LETTER TO THE EDITOR

Grebe syndrome: a second case with extremely severe manifestations

We read with great interest the report by Kulkarni *et al*¹ on Grebe syndrome in a severely affected child. We have recently seen a similar case, a 28 week preterm female infant with a birth weight of 600 g and a length of 25 cm, who died soon after birth (fig 1). She was the first child of a consanguineous couple (first cousins once removed) of Italian ancestry. The family history was unremarkable and the pregnancy had been uneventful. Clinical examination showed marked micrognathia, a normal neck and trunk, and shortening of all four limbs, the lower being more severely affected than the upper. The shortening was progressive, from proximal to distal, the fingers were bud-like (fig 2), the lower limbs very short, the hips abnormally jointed, and there was no clear limit between the thighs and legs. Distally, close to the ankles, there were osseous spurs protruding bilaterally. The feet were internally rotated and the toes, as well as the fingers, were knob-like (fig 3).

Figure 1 Full body view.

The radiographs showed normal humeri, absent ulnae, and very poorly ossified metacarpals and phalanges. Both femora were absent and, distally, there was only an unidentifiable rudimentary bone, the one observed clinically as a bony protrusion. Again, the metatarsals and phalanges were very poorly ossified or not at all. The skull, spine, ribs, and pelvis were normal (fig 4). No internal malformations could be detected at necropsy and cartilage histology was normal. Neither of the parents showed any clinical abnormality.

Because of the lack of trunk involvement and the radiographically normal bone struc-

Figure 2 Upper limbs. Note bulbous digits.

Figure 3 Lower limbs. Note bony spurs and bulbous toes.

Figure 4 Whole body radiograph. Note absence of femora and ulnae and only one bone in the legs bilaterally.

ture, lethal skeletal dysplasias were excluded as differential diagnoses, as were femoral hypoplasia-unusual facies² and femur-fibula-ulna³ syndromes. The whole clinical and radiographical appearance suggested Grebe syndrome.

Grebe syndrome is a rare genetic entity, which to date to our knowledge has been described in about 70 cases, belonging to 12 families or inbred groups. There seems to be no doubt about its autosomal recessive mode of inheritance, based on recurrence in sibs or parental consanguinity or both. Although the overall clinical picture in the different sib-

ships described was similar, the slight variations among them, as well as minor expression in heterozygous carriers mentioned by some of the authors,^{4,5} could indicate that different genetic entities or perhaps different mutations of the same gene are involved.

Our patient seems to be the second case with an extremely severe form of this condition, which could, as Kulkarni *et al*¹ suggested, reflect full expression of the gene, or, as already mentioned above, indicate that a different genetic entity or a different mutation of the same gene could be involved. Further studies on the recently described DCMP1 mutation⁶ apparently involved in Grebe syndrome should clarify this question.

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BOOK REVIEWS

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Chromosomes Today. Volume 12. Editors N Henriques-Gil, J S Parker, M J Puertas. (Pp 379; £60.00.) UK: Chapman & Hall. 1996. ISBN 0-412-75240-9.

This book contains all the invited lectures given at the 12th International Chromosome Conference held in September 1995 in Madrid, Spain. Not surprisingly, fluorescence in situ hybridisation has added colour to the classical beauty of chromosomes. The reader is attracted by a colourful cover and many colour plates. Indeed much progress has been made by using the new molecular cytogenetic techniques to study the complexities of chromosome structure, function, and evolution. However, I couldn't agree more with Peter Moens saying that "chromosome images have become exquisite but the line between fact and fancy is sometimes treacherously narrow", but he also states clearly that "nostalgia