LETTERS TO THE EDITOR

Bilateral retinal detachments at birth: the osteoporosis pseudoglioma syndrome

EDITOR,—The osteoporosis pseudoglioma syndrome (OPS) is a rare autosomal recessive disorder characterised by severe juvenile onset osteoporosis and congenital or juvenile onset blindness. Over 40 cases have been documented but reports in the ophthalmic literature are exceedingly rare and we believe this is the first recorded case in the United Kingdom.

CASE REPORT
A white, male infant was noted by his parents to have roving eye movements and poor vision at 5 weeks of age. The pregnancy, delivery, and neonatal period were normal. On examination at 12 weeks of age he had very poor visual responses and variable horizontal nystagmus. Fundal examination showed a disordered retina with bilateral retrolental masses (Fig 1). This was confirmed by ultrasound.

A clinical diagnosis of retinal dysplasia associated with probable Norrie disease (ND) was made. A blood sample was taken for DNA analysis of the Norrie gene. He was seen from time to time over the next year and it was clear that he was completely blind with no response to light. He was poking both eyes but no complications, in particular glaucoma, had arisen. At 1 year of age his elder brother fell on him in the bedroom resulting in a right fractured femur (Fig 2) which was treated with 2½ weeks of traction. One week later he sustained a left fractured femur while lying in his cot. This was treated with a hip spica. The combination of two fractures as a result of trivial trauma raised the possibility of non-accidental injury but review of the x-rays revealed generalised osteoporosis with coarse trabeculae and thin cortices. A DEXA bone scan showed a moderate degree of osteoporosis.

The combination of multiple fractures and blindness suggested a clinical diagnosis of the rare osteoporosis pseudoglioma syndrome (OPS) as fractures are not a feature of Norrie disease. A diagnosis was important to differentiate these two diseases, OPS being autosomal recessive and Norrie disease X linked. It was not until he was 2½ years of age that final results of molecular genetic analysis showed no abnormality of the Norrie gene.

He is now 5 years of age and has suffered a total of five fractures. For the past 2½ years he has received 3 monthly bisphosphonate infusions and DEXA bone scans show improved bone density. He is developmentally delayed and has just commenced “bum shuffling.” There is also intellectual and speech delay, short stature, but no hearing impairment. His mother is currently 5 months pregnant and has been counselled that future children have a 25% chance of being affected with OPS.

Figure 1 The 1 year old infant with bilateral leucocoria.

COMMENT
This case demonstrates the blindness and skeletal handicap that characterise OPS. Other manifestations may be present but it is the eye and skeletal components which are essential for the diagnosis. Frontali et al have reviewed OPS and shown that the clinical manifestations are highly variable.1 Eye features include vitreoretinal dysplasia resulting in retrolental masses. Some eyes have been mistakenly enucleated because they were thought to contain retinoblastoma.2 Other ocular features include microphthalmia, ante- rior chamber anomalies, cataract and phthisis bulbii, although these are all highly variable. Congenital blindness is the rule but a few patients have preserved useful vision into their teenage years.3 The osteoporosis results in multiple fractures and bone deformities. The time of onset and severity of the osteoporosis is highly variable and the history of minimal trauma is typi- cal. As the osteopoenic process seems to stabilize with age, prophylaxis and specialist care of fractures and deformities are essential to prevent incapacitating long term problems. Intravenous bisphosphonate therapy may prevent progressive skeletal de- formity.4 Other minor features of OPS include short stature, intellectual impairment, cardiac anomalies, hypotonia, and ligament laxity.5 The pathogenesis of OPS is unknown. It is clearly a connective tissue disorder. Clinical, biochemical, and microscopic analyses suggest the defective gene may encode a matrix protein expressed in eye and bone.6 The OPS locus has recently been mapped to 11q12–13 but the precise molecular pathology has yet to be identified.


Emmetropisation after Molteno implant insertion for buphthalmos

EDITOR,—We report a series of four infant patients who underwent insertion of Molteno implants for control of buphthalmos and congenital glaucoma. In addition to long term control of their glaucoma, they each demonstrated a return to emmetropia from myopia.

