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Autosomal dominant simple microphthalmos: incomplete penetrance and variable expression in a large family

We read with interest the well documented report by Vingolo *et al*¹ on "Autosomal dominant simple microphthalmos". The authors describe a large pedigree with 14 persons in four generations affected with bilateral microphthalmos without other ocular or systemic signs. The family data were most compatible with autosomal dominant inheritance with complete penetrance. Based on the findings in this family and a review of published reports the authors concluded that "simple, partial, posterior pure microphthalmos and nanophthalmos are similar clinical entities sharing total axial length and vitreous cavity length reduction".

During the past few years we have been contacted by several members of a large family (see pedigree in the figure) for genetic counselling after the birth in this family of three children (III-6, III-7, IV-1), two boys and one girl, with "uncomplicated" bilateral anophthalmos. All three are mentally normal at the respective ages of 12, 9, and 8 years.

Further clinical and laboratory examinations, including chromosome studies, were normal but CT scans of the brain showed complete absence of ocular structures but normal optic nerves in all three. Further familial investigation showed normal ophthalmological findings in all family members, except I-1 (paternal great grandfather of IV-1 and maternal grandfather of III-6 and III-7), II-1 (paternal grandfather of IV-1) and III-4. All three presented a unilateral left sided extreme form of microphthalmia with cloudy corneae and total axial lengths below 8 mm. Clinical and biometric findings of the contralateral eyes were normal.

The ocular anomalies in the affected members of the present family thus varied greatly from bilateral true anophthalmos to unilateral microphthalmos with small anterior segment and cloudy corneae. The findings in this family are most compatible with autosomal dominant inheritance with variable expression and incomplete penetrance and confirm the observations reported by Bateman² who described a three generation family with non-colobomatous microphthalmos dominantly inherited with incomplete penetrance and variable expressivity.

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Grebe syndrome: a very severely affected case

Grebe syndrome is a very rare form of short limb dwarfism, inherited as an autosomal recessive trait. It is characterised by shortening affecting the lower limbs more than the upper limbs and distal parts more than proximal parts resulting in bulbous fingers and toes, whereas the head, neck, and trunk are essentially normal.¹ The classical clinical and radiological features and other un-

usual clinical features have been described previously.^{2,3} In the present communication we report an extreme form of Grebe syndrome in which there was a total absence of bones in the lower limbs, features which have not been reported previously.

A male neonate was born at term to a consanguineous couple (uncle-niece) showing characteristic features of Grebe chondrodysplasia (fig 1). There was progressive shortening of the limb bones from the proximal to distal ends. The lower limbs were more severely affected than the upper limbs. The hands and feet were extremely small with bulbous digits. There were four fingers and a thumb on both hands and five toes on both feet. The head, neck, and trunk were essentially normal. His length was 30 cm, upper segment 24 cm, lower segment 6 cm, head circumference 30 cm, chest circumference 27 cm, upper limb length 10.5 cm, lower limb length 8 cm, and weight

Figure 1 Infant with Grebe syndrome.

Figure 2 Whole body radiograph of the infant.

Family pedigree.