Autosomal recessive postaxial polydactyly type A in a Sicilian family

F. MOLLIKA, S. LI VOLTI, AND G. SORGE

From Department of Paediatrics, University of Catania, Italy

SUMMARY Postaxial polydactyly type A was present in several members of a Sicilian family. The anomaly was probably transmitted as an autosomal recessive character. Two polydactylous subjects were also beta-thalassaemia carriers, but a linkage between the two mutant genes could be excluded. Two patients with hexadactyly had a fifth digital triradius.

Postaxial polydactyly, the presence of extra digits on the ulnar or fibular edge of the extremities, may be associated with other abnormalities as part of several genetic or chromosomal syndromes (McKusick, 1975), or with other defects of the hands and feet (Mohan, 1969; Holt, 1975), or may occur as a single birth defect. The extra digit(s) may be well developed ('type A' polydactyly) or may be vestigial ('type B' polydactyly). It is possible that type A and type B postaxial polydactyly are different genetic entities (Gates, 1946; McKusick, 1975) though they may coexist in the same kindred (Sverdrup, 1922/3).

Isolated postaxial polydactyly type A is usually transmitted as an autosomal dominant character with incomplete penetrance (Castilla *et al.*, 1973), the reports of possible or apparently recessive inheritance being very rare (Snyder, 1929; Gates, 1946; Mohan, 1969), and sometimes questionable (Kohler, 1929). The possibility that there are two (Walker, 1961) or even more loci for the trait cannot be excluded (Mohan, 1969).

We recently examined a boy with type A postaxial polydactyly, bilateral cryptorchidism, and beta-thalassaemia trait. Several other members of his family had postaxial polydactyly but no other associated

Received for publication 22 September 1977

Fig. 1 The pedigree.

Fig. 2 Radiographs of the hands (a) and feet (b) of the proband (V.3).

abnormalities. The study of this pedigree strongly suggests an autosomal recessive inheritance of the postaxial polydactyly in this family.

Proband

The proband (V.3, Fig. 1), a 16-month-old male infant, was admitted to the Department of Paediatrics of the University of Catania because he was moderately pale. Apart from the family data (see below), past history was irrelevant. His weight was 8.6 kg and height 76 cm. Moderate pallor, bilateral cryptorchidism, six toes on both feet, and an extra finger on the ulnar side of the right hand were the abnormal findings during physical examination.

An x-ray of the hands (Fig. 2a) showed partial duplication of the first phalanx and total duplication of the second and of the third phalanx of the right little finger; on the feet (Fig. 2b) there were partial duplication of the left fifth metatarsal and complete duplication of both the fifth toes. Radiographs of the

other bones were normal. For the dermatoglyphs see below.

There was anaemia of mild degree (haemoglobin 8.7 g/dl, red blood cells 3.17 millions/mm³, haematocrit 23%), with moderate anisopoikilocytosis, and frequent target cells. Fetal haemoglobin was 2% by alkali denaturation, and haemoglobin A₂ was 4.38% (normal up to 3.5 in this laboratory) at cellulose acetate electrophoresis. Urine analysis, white blood cells, and differential count, platelets, and serum glucose, Na, K, Ca, P, alkaline phosphatase, iron, iron-binding capacity, total proteins and fractions were normal, as well as electrocardiogram, electroencephalogram, karyotype (46,XY), and intravenous urogram. Ophthalmological examination was negative.

Family

Family L. lived in Bronte, a little town of eastern Sicily at the foot of mount Etna. Information about the family was obtained from three members of the

Fig. 3 Radiographs of the hands (a) and feet (b) of V.2.

Table Finger ridge counts and atd angles of V.2, V.3, and V.7

		VI		V		IV		III		II		I		Total ridge count (*)	atd	atd'
		r	u	r	u	r	u	r	u	r	u	r	u			
V.2	L	?	?	12	0	13	0	10	14	12	14	12	14	101	48°	—
	R	?	?	12	0	11	15	0	0	14	12	14	16	94	40°	49°
V.3	L	—	—	12	3	12	0	13	0	8	16	8	16	89	44°	—
	R	8	0	0	7	11	13	12	9	13	14	14	11	112	42°	—
V.7	L	?	?	12	0	14	0	12	0	14	9	14	9	80	48°	—
	R	?	?	12	0	13	0	12	0	13	14	14	0	78	48°	59°

*Extra fingers excluded.

pedigree (IV.2, III.1, and II.5, Fig. 1) directly in Bronte, where dermatoglyphs and blood samples for the haematological study were taken from the consenting members.