We are unaware of any similar case reports in the literature.

CASE REPORTS
All refractions discussed in cases were measured under cyclopia (cyclopentolate 1% × 3) using a streak retinoscope and trial lenses.

Case 1
A male patient presented at 6 months of age with bilateral congenital glaucoma. Bilateral Molteno implants were inserted without complications and long term intraocular pressure (IOP) control was achieved. Refraction 6 months postoperatively revealed myopia of −10.5 D in both eyes. Subsequent refraction at age 2 (18 months postoperatively) revealed reduced myopia of −4.5 D in both eyes. Refraction at age 6 (66 months postopera- tively) revealed essentially emmetropic refraction ( plano/−1.0D × 180 in both eyes).

Case 2
A male patient first presented to our department at age 6 months. He was diagnosed with Sturge-Weber syndrome with bilateral trigeminal nerve distribution naevus flammeus involving both upper and lower lids. He was noted to have bilateral buphthalmos, but with clear corneas and normal discs. He showed no evidence of visual attention at presentation. Examination under anaesthetic (EU A) revealed IOP of 32 mm Hg right and 37 mm Hg left and horizontal corneal diameters of 14 mm in both eyes. A one plate Molteno implant with Vycril tie, Sherwood slit, and donor sclera was inserted in the left eye at 8 months of age and the right eye at 9 months of age. EUA at 11 months of age (2 months postoperatively) revealed −6.5 D (myopia) in both eyes and normal IOP. Horizontal corneal diameters were 14 mm right and 13 mm left. Further EUA at 20 months of age (12 months postoperatively) revealed corneal diameters of 14 mm right and 13 mm left, with normal discs and IOPs (10, 12 mm Hg right and left). His myopia had increased to −8.5 D right and −8.0 D left and he was prescribed −5 D glasses in both eyes. At age 36 months of age (28 months postoperatively)
the parents questioned the need for glasses, and EUA revealed the patient was essentially emmetropic ( plano/ +1.25D × 0.45 right; plano/ +1.25DC × 135 left). Other glaucoma parameters were unchanged and glasses were stopped. EUA at age 42 months (36 months postoperatively) revealed refraction of +0.5D.SDS in both eyes which has remained stable on subsequent review to date (now 5 years postoperatively).

**Case 3**

A female patient presented at age 5 months (7 months postoperatively) with left corneal oedema and normal IOP. Refraction revealed myopia had reduced significantly to −1.75D right and −1D left with other parametrical changes. At 1 year (12 months postoperatively) revealed −1.5D right and −1D left in both eyes. While myopia had reduced significantly to −1.75D right and −1D left with other parameters unchanged.

**Case 4**

A male patient presented aged 3 months with the parents questioned the need for glasses, and EUA revealed the patient was essentially emmetropic ( plano/ +1.25D × 0.45 right; plano/ +1.25DC × 135 left). Other glaucoma parameters were unchanged and glasses were stopped. EUA at age 42 months (36 months postoperatively) revealed refraction of +0.5D.SDS in both eyes which has remained stable on subsequent review to date (now 5 years postoperatively).

Increased axial length (in particular vitreous length) in congenital glaucoma is related to the compliance of the connective tissue in children that allows distension of the globe. Furthermore, an increase of vitreous length indicates uncontrolled glaucoma and is a valuable method for follow up of glaucoma in children. Presumably the elasticity of scleral tissue returns vitreous/axial length relatively towards normal values on controlling IOP, until being proportionate with that buphthalmic eye’s flattened cornea and lens plus posterior lens position—again allowing emmetropia.

While this department now routinely performs biometry and keratometry on similar cases elsewhere should allow a better understanding of the emmetropisation process in congenital glaucoma. The ability of the globe to emmetropise probably depends on the age at surgical intervention, the degree and duration of elevation of IOP and its subsequent control, and the patient’s refractive genetic predisposition.

