first visit) the MHRD had not resolved and the BCVA remained at 20/50.

Case 2

A 73 year old woman was referred to our clinic with metamorphopsia in her left eye of 3 months' duration. The BCVA was 20/70 and the axial length was 29.39 mm. OCT revealed MHMF (fig 2A and C).

One month later, she reported visual loss in her left eye, and OCT showed the resolution of MF and consequent development of MHRD (fig 2D). The BCVA decreased to 20/100. Two months after the first visit, the fundus photograph and OCT still showed MHRD (fig 2B and E). Because the RD has extended and the BCVA remained 20/100, she chose vitrectomy with internal limiting membrane peeling and gas tamponade. After vitrectomy, the MHRD resolved, but the MH did not close. At the last visit (20 months after the first visit), the MH remained open and the BCVA was 20/200.

Comment

The pathogenesis of MHRD remains unclear, but the tangential traction of the vitreous cortex, the presence of an epiretinal membrane and posterior staphyloma are thought to have an important role in the development of MHRD,[4] while inflexibility of the retinal vessels and the internal limiting membrane is believed to be a cause of MF.[5] However, there is little information regarding this association. In this case series, we reported two cases of MHMF in which retinoschisis spontaneously was resolved and developed into RD.

The actual mechanism of the manner in which MF is resolved and develops into MHRD is unknown. The photoreceptor cells (the outer layer of MF) do not have a pump effect, which is one of the most important functions of the retinal pigment epithelial (RPE) cells. We hypothesise, therefore, that the pump effect of the RPE increased the osmolality of the subretinal fluid and that the intraretinal fluid moved into the subretinal space according to the incline of the osmotic pressure, resulting in the development of MHRD. Another possibility is that the photoreceptors are freed from the RPE according to RD, and MF may resolve because of the restitutive force of the intraretinal columns. In conclusion, spontaneous resolution of retinoschisis and consequent development of RD is one of the most important steps in causing MHRD, at least in some cases.

K Sayanagi, Y Ikuno, Y Tano
Department of Ophthalmology, Osaka University Medical School, Osaka, Japan

Correspondence to: Yasushi Ikuno, MD, Department of Ophthalmology E7, Osaka University Medical School, 2-2 Yamadaoka, Suita 565-0871, Japan; ikuno@ophthal.med.osaka-u.ac.jp

doi: 10.1136/bjo.2005.085233

Accepted for publication 2 January 2006

The authors have no proprietary interest in any aspect of this report.

References

1 **Takano M**, Kishi S. Foveal retinoschisis and retinal detachment in severely myopic eyes with posterior staphyloma. *Am J Ophthalmol* 1999;**128**:472–6.
2 **Benhamou N**, Massin P, Erginary A, *et al*. Macular retinoschisis in highly myopic eyes. *Am J Ophthalmol* 2002;**133**:794–800.
3 **Ikuno Y**, Tano Y. Early macular holes with retinoschisis in highly myopic eyes. *Am J Ophthalmol* 2003;**136**:741–4.
4 **Stirpe M**, Michels RG. Retinal detachment in highly myopic eyes due to macular holes and epiretinal traction. *Retina* 1990;**10**:113–14.
5 **Ikuno Y**, Gomi F, Tano Y. Potent retinal arteriolar traction as a possible cause of myopic foveoschisis. *Am J Ophthalmol* 2005;**139**:462–7.

Congenital stationary night blindness associated with mutations in GRM6 encoding glutamate receptor MGluR6

Congenital stationary night blindness (CSNB) is a non-progressive retinal disorder characterised by defective night vision from birth[1] that is clinically and genetically heterogeneous. It is most commonly inherited as an X linked disorder, but autosomal dominant (OMIM #163500) and recessive (OMIM#258100) forms have been described. A recent report describes mutations of the *GRM6* gene in three patients with autosomal recessive CSNB.[2] *GRM6* encodes the glutamate receptor MGluR6, which is expressed by the rod and cone ON bipolar cells.[3] Pharmacological block of this receptor in primates[4 5] leads to a similar CSNB phenotype as that described in subjects with *GRM6* mutations.[2] We have previously identified mutations in *CACNA1F* and *NYX* genes in males with X linked CSNB,[6 7] and have encountered several female patients with a similar phenotype. We screened these affected females for mutations in *RHO* which can cause autosomal dominant CSNB,[8–10] but failed to identify mutations. Recently, following the publication of *GRM6* mutations in CSNB[2] we have identified nonsense mutations in one female with CSNB.