Six of the 87 individuals reported in the pedigree were said to be polydactylous: 3 members of F-II (II.2, II.3, and II.9), and 3 living members of F-V, who were directly examined by us: the proband (V.3), one of his two brothers (V.2), and one of his first cousins (V.7). In all these 6 subjects the polydactyly was of the postaxial type.

II.2 Female, died at the age of about 60, was said to have had 6 digits on both hands and feet.

II.3 Male, died in old age, was described as having normal hands and 6 toes on both feet.

II.9 Female, died at the age of about 55, was said to have had 6 digits on both hands and feet.

V.2 Male, a 3-year-old boy, had six small 'fingers', which were amputated, on both hands, and has 6 well-formed toes on both feet. No skeletal vestigia of the extra fingers are visible on the x-rays of the hands (Fig. 3a). Both the fifth metatarsals are forked, and there are 6 complete toes on both feet (Fig. 3b). Physical examination is otherwise negative.

V.7 Female, an 11-year-old girl, had a sixth little finger, now amputated, on the ulnar edge of the right hand. The extra finger was amputated in infancy, and a little scar without radiological signs remained (Fig. 4a); there are 6 well-formed toes on both feet, and the radiographs (Fig. 4b) show malformed and partially duplicated fifth metatarsals. There are no other associated birth defects.

The other 81 individuals reported in the pedigree were normal during physical examination, or were described as having normal hands and feet.

Seven relatives of the proband were evaluated for beta-thalassaemia (see Fig. 1) by studying their erythrocytic morphology on blood smears, and by evaluating fetal haemoglobin (by alkali denaturation) and haemoglobin A₂ (by electrophoresis on cellulose acetate strips). Two of them (the mother IV.2 and the polydactylous cousin V.7) were found to be beta-thalassaemia carriers.

Dermatoglyphs

Finger- and palm-print configurations of the three living polydactylous members of the family are described in Fig. 5.

The only extra finger which we could directly examine, on the right hand of V.3, bore a pattern

Fig. 4 Radiographs of the hands (a) and feet (b) of V.7.

Fig. 5 Scheme of the finger- and palm-prints of V.2, V.3, and V.7

exactly similar to that of the neighbouring finger: a radial loop on the fifth, and an ulnar loop on the sixth digit.

In the right hands of V.2 and of V.7, who had the extra fingers amputated, an extra digital triradius (d') was present under the amputation scars. The left hands had no additional triradii.

The finger ridge-counts and atd angles of V.2, V.3, and V.7 are recorded in the Table. For the hands with extra digital triradii the width of the atd' angles is also reported.

Discussion

A dominant inheritance with complete penetrance of the polydactyly in this family can be ruled out, because it implies the absolutely unlikely occurrence of the same new gonadic mutation three times within a few generations in one family.

A dominant inheritance with incomplete penetrance

is theoretically possible but may hardly be advocated for the following reasons.

(a) The character does not appear in F-1 (either I.2 or I.3 should be a carrier).

(b) It does not appear in any of the 14 children of II.2, II.3, and II.9, who are all polydactylous (a probability of less than 1:16 000 if the character was dominant with complete penetrance).

(c) It also spares the two couples IV.1-IV.2 and IV.8-IV.26, who should carry the mutant gene in at least one member.

(d) Either IV.8 or IV.26 should be a carrier. Both have many sibs, none of whom is affected.

(e) If the character were dominant with very low penetrance 11.4 to 11.7 could be unexpressed carriers, but none of their 14 children is affected.

