Sir,

Duane syndrome associated with the Cat Eye syndrome: a case report

The Cat Eye syndrome is a rare condition with a wide spectrum of phenotypic variability. It has an estimated incidence between 1 : 50 000 and 1 : 150 000 and is thought to occur due to the presence of a supernumerary marker chromosome 22, which usually arises *de novo*, although transmission from a mildly affected parent has occasionally been reported *inter alia*[1] [CES, OMIM #115470]. Ocular motility defects are an infrequent feature.

Case Report

A baby girl was born via spontaneous vaginal delivery at 41 weeks and 4 days, weighing 3460 g. She was noted to have an imperforate anus. A laparotomy was performed and a sigmoid colostomy created to treat the distended sigmoid colon. An ejection systolic murmur was discovered and subsequent echocardiogram revealed totally anomalous pulmonary venous return (supracardiac type) and a right to left shunt. Renal ultrasound revealed a right hydronephrosis. Micturating cysto-urethrogram showed bilateral grade 4–5 reflux, a large, incompletely emptying bladder, and a left partial duplex system with a single renal pelvis. A rectovaginal fistula was also noted.

Cytogenetic investigation of lymphocyte cultures showed a chromosome count of 47 with an additional marker chromosome present in all cells examined (Figure 1). The marker chromosome was bisatellited, suggesting that it was derived from the short arms and proximal long arms of acrocentric chromosomes, but did not fluoresce with 4′,6-diamidino-2-phenylindole stain and therefore was not derived from chromosome 15, as are the majority of satellited marker chromosomes (this was confirmed by fluorescence *in situ* hybridization studies using a D15Z1 probe, specific for the centromere of chromosome 15). Further studies specific for the centromeres of chromosomes 14 and 22 (D14Z1/D22Z1) (Figure 2) and chromosome 22 only (D22Z4) showed two signals on the marker chromosome with both probes. Probe D22S75, localized to the proximal long arm of chromosome 22 at q11.2, showed no signal on the marker chromosome. The results, in combination with the morphological appearance, showed that this marker chromosome was derived from two different chromosomes 22, with break points close to the centromeres on the long arms of both chromosomes.

The karyotype was 47,XX,+mar.ish psudic (22;22)(q11.2;q11.2)(D14Z1/D22Z1++, D22Z4++, D22S75−). The imbalance from the resultant tetrasomy of the short arm and proximal long arm of chromosome 22 results in the Cat Eye syndrome (CES). The child had phenotypically unaffected parents. However, genetic analysis of the mother revealed a supernumerary

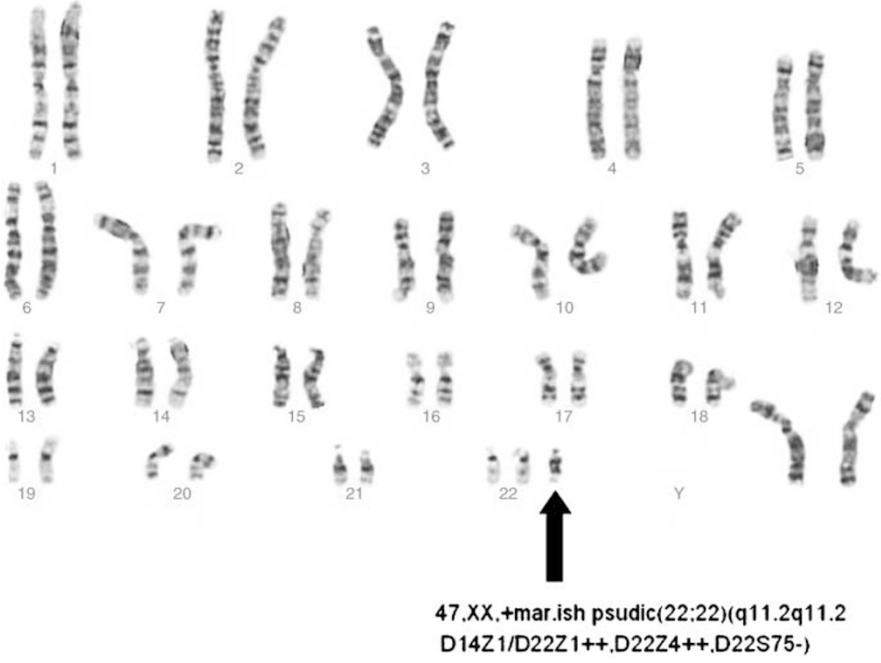

Figure 1 G-banded karyotype showing additional marker chromosome 22 (arrow).