**COMMENT**

Human adults show a non-Gaussian distribution of refractive errors with a predominance of refractions around emmetropia. Other ocular parameters such as corneal power, lens power, and axial length show a Gaussian distribution. Normal ocular development is towards emmetropia by corneal power, lens power, anterior chamber depth, and also by axial length. The comparison with X linked megalocornea where patients typically are emmetropic having symmetrically large but steep corneas with very deep anterior chamber depth and posteriorly placed lens but short vitreous length, both illustrate biometric differences between these two conditions and also that emmetropisation proceeds in other conditions with altered refractive parameters (the shorter vitreous length being the principal mechanism facilitating emmetropisation).

Conversely other ocular conditions also disturb the emmetropisation process when the refractive parameters do not enlarge proportionally. Retinopathy of prematurity is often associated with myopia, but with a small eye but relatively smaller anterior segment with steep cornea and possibly forward positioned lens. While nanophthalmos with a steep cornea and small eye results in high hyperopia.

We report four patients (seven eyes) with congenital glaucoma and myopia. Their myopia increased initially after surgical normalisation of pressures suggesting that disturbed growth of the globe continues for a period of time (up to 12 months postoperatively in these patients). Figure 1 illustrates the refractive changes with time. After some months of normalised IOP the myopia will return to emmetropia. Thus emmetropisation must be robust enough to withstand the effects of IOP and ocular enlargement on the various parameters that determine refraction, and furthermore appropriately influence them to achieve emmetropia (or at least result in an eye that is not nearly so myopic as its abnormal axial elongation would suggest). This would provide further support for some active process as part of emmetropisation, rather than just passive proportional enlargement.

**Figure 1** The time course of emmetropisation in four cases. Refractions shown as spherical equivalent and averaged between the two eyes (except case 4 which was a unilateral implant). A line of best fit has been drawn for each case.

8 Parsons JH. The refraction in buphthalmia. **Br J Ophthalmol** 1920;4:211–16.

Cerebral venous thrombosis presenting as acute visual loss

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revealed a haematoma in the right P-O region.

Urgent brain computed tomography (CT) showed left homonymous hemianopsia. An biomicroscopy, indirect ophthalmoscopy, and sluggish light reflex of both eyes, there being counting fingers in the left eye. Both eyes visual acuity of 1/60 in the right eye and ophthalmic examinations disclosed corrected neurological examinations were normal. Ophthalmic features of cerebral venous obstruction. Arch Neurol 1995;52:880–5.


The acute reversible visual loss, a rarely reported presentation of CVT, could be attributed to the coexistence of extensive cerebral oedema and the relatively unusual site of venous thrombosis in the present case.

CASE REPORT

A 54 year old woman suffered from sudden onset of severe headache and progressive visual loss in both eyes within 1 day. Her past history was unremarkable but her family history was significant for thrombophilia, pulmonary embolism (her father), and deep vein thrombosis (her son). She had just undergone hormone replacement therapy with oral conjugated oestrogen and medroxyprogesterone for 1 month.

On admission, she was conscious. Blood pressure was 156/84 mm Hg. Physical and neurological examinations were normal. Ophthalmic examinations disclosed corrected visual acuity of 1/60 in the right eye and counting fingers in the left eye. Both eyes exhibited orthophoria with full and free extraocular movement in all directions. The pupils were isocoric, 4 mm in diameter, with sluggish light reflex of both eyes, there being no relative afferent pupillary defect. Slit lamp biomicroscopy, indirect ophthalmoscopy, and fluorescein angiography did not reveal any abnormality. A Goldmann visual field test revealed left homonymous hemianopsia. An urgent brain computed tomography (CT) revealed a haematoma in the right P-O region.

with marked cerebral oedema and a left shifted midline. A brain magnetic resonance image (MRI) indicated hyperintensities on T1 and T2 weighted images in the corresponding area (Fig 1), although the initial brain MRI was also characterised by a lesion in the left P-O region, which revealed a hypointense signal without contrast enhancement on T1 weighted images (T1WI) and hyperintense signal on T2 weighted images (T2WI), indicating cerebral oedema or infarction (Fig 1). A further brain magnetic resonance venography (MRV) indicated a loss of signal in the posterior half of the superior sagittal sinus and adjacent cortical veins (Fig 2). Other laboratory investigations including blood cell counts, PT, APTT, and immunological profiles all returned normal results.

