Case reports

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Unilateral absence of the hand in second cousins

MARGARET LAMONT* AND A J SALISBURY†

*Department of Child Health, Southampton General Hospital, Southampton SO9 4XY; and †Department of Paediatrics, Princess Margaret Hospital, Swindon SN1 4JU

SUMMARY This paper reports two second cousins with absence of the left hand.

Congenital absence of the hand, acheiria, is a rare defect occurring in 1:65 000 live births.¹ It is always unilateral and almost always sporadic; reports of acheiria recurring in a family are sparse. They include those of Hecht and Scott,² in which two sibs born to consanguineous parents were affected, and of Pilarski *et al*³ who recorded two affected first cousins. Familial occurrence of acheiria and forearm

amputation has been recorded, in sibs,¹ uncle and niece,⁴ uncle and nephew,³ and in a great grandmother and her great granddaughter.⁵ However, we know of no previous reports of acheiria occurring in children sharing great grandparents.

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Case 1 is the younger child of healthy, unrelated parents. His father was aged 33 and his mother 29 years at the time of his birth. Neither they, nor his older sib, have any hand abnormality. His mother had primary amenorrhoea and both pregnancies were induced with clomiphene. The pregnancy was

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FIG 1 Case 1 aged two and a half years with rudimentary digits on the left arm. X ray at 15 months old shows two ossification centres.

uneventful with no illness or medication. Birth weight at term was 2890 g. He was noted at birth to have an absent left hand with rudimentary digits. Apart from this (fig 1) he has no physical defect and is developing normally. His right hand and both feet are of normal size with no digital anomalies. X ray at 17 months (fig 1) showed a normal radius and ulna with two ossification centres in the central region.

Case 2 was born 17 months after case 1 to a first

cousin of his mother (fig 2). The two families live some 60 miles apart. She is the only child of a 28 year old father and a 29 year old mother. There was no history of menstrual problems. The pregnancy was uneventful with no medication apart from iron therapy and no history of illness. Her birth weight at 40 weeks' gestation was 2700 g. She was born with absence of the left hand (fig 3).

The defect is similar to that of case 1 but with greater reduction of digital development. She has no other physical defects and, like her cousin, is developing normally. An x ray (fig 3) done just after birth shows a normal left radius and ulna.

No other family members have any known anomalies of their hands or feet. The hands of the mother and maternal aunt of case 1 have been personally examined and show no clinical or radiological abnormality.

Discussion

The occurrence of this identical defect in two cousins suggests a genetic basis. The possibility that both children could have been affected by chance alone, when the incidence of acheiria is 1:65 000, is too remote to be considered. The parents of the two children live in different towns and environmental factors are unlikely to have any aetiological signifi-

FIG 2 Family pedigree.

FIG 3 Case 2 at 11 months old, showing small rudimentary digits on the left arm, and x ray appearance at birth.

cance. The inheritance of a common mutant dominant gene from one or other great grandparent is the most cogent explanation. However, the gene is not expressed in any relatives in the two intervening generations. This raises the possibility, discussed by David⁶ in relation to ectrodactyly, of a single mutant autosomal dominant gene under epistatic control of a gene, or genes, elsewhere in the genome. When the mutant gene is inherited without the 'protective' gene or genes, deformity will occur. That more than one 'protective' gene may be involved is suggested by the reports of acheiria and mid forearm amputation occurring within the same family.¹⁻⁵ Forearm amputation is, like acheiria, a rare defect (1:25 000) and would be unlikely to be associated, by chance alone, with acheiria in the same family. The extent to which the mutant gene is expressed could be dependent on the number of 'protective' genes also inherited.

Another possible issue to consider is germinal mosaicism, but the reports of acheiria and mid forearm amputation in the same family do not favour the presence of a single mosaic mutant gene.

Delayed gene mutation could be a theoretical explanation in the family reported here, but the family in which a great grandmother had acheiria and her great granddaughter a mid forearm amputation⁵ would be rather against such a factor operating. The suggestion that the sex of the parent may be relevant to gene expression in the offspring, owing to differential 'genome imprinting' during oogenesis and spermatogenesis,^{7,8} is not of rele-

vance in this context. Inheritance in case 1 was male-female-male and in case 2 female-female-female; neither is there any sex differential in any other reported familial cases of acheiria or acheiria and mid forearm amputation.

From the relatively few case reports where acheiria has recurred within a family, or has been associated with mid forearm amputation, we would favour the presence of a mutant gene, in the absence of a 'protective' gene or genes to account for the deformity.

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Correspondence to Dr M Lamont, Department of Child Health, Southampton General Hospital, Southampton SO9 4XY.

Identification and characterisation of a small marker chromosome using non-isotopic in situ hybridisation with X and Y specific probes

JOHN A CROLLA*, MARY SMITH, AND ZOE DOCHERTY

From the Paediatric Research Unit, Division of Medical and Molecular Genetics, United Medical and Dental Schools of Guy's and St Thomas's Hospitals, Guy's Hospital, London SE1 9RT.

SUMMARY A 13 year old male with mild mental retardation, obesity, and poor secondary sexual differentiation was found to have a 46,X,+mar karyotype. In situ hybridisation with X and Y specific probes proved the marker to be composed of Y centromeric and short arm material.

*Present address: MRC Experimental Embryology and Teratology Unit, MRC Laboratories, Woodmansterne Road, Carshalton, Surrey SM5 4EF.

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Case report

The proband, a 13 year old mentally retarded male, was referred because of poor secondary sexual development and gynaecomastia. He was thought to be a possible case of Prader-Willi syndrome. He was born at 37 weeks' gestation weighing 1956 g to healthy and unrelated parents. Two sibs, one younger and one older, are both healthy and normal. At two years, the patient's right testis was brought down surgically and the other descended spontaneously at seven years. His development has