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 ultrason sound scan and examination under anaesthesia.

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. To light. He was poking both eyes but no complications, in particular glaucoma, had arisen.

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 “bump 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.

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 vitreal dystasia resulting in retrolental masses. Some eyes have been mistakenly enucleated because they were thought to contain retinoblastoma.2 Other ocular features include microphthalmia, anterior 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 through their teenage years.2

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 typical. As the osteopenic process seems to stabilise with age, prophylaxis and specialist care of fractures and deformities are essential to prevent incapacitating long term problems.3 Intravenous bisphosphonate therapy may prevent progressive skeletal deformity.4 Other minor features of OPS include short stature, intellectual impairment, cardiac anomalies, hypothyria, and ligament laxity.5 The pathogenesis of OPS is unknown. It is clearly a connective tissue disorder. Clinical, biochemical, and microscopic analyses suggest a 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.

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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 referrals discussed in cases were measured under cycloplegia (cyclopentolate 1% X 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 −4.5D in both eyes. Refraction at age 6 (66 months postoperatively) revealed essentially normal refraction ( plano−1/1DC × 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 (EUA) 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 Vicryl 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 −6.5D (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 −8.5D right and −8.0D left and he was prescribed −5D phakic lenses 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/+1.25DC × 045 right; plano/+1.25DC × 135 left). Other glaucoma parameters were unchanged and glasses were stopped. EUA at age 42 months (36 months postoperatively) revealed refractions of +0.5DS in both eyes which has remained stable on subsequent review to date (now 5 years postoperatively).

Case 2

A female patient presented at age 5 months with buphthalmos. EUA next day revealed normal corneal diameters 14 mm right and 13.5 mm left with IOPs of 33 mm Hg right and 30 mm Hg left. There was corneal oedema but no haemorrhage. EUA at 15 months (10 months postoperatively) revealed normal IOP. This was followed by deterioration in vision and EUA at 24 months of age (16 months postoperatively) revealed normal corneal diameter of 12 mm Hg left and normal discs. Refraction revealed +1.75DS right and −0.5DS left. Subsequent refraction at 9 months of age (6 months postoperatively) revealed +1.75DS right and −0.5DS left. EUA at 15 months (10 months postoperatively) revealed normal IOP. Thus, after an initial period of emmetropia there was a return to emmetropia. There was, therefore, no lasting effect of the initial use of glasses.

Case 3

A male patient presented aged 3 months with buphthalmos. EUA at 1 month of age revealed +2.75DS and −3.75DS and a relative afferent visual field defect. Haab striae were seen but no disc haemorrhage. EUA at 15 months of age (16 months postoperatively) revealed normal IOP. EUA at 24 months of age (21 months postoperatively) revealed normal IOP. Refraction revealed −5.5D left and the patient was prescribed −5D right and −6D left.

Case 4

A male patient presented aged 3 months with buphthalmos. EUA at 1 month of age revealed +3DS right and −3DS left. Refraction revealed −7DS right and −7.5DS left. EUA at 15 months of age (16 months postoperatively) revealed normal IOP. EUA at 24 months of age (21 months postoperatively) revealed normal IOP. Refraction revealed −7DS right and −7.5DS left. EUA at 24 months of age (21 months postoperatively) revealed normal IOP. Refraction revealed −7DS right and −7.5DS left.

Results in flattening of the cornea, deepening of the anterior chamber, flattening and posterior displacement of the lens, and an increase in axial length (especially vitreous length), often asymmetrical. The myopia due to increased axial length is only partially compensated by flattening of the cornea and lens and postvention may result in a return to emmetropia. Thus, emmetropisation must be considered a progressive process and cannot be envisaged as a result of a single surgical intervention.

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 one of proportional enlargement. Emmetropisation occurs by active and passive processes. The active process is one of proportional enlargement of the eye and the active mechanism probably involves the feedback of image focus information from the retina. Congenital glaucoma has an incidence of 1 in 10 000 live births. In congenital glaucoma trabeculodysgenesis causes elevated IOP. The eye in utero and in the neonatal period enlarges in response to elevated IOP. It is likely that globe expansion is most sensitive to abnormal IOP before 6–12 months of age and that ocular desity eventually results in ocular enlargement through elevated IOP.
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 contraceptive medication.

CASE REPORT

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 obstruction, 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 hemianopia. 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 occlusive disease 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 haematomas, as was the right P-O haematomata and the persistent left homonymous hemianopia in this case.4

Of note, a combination of a hereditary AT III deficiency, which is extremely rare in orientials, and hormone replacement therapy may have been the culprits leading to an extensive CVT for this patient.1 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.1 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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5 Bessen JH, Duda EE. Computed axial tomography scan demonstration of cerebral edema in eclampsia preceded by blindness. Obstet Gynecol 1982;60:529–32.
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 known as fomivirsen sodium) is a phosphorothioate sense oligonucleotide complementary to 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).

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 6/6 in the amblyopic right eye, 6/4 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 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).

COMMENT

Two cases of CMVR with negative ERGs following intravitreal vitravene are described. A “negative” ERG indicates post-phototransduction dysfunction, usually post-receptorial. The normal a-wave is consistent with normal photoreceptor function; the reduced EOG light rise may be reduced. Right eye rod b-wave is 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. ERGs and EOG light rise (not shown) are normal.

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3 Lieberman RM, Grillole 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).


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).

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; website: 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: ophthalm@icmsaust.com.au; website: www.ophthalmology.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 Shigeki 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: zobbere@zedat.fu-berlin.de).