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 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.

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.

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.

Eye features include vitreoretinal dysplasia resulting in retrolental masses. Some eyes have been mistakenly enucleated because they were thought to contain retinoblastoma. 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 into their teenage years.

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 osteopetrotic process seems to stabilise 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 deformity.

Other minor features of OPS include short stature, intellectual impairment, cardiac anomalies, hypothyroidism, and ligament laxity.

The pathogenesis of OPS is unknown. It is clearly a connective tissue disease. Clinical, biochemical, and microscopic analyses suggest the defective gene may encode a matrix protein expressed in eye and bone. The OPS locus has recently been mapped to 11q12–13 but the precise molecular pathology has yet to be identified.

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REFERENCES

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 cycloplegia (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 −4.5D in both eyes. Refraction at age 6 (66 months postoperatively) revealed essentially emmetropic refraction ( plano/−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 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/+1.25DC × 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 refraction of +0.5DS in both eyes which has remained stable on subsequent review to date (now 5 years postoperatively).

**Case 3**

A male patient presented at age 5 months with buphthalmos. EUA next day revealed horizontal corneal diameters 14 mm right and 13.5 mm left with IOP’s of 33 mm Hg right and 30 mm Hg left. There was corneal oedema worse right than left and bilateral Haab striae. We proceeded to right one plate Molteno implant with Vycril tie and slit, with a similar procedure in the left 1 week later. Subsequent EUA at 13 months (8 months postoperatively) revealed normal IOP (14 mm Hg in both eyes) with horizontal corneal diameters of 13 mm Hg right and 13.5 mm Hg left and normal disc. Refraction revealed myopia of −4.0D right and −4.5D left. EUA at 15 months (10 months postoperatively) revealed greater myopia of −7.0D right and −5.5D left and the patient was prescribed glasses (−4D right and −3D left). EUA at 21 months of age (16 months postoperatively) revealed reduced reduced significantly to −1.75D right and −1D left with other parameters unchanged.

**Case 4**

A male patient presented aged 3 months with a history of cloudy left cornea from 4 weeks of age. EUA revealed left corneal diameter of 12 mm and IOP of 50 mm Hg. The patient proceeded to a left one plate Molteno implant with Vycril tie and Sherwood slit and donor sclera. At EUA 1 week later the eye showed marked improvement with resolution of corneal oedema and normal IOP. Refraction at 4 months of age (1 month postoperatively) revealed plano/+1.75DS right and −3.5DS left. Subsequent refraction 9 months of age (6 months postoperatively) revealed plano/+1DC × 900 in both eyes. Refraction at 24 months of age (21 months postoperatively) revealed −0.5DS right and +0.75DS/+1.0DC × 045.

**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.1–4 Normal ocular development is towards emmetropia by corneal power, lens flattening of the cornea and lens and posterior lens position so that enlargement causes myopia which is a feature of congenital glaucoma.**5** This suggests that congenital glaucoma disturbs emmetropisation as a result of ocular enlargement, but does not disrupt it as these partially compensatory measures in themselves are tending to emmetropise a buphthalmic eye that otherwise would be much more myopic than in the absence of axial length alone increased. 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 conditions6 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 pressure 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 there is a return to emmetropia. Thus emmetropisation must be acquired enough to withstand the effects of IOP and ocular enlargement on the various parameters that determine refraction, and furthermore more 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.

**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.1 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 perform keratometry and keratometry on similar cases elsewhere should allow a better understanding of the emmetropisation process in congenital glaucoma. The ability of the globe to grow normally 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.

Disclaimer: One of the authors (ACBM) has a financial interest in Molteno implants.

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Cerebral venous thrombosis presenting as acute visual loss

EDITOR.—The common features associated with cerebral venous thrombosis (CVT) are headache, papilloedema, motor or sensory deficits, seizures, and conscious disturbance.1 Ophthalmological manifestations including diplopia, subnormal visual acuity, or visual field defect are primarily the consequence of increased intracranial pressure (ICP).2 Visual disorientation, psychic gaze paralysis, and inferior altitudinal hemianopia may develop if cerebral infarction is complicated in the parieto-occipital (P-O) region.3 We describe an unusual oriental case of CVT presenting uncommon transient visual loss to stress the diversity of the manifestations of CVT.

Figure 1 The time course of emmetropisation in four cases. Refraction has been 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.

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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 contraceptive medication.

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 showed left homonymous hemianopsia. An urgent brain computed tomography (CT) revealed a haematoma in the right P-O region.

Figure 1  Axial T1 weighted MRI of the brain revealing a haematoma (arrowhead, A) in the right P-O region with substantial perifocal oedema (arrow, B) and marked cerebral oedema in the left P-O region (arrow, A), which exhibiting hyperintense signal on T2 weighted images (arrow, B).

Figure 2  Brain MRV revealing the loss of signal in the posterior half of the superior sagittal sinus (arrows).

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 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.

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. 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. 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

**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). Electroretinography 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 6/5 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-transduction dysfunction, usually post-receptorial. The normal a-wave is consistent with normal photoreceptor function; the reduced EOQ light rise also observed therefore suggests additional dysfunction at the level of the RPE/photoreceptor complex. The abnor- mal pattern ERGs show macular involvement. RPE involvement in AIDS CMVR has been demonstrated ophthalmoscopically and confirmed by histology, immunohistochemistry and electro-oculography. The magnitude of EOQ light rise reduction in AIDS related CMVR does not correlate with ERG a-wave amplitude, suggesting that the EOQ changes are not secondary to photoreceptor dysfunction. There is however good correlation with the extent of RPE involvement, and EOQ may thus be a good indicator of disease activity. Although ERG b-wave reduction may occur in AIDS related CMVR, the occurrence of a negative ERG in two eyes following intravitreal vitravene, and the normal ERG in a control eye with CMVR of similar magnitude which also received intravitreal medica- tion, are in keeping with a causal relation.

**Figure 2**

Patient 1: Right eye ERGs fall within the normal range. Left eye rod b-wave is normal; the maximal response shows a negative waveform; cone flicker ERGs show relative reduction and implicit time increase; the PERG is reduced in keeping with macular involvement. The EOQ 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 normal; 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 EOQ 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 EOQ light rise (not shown) are normal.

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

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3. Lieberman RM, Grillon LR, Chandler JW. Safety profile of low (3.0 mg/ml) and high (6.6 mg/ml) dose fomiviren 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@easynet.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 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).
Electrophysiological abnormalities following intravitreal vitravene (ISIS 2922) in two patients with CMV retinitis
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