Case report

The patient was 7 years of age at the time of clinical examination. Her parents thought that she had always had poor night vision and had noticed horizontal nystagmus since early infancy. She had worn spectacle correction for myopic astigmatism since the age of 3 (right eye: −2.50DS/−3.5DC×85, left eye: −2.50DS/−4.00DC×100). She was otherwise fit and well, and had no family history of ocular disorders. Her distance visual acuity was logMAR +0.3 (6/12, 20/40) in each eye and she was able to read N5 print. Colour vision was full (Ishihara and City University plates). She had no nystagmus in primary position but a small amplitude horizontal nystagmus was noted in lateral gaze. She had a small angle esophoria and 500 seconds of arc stereoacuity. Funduscopy showed inferotemporally tilted discs with mild hypopigmentation in the inferotemporal fundus. There was no ophthalmoscopic evidence of foveal hypoplasia. The patient underwent ISCEV standardised electroretinographic testing using contact gold foil electrodes (protocol previously described)[7] (fig 1). Subjects with AR or XLCSNB characteristically have a ''negative wave'' electroretinogram (ERG) with grossly subnormal scotopic (rod photoreceptor pathway) b-wave amplitudes. The patient's ERG waveform was more similar to that in XLCSNB1 (''complete'') rather than XLCSNB2 (''incomplete''): the differences being the absence of recordable scotopic oscillatory potentials differences and the presence of a 30 Hz flicker response in this and the XLCSNB1 subjects. Blood was taken, with informed consent, from the patient and DNA extracted using standard techniques. Using polymerase chain reaction (PCR) we amplified each of her *GRM6* gene exons[2] and sequenced the coding region and intron-exon boundaries. We identified two nonsense mutations: R238X and Y409X, in exons 2 and 4 respectively (fig 2). These mutations specific have not been previously reported in CSNB but other nonsense mutations are described.[2]

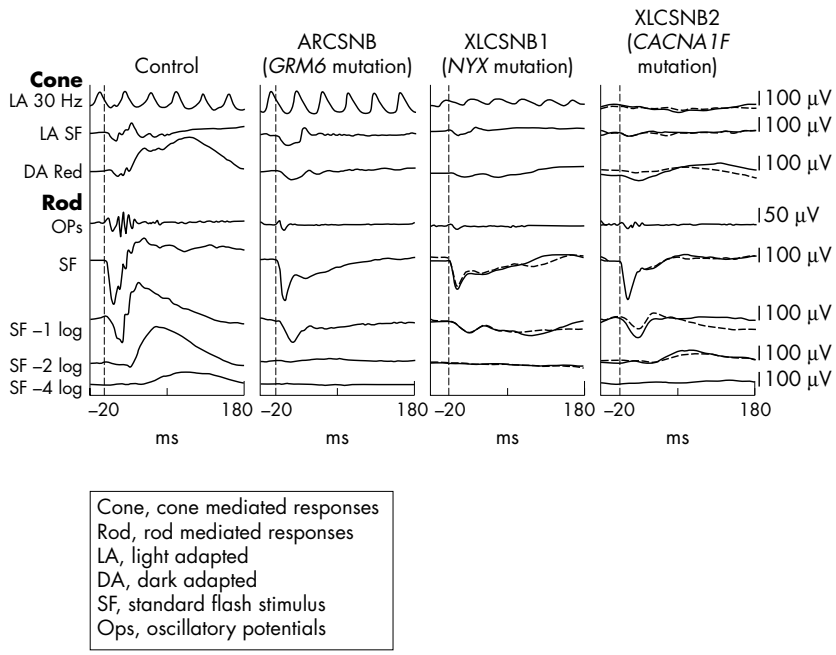

Figure 1 Comparison of ERG waveforms. The absence of oscillatory potentials and the presence of a 30 Hz flicker response make the ERG in this case more similar to that seen in subjects with the X linked CSNB1 genotype than those with CSNB2.