Warfarin and glycerol were administered. Her headache subsided 4 days later. A follow up brain CT 2 weeks after admission revealed the subsidence of cerebral oedema and a partial resolution of the haematoma. The patient’s vision recovered to 6/6 in both eyes 3 weeks subsequently, but the visual field defect persisted. Serial quantitative measurements of anticoagulant factors revealed an inadequate antithrombin III (AT III) level of 57% (normal range 80–120%). Her son and daughter also demonstrated a subnormal AT III level. Now she is doing well with a daily dose of warfarin (5 mg/day).

COMMENT

Acute reversible visual loss in this case was an unusual presentation for CVT. Pathogenetically, CVT may result in visual disturbance through several different mechanisms including long term ICP and complicated venous infarction involving the bilateral visual cortex. The sluggish light reflex with normal disc appearance for this patient may indicate optic nerve dysfunction secondary to acute ICP. Although acute ICP itself may result in transient visual obscuration, severe visual loss only complicates end stage ICP with optic atrophy. On the other hand, CVT associated venous infarction involving the bilateral primary visual cortex may lead to cortical blindness; however, for the present case, the rapid recovery of vision and the absence of any low density regions representing cerebral infarction over the left P-O region on the follow up brain CT excluded such a possibility.

The possible explanation for the acute, reversible visual loss in this case may be the severe left occipital lobe oedema secondary to venous congestion, concurrent with a haemorrhagic infarction in the right P-O region that resulted in the left hemianopsia. In fact, it has been reported that patients with eclampsia may demonstrate transient blindness due to occipital oedema, which may then resolve within 24 hours after delivery and the application of medication to reduce cerebral oedema.1 Further, when relating brain MRI of venous sinus occlusion to the underlying pathophysiology, Yuh et al noted a rapid resolution of the hyperintense signal on T2WI after restoration of venous drainage, which indicated that the signal change on T2WI represented reversible venous congestion and pressure driven interstitial oedema. Thus, these authors concluded that early intervention might resolve the clinical symptoms and normalise the MR appearance of certain venous sinus occlusive diseases.1 Tissue damage for these patients was reported to be predominantly resulted from the haematoma, as was the right P-O haematoma and the persistent left homonymous hemianopsia in this case.4

Of note, a combination of a hereditary AT III deficiency, which is extremely rare in orientals, and hormone replacement therapy may have been the culprits leading to an extensive CVT for this patient.3 In addition, in patients with superior sagittal sinus thrombosis, only one third have a thrombosis involving the posterior third of the sinus, just as in the present case.7 The acute reversible visual loss, a rarely reported presentation of CVT, could be attributed to the coexistence of extensive cerebral oedema and the relatively unusual site of venous thrombosis in the present case.


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Electrophysiological abnormalities following intravitreal vitravene (ISIS 2922) in two patients with CMV retinitis

EDITOR—Vitravene (ISIS 2922, formerly known as fomivirsen sodium) is a phosphorothioate oligonucleotide with potent and specific anticytomegalovirus (CMV) activity.

Vitravene binds to human CMV mRNA and inhibits the synthesis of proteins responsible for regulating virus gene expression. It is given intravitreally and its site of action differs from currently available therapies therefore reducing viral cross resistance. Minimal adverse effects have been reported including peripheral visual field loss and retinal pigment changes at high doses but the mechanism of this is not known.

We report two patients in whom negative electroretinograms (ERGs) were observed following prolonged intravitreal vitravene.

CASE REPORTS

Patient 1

A 51 year old man with AIDS developed CMV retinitis (CMVR) in the left eye in zones 2–3. The right eye was normal and visual acuity was 6/5 right, 6/6 left. The patient failed to respond to standard intravenous therapies or intravitreal ganciclovir. Intravitreal vitravene (330 µg in 0.05 ml) was administered on days 1, 8, and 15, and then fortnightly for 6 months, with good effect. Although vision remained at 6/6 without active CMVR and no zone 1 involvement, the patient described mild photophobia, colour desaturation, and poor dark adaptation in the left eye. An altered macular reflex was noted and fluorescein angiography demonstrated slow choroidal filling and capillary dropout at the macula (Fig 1). Electrophysiology was performed to look at retinal function (Fig 2).