Polygenic inheritance may be an alternative explanation for the polydactyly of this family. Pipkin and Pipkin (1946) described 4 polydactylous subjects of a white family born from unaffected parents, and suggested that the anomaly was the result of the coexistence of two dominant genes, one being rare and the other relatively common. According to this suggestion, Walker (1961) interpreted the polydactyly of a Batutsi family, in which there was an asymptomatic obligate carrier, as being the result of two dominant genes, a rare polydactyly gene P (normal allele p) and an accessory gene A (normal allele a) which controls the penetrance of P . But the hypothesis of two dominant genes can hardly be accepted for the present family, in which none of the 14 children of affected persons is also affected (a 0:14 ratio, while the expected ratio from matings between affected and unaffected persons is at least 1:4).

A recessive inheritance is, therefore, far more probable. The following aspects fit well with recessive inheritance.

(a) The distribution of the character in the pedigree is clearly 'horizontally orientated', that is, it affects only 2 non-consecutive generations out of 5.

(b) Of the 3 couples of parents of the affected individuals, 2 are consanguineous.

If the hypothesis of a recessive inheritance is true, I.2 and I.3 are heterozygotes, with 3 of their 7 children being homozygous affected (a probability of 0.17). All the children of the 3 polydactylous persons are of course obligate heterozygotes, as well as the 2 couples IV.1-IV.2 and IV.8-IV.26, who gave birth to affected children.

Whatever the mechanism is of inheritance of polydactyly in this family, a close linkage between the genes of 'polydactyly' and of 'beta-thalassaemia' appears extremely unlikely. If the polydactylous character is a recessive one, a linkage between the two mutant genes can be excluded, because IV.2 has

transmitted to V.2 the 'polydactyly' and not the 'thalassaemia' gene. Moreover, only one of the two sisters IV.2 and IV.8, who are both heterozygotes for polydactyly, also carries the thalassaemia gene.

Two of the five hands with extra fingers which we directly examined had an additional digital triradius. In both, the extra fingers had been amputated, but the extra triradius was clearly visible near the amputation scar. The finding of extra digital triradii in hexadactyly is well known (Cummins and Midlo, 1943; Holt, 1968) but uncommon. Holt (1975) examined 9 hands with postaxial hexadactyly from 5 patients belonging to 2 English families, and found only one atypical triradius in the fourth interdigital area between triradii *c* and *d*.

References

- Castilla, E., Paz, J., Mutchinick, O., Munoz, E., Giorgiutti, E., and Gelman, Z. (1973) Polydactyly: a genetic study in South America. *American Journal of Human Genetics*, **25**, 405-412.
- Cummins, H., and Midlo, C. (1943). *Finger Prints, Palms and Soles*. Blackiston, Philadelphia.
- Gates, R. R. (1946). *Human Genetics*. Macmillan, New York.
- Holt, S. B. (1968). *The Genetics of Dermal Ridges*. Thomas, Springfield, Illinois.
- Holt, S. B. (1975). Polydactyly and brachymetapody in two English families. *Journal of Medical Genetics*, **12**, 355-366.
- Koehler, O. (1929). Zur Frage der Vererbung der menschlichen Vielfingerigkeit. *Biologisches Zentralblatt*, **49**, 705-717.
- McKusick, V. A. (1975). *Mendelian Inheritance in Man*, 4th ed. Johns Hopkins Press, Baltimore.
- Mohan, J. (1969). Postaxial polydactyly in three Indian Families. *Journal of Medical Genetics*, **6**, 196-200.
- Pipkin, S. B., and Pipkin, A. C. (1946). Two new pedigrees of zygodactyly. Variations of expression of polydactyly. *Journal of Heredity*, **37**, 93-96.
- Snyder, L. H. (1929). A recessive factor for polydactylism in Man. *Journal of Heredity*, **20**, 73-77.
- Sverdrup, A. (1922/23). Postaxial polydactylism in six generations of a Norwegian family. *Journal of Genetics*, **12**, 217-240.
- Walker, J. T. (1961). A pedigree of extra-digit-V polydactyly in a Batutsi family. *Annals of Human Genetics*, **25**, 65-68.

Requests for reprints to Professor F. Mollica, Clinica Pediatrica Università, Viale Andrea Doria, 95125 Catania, Italy.