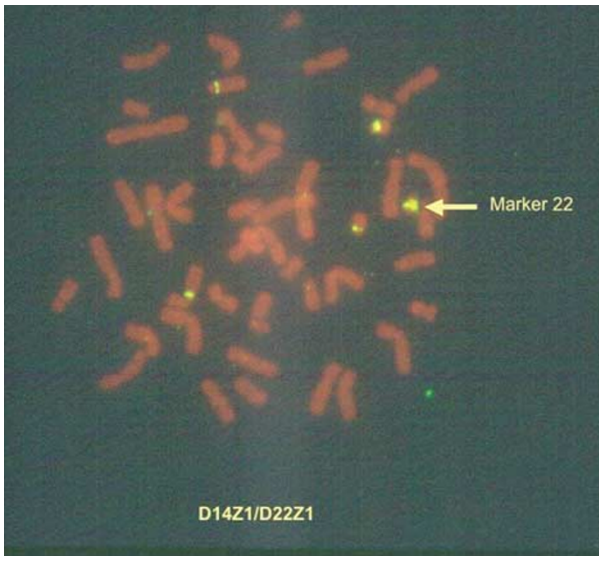

Figure 2 Metaphase spread showing fluorescence *in situ* hybridization investigations with D14Z1/D22Z1 probe set.

bisatellited marker chromosome, identical to that found in the daughter in 33 out of 175 (19%) cells examined.

(karyotype: mos 47,XX, + psudic(22;22)(q11.2;q11.2) [33]/46,XX[142])

The patient was referred for ophthalmological review and was seen at the age of 4 years with concerns regarding a left convergent squint from birth. Vision was 6/6 bilaterally. Cover test, ocular movements, and Frisby testing were all unremarkable. Refraction was within normal limits for age. No lid abnormalities, iris, or choroidal colobomata were noted.

The patient was also receiving speech and language therapy for a right-sided hypoplastic palate and very narrow ear canals with possible unilateral sensorineural hearing loss.

At the age of 7 years, the patient was noted to have moderate restriction of abduction in the right eye, associated with narrowing of the palpebral fissure on attempted adduction, with an upshoot in adduction. Cover testing showed minimal exophoria for near and distance. Duane anomaly was diagnosed. No abnormal head posture was evident and the patient thus managed conservatively.

Comment

In 1878, Haab[2] described a triad of congenital malformations consisting of uveal coloboma, imperforate anus, and renal malformations. This was later named the CES by Gerald *et al*,[3] in reference to the vertical iridochoroidal coloboma frequently present.

The major clinical features of CES include preauricular skin tags and/or pits (the most common), anorectal malformation, urogenital malformation, ocular coloboma, and congenital heart defect. Minor features include down-slanting palpebral fissures, hypertelorism, orthopaedic malformations, low set/dysplastic ears, gut malformations, micrognathia, microcephaly, microphthalmia, and cleft palate. Mental function can be normal to severe retardation. Neurological features, of which ocular motility disorders are most common, include hearing impairment, spasticity, ataxia, and seizures.[4] Not all major features are necessarily present in all cases, thus demonstrating the phenotypic variability of the condition. Severe forms can lead to death.[5] Several forms of ocular motility disorders are known to be associated with CES, but to our knowledge, there have only been a few cases reported specifically describing Duane syndrome (DS).[1,6,7]

Duane retraction syndrome has been subjected to several classifications, but its most characteristic presentation is the absence of abduction with some degree of restriction of adduction associated with globe retraction, with narrowing of the palpebral fissure on attempted adduction. It most commonly affects the left eye and several studies confirm a preponderance towards females.[8] It is evident, according to a literature review by Kalpakian *et al*[6], that DS has been coexistent with other ocular and systemic conditions[4] but for the majority of cases, this is not so.

We believe that our case supports DS as a recognized feature of the rare CES. Furthermore, it emphasizes that despite the appellation, patients may not necessarily exhibit the classic vertical iridochoroidal coloboma or indeed, any other ocular signs, at diagnosis. Should this be the case, periodic review may still be warranted to detect ocular motor dysfunction developing later in childhood. Our patient differs from previously described cases insofar as she did not exhibit any detectable iridochoroidal colobomata. Cullen *et al*[1] described a case of DS in a patient with urogenital abnormalities with a bisatellited marker derived from chromosome 22, who also lacked colobomata. However, their case also demonstrated notable differences from CES, for example, lack of heart defects, short stature, and primary amenorrhoea owing to absent uterus. Our case also raises the question as to whether chromosome 22 is involved in ocular motility abnormalities. Several reports have localized DS to various chromosomes, which include chromosomes 2, 4, 8, and 22.[8] This is beyond the scope of this report and further studies on chromosome 22 would be needed to establish this link.