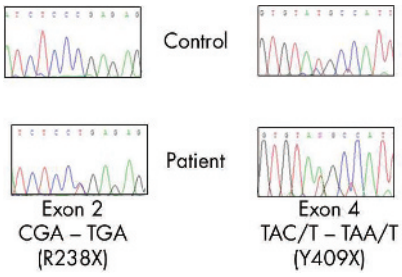

Figure 2 Mutations in GRM6 gene.

Comment

Mutations in *GRM6* cause some cases of ARCSNB. In darkness, glutamate is tonically released from the photoreceptor presynaptic terminal while light induced photoreceptor hyperpolarisation diminishes its release. The reduced stimulation of the ''on'' bipolar cell in light conditions results in it depolarisation. Absence of the MgluR6 receptor as a result of *GRM6* gene mutation causes the ''on'' bipolar cells to be relatively depolarised (light adapted) in darkness, causing the symptom of night blindness. Both this form of ARCSNB and XLCSNB1 appear to profoundly affect the ''on'' bipolar cell retinal pathway only and therefore have similar waveforms: specifically grossly subnormal, often absent scotopic b-wave response, an absence of scotopic oscillatory potentials but a relatively well preserved 30 Hz flicker response. In subjects with XLCSNB2, in which abnormalities in function of the L-type calcium channel appears to impair both the ON and ''off'' bipolar pathway: scotopic b-waves and oscillatory potentials are usually recordable but the 30 Hz flicker response is grossly subnormal.

The striking similarities between *GRM6* CSNB and CSNB1 caused by *NYX* mutations suggest that nyctalopin (encoded by *NYX*) plays an important part in signalling through the ''on'' bipolar pathway. Since little is known about the function of nyctalopin these clinical observations may help to guide further studies of its function and any interaction with mGluR6 in bipolar cell function.

E O'Connor
Academic Unit of Medical Genetics, Division of Human Development. School of Medicine, and Centre for Molecular Medicine, Faculty of Medical and Human Sciences, University of Manchester, Manchester, UK

L E Allen, K Bradshaw
Department of Ophthalmology, Addenbrooke's Hospital Trust, Cambridge, UK

J Boylan
Academic Unit of Medical Genetics, Division of Human Development, School of Medicine, and Centre for Molecular Medicine, Faculty of Medical and Human Sciences, University of Manchester, Manchester, UK

A T Moore
Institute of Ophthalmology and Moorfields Eye Hospital, London, UK

D Trump
Academic Unit of Medical Genetics, Division of Human Development, School of Medicine, and Centre for Molecular Medicine, Faculty of Medical and Human Sciences, University of Manchester, Manchester, UK

Correspondence to: Professor Dorothy Trump, Academic Unit of Medical Genetics, St Mary's Hospital, Hathersage Road, Manchester M13 0JH, UK; dorothy.trump@manchester.ac.uk

doi: 10.1136/bjo.2005.086678

Accepted for publication 3 January 2006

References

1 **Jacobi FK**, *et al*. Phenotypic expression of the complete type of X-linked congenital stationary night blindness in patients with different mutations in the NYX gene. *Graefes Arch Clin Exp Ophthalmol* 2002;**240**:822–8.
2 **Dryja TP**, *et al*. Night blindness and abnormal cone electroretinogram ON responses in patients with mutations in the GRM6 gene encoding mGluR6. *Proc Natl Acad Sci USA* 2005;**102**:4884–9.
3 **Nakajima Y**, *et al*. Molecular characterization of a novel retinal metabotropic glutamate receptor mGluR6 with a high agonist selectivity for L-2-amino-4-phosphonobutyrate. *J Biol Chem* 1993;**268**:11868–73.
4 **Slaughter MM**, Miller RF. 2-amino-4-phosphonobutyric acid: a new pharmacological tool for retina research. *Science* 1981;**211**:182–5.
5 **Schiller PH**, Sandell JH, Maunsell JH. Functions of the ON and OFF channels of the visual system. *Nature* 1986;**322**:824–5.
6 **Zito I**, *et al*. Mutations in the CACNA1F and NYX genes in British CSNBX families. *Hum Mutat* 2003;**21**:169.
7 **Allen LE**, *et al*. Genotype-phenotype correlation in British families with X linked congenital stationary night blindness. *Br J Ophthalmol* 2003;**87**:1413–20.
8 **Sieving PA**, *et al*. Dark-light: model for nightblindness from the human rhodopsin Gly-90→Asp mutation. *Proc Natl Acad Sci USA* 1995;**92**:880–4.
9 **Al-Jandal N**, *et al*. A novel mutation within the rhodopsin gene (Thr-94-Ile) causing autosomal dominant congenital stationary night blindness. *Hum Mutat* 1999;**13**:75–81.
10 **Dryja TP**, *et al*. Heterozygous missense mutation in the rhodopsin gene as a cause of congenital stationary night blindness. *Nat Genet* 1993;**4**:280–3.