Comment

Two cases of CMVR with negative ERGs following intravitreal vitravene are described. A “negative” ERG indicates post-photorceptor dysfunction, usually without photoreceptor dysfunction. The normal a-wave is consistent with normal photoreceptor function; the reduced EOG light rise was normal on the right but undetectable on the left (not shown). Patient 2: All left eye findings are severely reduced. Right eye rod ERG is borderline subnormal; the maximal ERG is of markedly increased implicit time; the PERG shows only residual activity. The EOG light rise was reduced on the right, undetectable on the left (not shown). Patient 3: This patient with AIDS had CMVR, of similar extent to patients 1 and 2, treated with intravenous foscarnet and real ganciclovir and foscarnet. Intravitreal vitravene was successful. The left eye visual acuity was 6/36 in the amblyopic right eye.

Patient 2

A 52 year old man with AIDS developed CMVR in the right eye of similar extent to that in patient 1. His left eye was normal and visual acuity was 6/36 in the amblyopic right eye, 6/6 on the left. Treatment with intravenous cidofovir was successful. The left eye developed macular CMVR, which failed to respond to intravenous ganciclovir or intravitreal ganciclovir and foscarnet.

CMVR reactivated 1 year later in the right eye. Intravitreal vitravene (330 µg in 0.05 ml) was administered on days 1, 8, and 15 and then monthly for 14 months. No further CMVR reactivation was observed in the vitravene treated eye and no new ocular symptoms developed. Retinal function was examined by electrophysiology (Fig 2).

Figure 2 Patient 1: Right eye ERGs fall within the normal range. Left eye rod a-wave is subnormal; the maximal response shows a negative waveform; cone flicker ERG shows relative reduction and implicit time increase; the PERG is reduced in keeping with macular involvement. The EOG light rise was normal on the right but undetectable on the left (not shown). Patient 2: All left eye findings are severely reduced. Right eye rod ERG is borderline subnormal; the maximal ERG has a negative waveform; the 30 Hz flicker ERG is of markedly increased implicit time; the PERG shows only residual activity. The EOG light rise was reduced on the right, undetectable on the left (not shown). Patient 3: This patient with AIDS had CMVR, of similar extent to patients 1 and 2, treated with intravenous foscarnet and intravitreal ganciclovir. ERG and EOG light rise (not shown) are normal.

Figure 1 Fundus fluorescein angiogram of the left eye of patient 1 demonstrates macular capillary dropout.

3 Lieberman RM, Grillone LR, Chandler JW. Safety profile of low (3.0 mg/ml) and high (6.6 mg/ml) dose fomivirsen for the treatment of CMV retinitis. Int Conf AIDS 1998; 12: 311 (abstract no 22245).

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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: eyeresource@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: eyeresource@ucl.ac.uk).

31st Cambridge Ophthalmological Symposium
The 31st Cambridge Ophthalmological Symposium will be held 3–5 September 2001 at St John’s College Cambridge. The subject is Retinal Detachment. Further details: COS Secretariat, Cambridge Conferences, The Lawn, 33 Church Street, Great Shelford, Cambridge CB2 5EL, UK (tel: 01223 847464; fax: 01223 847465; email: b.ashworth@easy.net.co.uk).

1st Asia Pacific Forum on Quality Improvement in Health Care
The 1st Asia Pacific Forum on Quality Improvement in Health Care will be held from 19–21 September 2001 in Sydney, Australia. Presented by the BMJ Publishing Group (London, UK) and Institute for Healthcare Improvement (Boston, USA), with the support of the Commonwealth Department of Health and Aged Care (Australia), Safety and Quality Council (Australia), NSW Health (Australia) and Ministry of Health (New Zealand). Further details: quality@bma.org.uk; fax +44 (0) 7383 6869.

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; website: www.rcpe.ac.uk).

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). 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).
Emmetropisation after Molteno implant insertion for buphthalmos

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