long-term prognosis is still unknown. The diagnosis of L-ORD is either based on the above clinical picture or on the pathological appearance of a thick sub-RPE deposit throughout the retina^{1,3,4} like that found in Sorsby's fundus dystrophy⁶ and sometimes in age-related macular degeneration.⁷ It is postulated that this deposit may act as a barrier to nutrient transport to the retina. In the later stages, there is widespread loss of RPE and photoreceptors.⁴

In the early stages, the disease can mimic other ophthalmic conditions as in our two cases. Our first patient was seen relatively early in the disease course but the diagnosis was not made in the patient or her sister until the peripheral retinal changes were present. Asking about night vision problems, family history and careful examination of the fundus including peripheral retina can be helpful in detecting this unusual disease. Our patients' diagnosis was further confirmed when they were found to be distantly related members of a fully investigated L-ORD family.²

These cases are important to raise awareness of L-ORD in the ophthalmic community. We often try to reassure our patients with ARM that they will not lose their peripheral vision. This rare subgroup of patients does lose this vital visual function with devastating visual results.

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Sir,

Ocular coloboma and radial aplasia: syndrome or association

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Ocular colobomata are relatively common malformations and are often associated with microphthalmos. A typical coloboma is located in the inferonasal quadrant, and may affect any part of the globe traversed by the fissure from the iris to the optic nerve. The majority of cases are isolated defects; however, sometimes they may be seen with other defects. Patients with multiple malformations and coloboma often present diagnostic and therapeutic challenges especially in infants.

Case report

The affected proband is a female born at 41 weeks gestations. The delivery was by emergency caesarean section because of meconium stained liquor and prolonged rupture of membranes. Apgar scores were 8 at 1 min and 10 at 5 min. The birth weight was 2420 g (below third centile) and head circumference was 33 cm (third centile). The baby was admitted to the neonatal unit because of respiratory grunting, and received oxygen for 24 h and 3 days of intravenous antibiotics. Clinical examination revealed a congenital right upper limb abnormality with an absent thumb.

Radiography of the right upper limb showed absence of the radius and thumb with only four metacarpals (Figure 1). Chest X-ray showed normal mediastinum and

Figure 1 X-ray of the right upper limb showing radial aplasia, absent thumb, and four metacarpals.

heart size and clear lungs. On abdominal ultrasounds, both kidneys were normal in size and appearance as well as the liver, gall bladder, pancreas, and spleen. Cranial ultrasound showed a normal appearance as well.

Both parents were healthy and nonconsanguineous. The mother was 38 years old at the time of delivery and did not experience any illness during the pregnancy. She was previously gravida 5 para 5 and no significant past medical history. The first sibling, a male, had been diagnosed with polycystic kidneys. The other four siblings, two boys and two girls, are all healthy. The father was 43 years old with no known medical problems. He is the biological father of this patient but not of the other five children. He has two other children who are both normal.

The infant was seen in the Eye clinic at the age of 10 months. She was found to have a coloboma involving the iris, retina, choroids, and optic nerve in the right eye (Figures 2 and 3). The left eye was normal. The corneal diameters were RE 10.1 mm and LE 10.2 mm and the axial lengths were RE 22.05 mm and LE 22.38 mm.

Careful inspection of the face did not reveal any facial dysmorphic features. Although the infant was noted to have features of intrauterine growth retardation at birth, further assessments by the paediatrician showed that subsequent growth and development was normal. A further referral to the paediatrician to carry out a complete physical examination, with emphasis on the vertebrae and cardiovascular system, was requested. However, no other congenital abnormalities were detected.

Karyotyping in our patient using G-banded analysis showed an apparently normal female pattern. No visible cytogenetic abnormality was observed. Molecular analysis by fluorescent *in situ* hybridization (FISH) studies using a DNA probe that hybridizes to 22q11.2 did not detect any deletion in this region. Further chromosomal analysis was requested to rule out tetrasomy 22pter-q11 and Fanconi anaemia by looking

Figure 2 Iris coloboma of the right eye located inferonasally.

Figure 3 Chorioretinal coloboma located inferiorly and involving the optic nerve.

for increased chromosomal breakage in cultured blood lymphocytes after exposure to Mitomycin C. These results were also negative.

Comment

Ocular colobomata are because of a defective closure of the fetal fissure during the 5th to 7th weeks of fetal life. Isolated coloboma is often inherited as an autosomal dominant trait with variable expression;¹ an autosomal recessive pattern has been suggested in some cases.² Patients with multiple systemic malformations and coloboma may have a recognized syndrome or one of several chromosomal aberrations. The inheritance pattern may be autosomal dominant, autosomal recessive or X-linked.³ Environmental and intrauterine insults have been linked with

ocular colobomata and would seem plausible in sporadic cases. Thalidomide 'A' is a well-documented environmental cause of coloboma with or without phocomelia.⁴ The use of anticonvulsants in pregnancy,⁵ as well as alcohol,⁶ has also been implicated in the formation of coloboma and other multiple systemic malformations.

The finding of a coloboma should alert the physician to the possibility of chromosomal aberration and the need for a complete systemic evaluation. Accurate refraction is fundamental since there is a wide range of refractive errors in eyes with coloboma. Cycloplegic refraction was performed in our patient and was within the normal limits for this age group. Essential in the treatment of children with colobomata is the determination of visual prognosis. Measurements of corneal diameter and axial length are useful parameters in assessing the visual potential in infants with coloboma. Hornby *et al*⁷ have shown that microphthalmos with cyst had the worst prognosis, coloboma with microcornea and microphthalmos had a poor prognosis, coloboma with microcornea had an intermediate prognosis, and simple coloboma had the best prognosis. Our patient had corneal diameters of 10.1 and 10.2 mm and axial lengths of 22.05 and 22.38 mm in the right and the left eye, respectively. However, the coloboma extended posteriorly to involve the optic nerve and therefore associated with a poor visual prognosis.

Genetic evaluation is becoming increasingly more important in the understanding of molecular disorders and is warranted in all cases of ocular colobomata associated with other malformations. Recent reports have shown that there are over 20 reported cases of interstitial deletion in 2q, the most common single deletion being del 2(q31q33) with 14 cases in the literature.⁸ Nixon *et al* reported on a 9-year-old boy with *de novo* deletion of chromosome 2q, including bands 2q24.3 and 2q31.⁸ The clinical findings included growth failure, minor facial anomalies, craniosynostosis, heart defects, coloboma of the iris, retina and optic nerve and limb abnormalities. Boles *et al*⁹ have drawn attention to the emerging association between del 2q31.1 and limb defects. Deletion of chromosome 22q11 has been well documented and is a major cause of DiGeorge syndrome.¹⁰ Digilio *et al*¹¹ reported on a neonate with del 22q11 presenting with facial dysmorphism, congenital heart defect, urogenital malformation, ocular coloboma, and unilateral radial aplasia. We believe that there may be other genes responsible for producing ocular coloboma and other systematic malformations. Further delineation of genes involved in these disorders may help in understanding the molecular defects causing ocular colobomata.

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Sir,

Interferon-associated retinopathy

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Interferon (INF) alpha is known to have antiviral, antifibroblastic and antitumour effects.^{1,2} It has been tried in the treatment of ocular disorders such as dendritic keratitis, subretinal neovascularisation in age-related macular degeneration,³ glaucoma filtering surgery, and