Congenital Absence of the Fibula and Craniosynostosis in Sibs

R. B. LOWRY*

*The Division of Medical Genetics, Department of Paediatrics, University of British Columbia,
and the Vancouver General Hospital, Vancouver, British Columbia, Canada*

Total or partial congenital absence of the fibula is the most frequent defect involving the long bones. More than 300 cases have been recorded in the literature. It is usually a sporadic event and, with the exception of absent tarsal bones and toes, other malformations are infrequent. The present paper deals with what is possibly a new genetic syndrome.

Case Reports

Case 1. The propositus was born in 1965, the first child of healthy young Greek parents who were second cousins; the father was 28 and the mother 19 at his birth. The pregnancy was notable for excessive vomiting throughout for which antacids and an unknown antinauseant were taken. The gestation period and delivery were normal. The main clinical features are listed in Table I. The craniosynostosis (Figs. 1 and 2)

normal intelligence having just completed a year of kindergarten. His chromosome karyotype was normal, and apart from the simian creases his dermatoglyphics were unremarkable. He did not have a cleft palate though the palate was highly arched.

Case 2 was born 2 years later after a normal, full-term pregnancy. No drugs were taken during this pregnancy. He sustained a fracture of the left humerus during the delivery which was by breech extraction, and was very limp, requiring resuscitation. He subsequently developed respiratory distress and died within 12 hours so

TABLE I
CLINICAL FEATURES

	Case 1	Case 2
Sex	Male	Male
Birth weight (g)	2920	2400
Craniosynostosis	+	+
Both coronals	+	+
Sagittal	+	-
Prominent eyes	+	+
Strabismus	+	NK
Partial cleft palate	-	+
Bilateral simian creases	+	+
Cryptorchidism	+	+
Bilateral absent fibulae	+	+
Bilateral equino varus	+	+
Short sternum	+	NK
Pilonidal dimple	+	NK

+ = present, - = absent, NK = not known.

was of such severity that a craniectomy was performed. Five toes were present bilaterally and no abnormalities were noted in the bony configuration of the feet though both were in marked equinovarus position (Fig. 3). He has been raised in a foster home, and appears to have

FIG. 1.

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* Present address: 715 West 12th Avenue, Vancouver 9, British Columbia, Canada.

FIG. 2.

FIG. 3.

that antemortem investigations were limited. Chromosome studies were not done. There were some differences from the previous case, namely a short webbed neck, low set ears with pointed helices, and there was a mild chordee of the penis. Although there was bilateral incomplete coronal synostosis there was also a midline skull defect in the anterior occipital region giving a large posterior fontanelle measuring 4×6 cm and wide occipital sutures. The sagittal suture was not fused. However the anterior fontanelle was very small, and there were several small wormian bones adjacent to the occipital bone. There was a partial cleft of the hard palate with an intact soft palate and single uvula. Necropsy examination disclosed marked congestion of the blood vessels on the surface of the brain with diffuse subdural and intradural haemorrhages. The lungs showed hyaline membrane disease and the testes, which were normal, were in the abdomen. The lower limbs were identical to those of his brother (Table I).

Discussion

Congenital absence of the fibulae, either total or partial, is frequently associated with absence of the lateral two or three toes as well as the talus and cuboid. O'Rahilly (1951) lists 296 cases in the literature and there have been many reports since that time. Frantz and O'Rahilly (1961) classify this as paraxial fibular hemimelia with two subtypes: terminal longitudinal (absence of lateral toes and tarsal bones) and intercalary (normal distal structures). They quote the genetics as being 'recessive or possibly sporadic'. The vast majority of the more than 300 cases previously described have been sporadic but it should be realized that in many instances adequate family history details are not given. It is more likely that familial cases would have been reported and their absence is all the more significant. As with most congenital malformations heterogeneity is likely. Bilateral partial absence of the fibula was reported by Volkmann (1873) in 3 generations of a family and occurring in both sexes thus suggesting autosomal dominant inheritance. Mau (1927) reported 2 brothers with the same ankle deformity as Volkmann's patients (1873). However, only one had a fibular defect which was partial. The parents and remaining 6 sibs were normal which suggested a recessive mode of inheritance with variable expressivity. Aschner (1929) cites a number of familial instances of congenital fibular aplasia some of which appear to be dominant traits (Meusel, 1882; Friebe, 1903) and some suggestive of recessive inheritance (Jakobi, 1891; Hiromoto, 1913). Fibular aplasia or hypoplasia has been described in association with malformations involving other limbs (Grebe, 1955; Langer, 1967)

and with cleft lip and palate (Roberts, 1919). Robert's cases appear to be a different syndrome. Nevertheless they are of interest as the lateral photograph of one shows prominent eyes suggestive of craniosynostosis and shallow orbits. No other cases of absent fibulae and craniosynostosis are recorded in the literature though Scharff (1909) quotes a case (no. 36 in his table) with 'defects of the skull bones' and Haudek (1896) quotes two cases (no. 2 and no. 45 in his table) with either deformities or defects of the skull.

Craniosynostosis can, of course, be due to single mutant genes as in several syndromes. However, I am unaware of fibular aplasia in any of these. The treatment of the latter malformation has been discussed by others (Farmer and Laurin, 1960) and no further comments will be made. The partial hard palatal cleft with an intact soft palate and uvula is unusual and at present cannot be explained by any current embryologic theory (Lynch, Lewis, and Blocker, 1966).

The patients described in this report appear to have an unique combination of malformations and this together with the parental consanguinity suggests an autosomal recessive mode of inheritance.

Summary

Two brothers have been described with a syndrome of bilateral absent fibulae, craniosynostosis, cryptorchidism, and bilateral simian creases. The parents are second cousins and the tentative conclusion is that this is an autosomal recessive trait.

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