Metastastic choriocarcinoma causing cavernous sinus syndrome

Choriocarcinoma is a rare trophoblastic tumour.[1 2] We describe a case of metastatic choriocarcinoma to the cavernous sinus causing complete ophthalmoplegia and ptosis, following an uneventful pregnancy.

Case report

A 28 year old woman was referred to the oculoplastic and orbital service with a 1 week history of right sided ptosis and 6 weeks of right facial pain. Six weeks earlier she underwent evacuation of retained products of conception, following spontaneous vaginal delivery. Facial pain immediately ensued and her dentist extracted a right wisdom tooth, but the pain continued to worsen. The visual acuity was 6/9 right eye, 6/5 left eye, with complete right sided ptosis, total ophthalmoplegia, and a dilated unreactive pupil (fig 1A, B). Reduced sensation in the distribution of right trigeminal branches V1 (including cornea) and V2 was noted. There was no relative afferent pupillary defect, visual field or colour vision defects, or proptosis.

Magnetic resonance imaging (MRI) scans of brain and orbits (fig 1C, D), revealed a right cavernous sinus mass extending to right temporal lobe. Image guided biopsy of the temporal lobe revealed a dural encased highly vascular choriocarcinoma. Subsequent computed tomography (CT) imaging revealed a grossly enlarged uterus and multiple large pulmonary metastases. Serum β-HCG levels were markedly elevated at 2.5×10^7 IU/l, consistent with choriocarcinoma. She was commenced on systemic and intrathecal chemotherapy. Five months later, β-HCG levels returned to normal, her facial pain and sensation improved, and her ptosis resolved. Between 9 months and 18 months, ocular motility examinations revealed a stable right esotropia with poor abduction and reduced elevation. She underwent lateral transposition surgery to superior and inferior recti (combined with botulinum toxin chemodenervation of ipsilateral medial rectus) to improve ocular alignment.

MRI scans at 6 months revealed a reduced tumour size (fig 1E and F). She remains clinically stable 18 months after presentation with a useful field of binocular single vision.

Comment

This patient had a potentially fatal cavernous sinus and intracranial metastasis from choriocarcinoma. Patients can become symptomatic long after an uneventful pregnancy,[1–3]

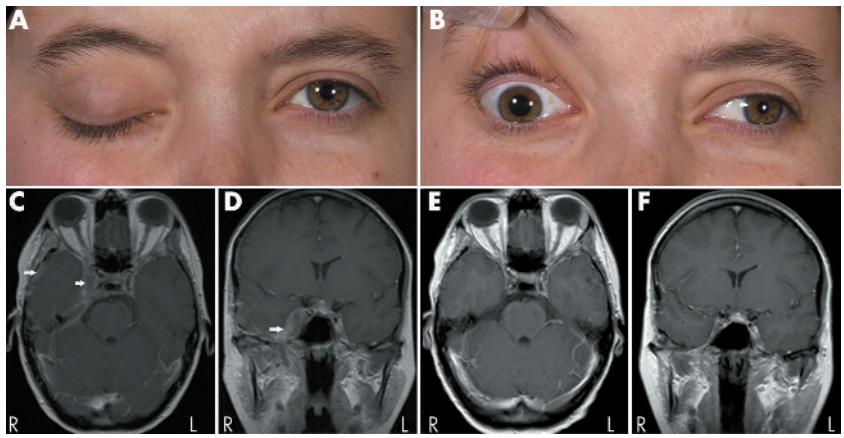

Figure 1 (A, B) Right sided complete ptosis, fixed dilated pupil, and total ophthalmoplegia. (C, D) Axial and coronal post gadolinium T1 MRI brain scans, showing enhancing right cavernous sinus mass extending to right temporal lobe surface. Arrows illustrate tumour location. (E, F) MRI scans 6 months after chemotherapy, showing reduction in tumour size. Reproduced with permission.