References

1 Cullen P, Rodgers CS, Callen DF, Connolly VM, Eyre IL, Fells P *et al*. Association of familial Duane anomaly and urogenital

abnormalities with a bisatellited marker derived from chromosome 22. *Am J Med Genet* 1993; **47**: 925–930.
2 Haab O. Bieträge zu den angeborenen Fehlern des Auges. *Von Graefe's Arch. Ophthalmol* 1878; **24**: 257.
3 Gerald PS, Davis C, Say BM, Wilkins JL. A novel chromosome basis for imperforate anus (the 'cat's-eye syndrome'). *Pediatr Res* 1968; **2**: 297.
4 Rosias PR, Sijstermans JM, Theunissen PM, Pulles-Heintzberger CF, De Die-Smulders CE, Engelen JJ *et al.* Phenotypic variability of the Cat Eye Syndrome. Case report and review of the literature. *Genet Counsel* 2001; **12**(3): 273–282.
5 Denavit TM, Malan V, Grillon C, Sanlaville D, Ardalan A, Jaquemont ML *et al*. A new case of severe clinical phenotype of the Cat Eye Syndrome. *Genet Counsel* 2004; **15**(4): 443–448.
6 Kalpakian B, Choy AE, Sparkes RS, Schreck RR. Duane Syndrome associated with features of the Cat-Eye Syndrome and mosaicism for a supernumerary chromosome probably derived from number 22. *J Paediatr Ophthalmol Strabismus* 1988; **25**: 293–297.
7 Weleber RG, Walknowska J, Peakman D. Cytogenetic investigation of Cat-Eye Syndrome. *Am J Ophthalmol* 1977; **84**: 477.
8 Mitchell PR, Parks MM. Ophthalmic syndromes and trauma. In: Jaeger EA, Tasman WS (eds). *Duane's Ophthalmology.* Lippincott Williams and Wilkins, New York, 2005, pp 1–6.

TN Win[1], Selwyn Roberts[2] and David Laws[1]

[1]Department of Ophthalmology, Singleton Hospital, Sketty Lane, Sketty, Swansea, UK

[2]Department of Cytogenetics, Institute of Medical Genetics, University Hospital Wales, Heath Park, Cardiff, UK

Correspondence: David Laws, Department of Ophthalmology, Singleton Hospital, Sketty Lane, Sketty, Swansea SA2 8QA, UK
Tel: +44 1792 205666, ext 5912;
Fax: +44 1792 205666.
E-mail: dave@sailwave.com

Eye (2007) **21,** 289–291. doi:10.1038/sj.eye.6702538; published online 22 September 2006

Sir,

Palpebral pleomorphic rhabdomyosarcoma in a teenager

Rhabdomyosarcoma (RMS) is the most common childhood primary soft tissue sarcoma. Ocular lesions represent about 10% of all RMSs. The majority of ocular RMS arises from the orbit and is of the alveolar cell type. Pure eyelid lesion of the pleomorphic cell type is extremely rare especially in children. We would like to present a case of palpebral pleomorphic RMS and its management.

Case report

An 11-year-old Indonesian Chinese boy who was previously well, developed an itchy lump in his left upper lid in December 2004. The lump was excised at a local hospital in February 2005 without histological diagnosis. The lump recurred 3 months later resulting in a mechanical ptosis. The patient consulted a private ophthalmologist in Kuching, Sarawak in August 2005 and the lump was biopsied. Histology showed pleomorphic cells with enlarged hyperchromatic nuclei and eosinophilic cytoplasm. Some tadpole-shaped cells were also seen (Figure 1). The diagnosis of RMS was confirmed with immunohistochemistry, which revealed the presence of desmin (see inset in Figure 1). The patient was referred to the oncologist. CT scan of the orbits and brain showed the tumour was confined to the upper lid measuring $2.5 \times 3.0 \times 3.5$ cm. He was started on chemotherapy and two cycles of uncomplicated chemotherapy were given in August and September 2005. However, the tumour failed to respond to the treatments and doubled in size (Figure 2). Central necrosis also developed on the surface of the tumour.

The patient was referred to our eye centre for further management. Despite difficulty in opening the eye, the patient was able to perceive light in the left eye. A repeated CT scan showed the tumour had extended into the anterior orbit (Figure 3). However, the orbital bone showed no signs of involvement. Using the

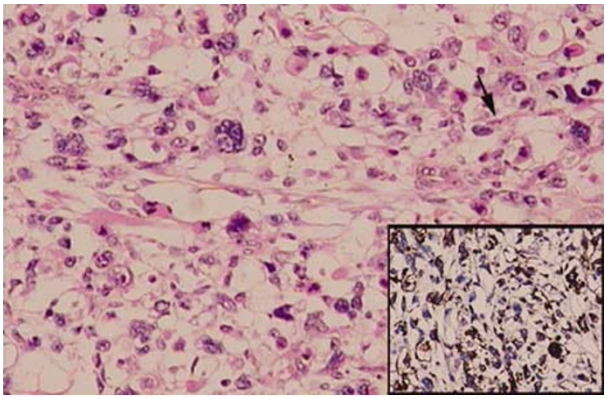

Figure 1 Histology of the tumour showing pleomorphic cells with tadpole-shaped cell (arrowed) and the inset shows positive desmin immunostaining of the tumour cells.