, Jost B Jonas

Department of Ophthalmology, University of Heidelberg, Mannheim, Germany

Correspondence to: Dr J B Jonas, Universitäts-Augenklinik, Theodor-Kutzer-Ufer 1–3, 68167 Mannheim, Germany; Jost.Jonas@augen.ma.uni-heidelberg.de

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Late-stage inclusion body conjunctivitis: trachoma?

Chlamydia trachomatis is the most commonly found infectious agent in chronic conjunctivitis. Diagnosis is often delayed due to the oligosymptomatic course of the disease and the difficulty of obtaining enough infected cells in the conjunctival swab to confirm the diagnosis. These difficulties often lead to a prolonged course of the infection and possibly to scarring when infection occurs owing to chronic inflammation. We report on a 30-year-old Swiss patient having trachomatous entropion with trichiasis of the upper eyelid requiring corrective surgery, but with no history of travelling to trachoma endemic areas.

Figure 1 Cicatricial changes of the palpebral conjunctiva. Informed consent was obtained for publication of this figure.

Case report

A 34-year-old patient was seen in consultation for trichiasis involving both upper eyelids causing keratopathy. According to the patient, the development of entropion was preceded by a 1-year episode of recurrent conjunctivitis. Except for hay fever there was no other relevant ophthalmic or medical history, especially no history of possible infection elsewhere. On eversion of the eyelid, there were cicatricial changes and inflammation involving the entire palpebral conjunctiva with marked papillae (fig 1). Infection with *C trachomatis* was suspected and confirmed by a polymerase chain reaction. The patient was treated with a 2×100 mg doxycycline regimen for 2 weeks, with topical ofloxacin ointment treatment for 4 weeks. Owing to advanced entropion and trichiasis, a lid margin rotation (Trabut) procedure was performed (fig 2). The post-operative course was uneventful, with successful anatomical correction of the upper eyelids.

Comment

Chlamydiae are obligate intracellular Gram-negative eubacteria that lack cytochromes and the ability to synthesise their own ATP. *C trachomatis* has been a source of human disease especially in the eye and urogenital system for millennia, thriving in poor, crowded and unsanitary conditions. It has been known as a blinding disease for more than 3500 years.¹ Trachoma was rampant throughout Europe and North America in the 1800s, but disappeared in England before the Second World War. In the 1950s, trachoma also disappeared in Italy and the Soviet Union. This was mainly due to improved hygiene standards.

In the developing world, trachoma is still the leading infectious cause of blindness. The World Health Organisation estimates that 70

Figure 2 Lid margin rotation procedure. Informed consent was obtained for publication of this figure.

million people are infected with trachoma. Five million people are infected with its late stages and two million are blind because of it.

The trachoma biovar of *C. trachomatis* can be subdivided into 15 serovars which are designated by the letters A–K based on the polymorphism in the sequence of the major outer membrane protein.^{2,3} Serovars A–C can usually be isolated from patients with clinical trachoma in regions where trachoma is endemic.

Oculogenital infection caused by serovars D–K is common in developed countries and leads to inclusion conjunctivitis, also called paratrachoma. Up to 90% have concurrent urogenital infections.

Although the different groups of serovars display unique tissue tropisms, they are not tissue selective, and serovars D–F, J and K have all been isolated from conjunctival swabs taken from individuals with typical clinical signs of active trachoma.^{4–7} However, all these reports are from areas where trachoma is endemic.

Therefore, the traditional distinction between ocular and genital strains may have to be reconsidered.

Clinically, it is difficult to diagnose the beginning of trachoma or inclusion body conjunctivitis, and it is only by laboratory testing that the diagnosis can be confirmed. Among the available assays, nucleic acid amplification tests have proven superior in detecting, quantifying and genotyping *C. trachomatis*.⁸ Because chlamydia is an intracellular organism, the correct swab technique is very important to obtain a positive test result. This includes firm rubbing with the swab in the fornix, which is unpleasant for the patient. Because chlamydial infection is frequently oligosymptomatic and routine laboratory screening is seldom not readily available for the ophthalmologist practitioner, the diagnosis of the disease is often delayed or even missed. Additionally, repeated reinfection occurs when the sexual partner is not treated as well.

These difficulties lead to a prolonged course of the infection and possibly to scarring due to chronic inflammation and repeated reinfections. Unfortunately, we were not able to differentiate the serovar of the *C. trachomatis* isolate in our case, as serotyping is not routinely performed in Switzerland. However, the advanced clinical findings leading to entropion necessitating surgery emphasise not only the need for early diagnosis and treatment of this disease but also the need for thorough clinical examination including eversion of the upper lid and inspection of the tarsal conjunctiva in any patient with conjunctivitis.

Martin Zinkernagel, Elena Catalano, Dagmar Ammann-Rauch, Martin Zinkernagel, Elena Catalano, Dagmar Ammann-Rauch
Department of Ophthalmology, Cantonal Hospital St Gallen, St Gallen, Switzerland

Correspondence to: Dr M Zinkernagel, Department of Ophthalmology, Cantonal Hospital St Gallen, 9007 St Gallen, Switzerland; martin.zinkernagel@kssg.ch

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CORRECTIONS

doi: 10.1136/bjo.2006.102541corr1

Several errors occurred in the paper titled, Linezolid-induced optic neuropathy: a mitochondrial disorder? (*Br J Ophthalmol* 2007;**31**:111–5). A fully corrected pdf is available online at <http://bjo.bmj.com/>. The journal apologises for these errors.

doi: 10.1136/bjo.2006.93856corr1

In the paper titled, Plasma apolipoproteins and risk for age-related maculopathy (*Br J Ophthalmol* 2006;**90**:1028–33) previous literature has been incorrectly cited within the text.

In second paragraph of the Discussion section (page 1030, right column), the authors refer to "large associations between neovascularisation and plasma cholesterol (OR = 4.1) in the Eye Disease Case Control Study (EDCCS)⁴⁸ and neovascularisation and apoB (OR = 9.2) in the Beaver Dam Eye Study (BDES).⁴⁹" Further on in the same paragraph, we state, "It is not clear why the EDCCS and BDES obtained the strong effects they did".

In both cases these results were incorrectly attributed to the BDES. These two sentences should have instead cited Reference 79, which pertains to data from the NHANES III study. Citations to References 49 (BDES) and 79 (NHANES II) are correct in the 3 tables.