Family study of inherited syndrome with multiple congenital deformities: symphalangism, carpal and tarsal fusion, brachydactyly, craniosynostosis, strabismus, hip osteochondritis

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Summary. A syndrome of brachydactyly (absence of some middle or distal phalanges), aplastic or hypoplastic nails, symphalangism (ankylosis of proximal interphalangeal joints), synostosis of some carpal and tarsal bones, craniosynostosis, and dysplastic hip joints is reported in five members of an Italian family. It may represent a previously undescribed autosomal dominant trait.

Brachydactyly and symphalangism are well-known hereditary anomalies of the hands and feet. In brachydactyly, digits or specific phalanges may be affected, sometimes in association with shortening of metacarpal and metatarsal bones, and classification has been based on specific patterns (Bell, 1951). The thumbs and big toes are not usually involved. There may be various degrees of dysplasia of the nails (Cuevas-Sosa and Garcia-Segur, 1971). Symphalangism is the result of failure of differentiation of the interphalangeal joints, and leads to ankylosis between proximal or, more rarely, distal interphalangeal joints. Other congenital anomalies may be associated with symphalangism, the most common of which is synostosis of the carpal and tarsal bones.

We report here five cases in three generations of a syndrome of brachydactyly with symphalangism, and other features including craniosynostosis. This may be a hitherto undescribed autosomal dominant trait.

Family study

The proband, III.3, was first seen because of acute leukaemia, and the bone anomalies were observed in four other members of her family in three generations (Fig. 1). The anomalies were in the hip, the cranium, and both

hands and feet (Fig. 2-5). They varied in severity, and the malformations were not symmetrical in all affected individuals (Appendix). The nails presented various degrees of dystrophy (including total absence), solely on the brachydactylous fingers, while they appeared normal where there was symphalangism without brachydactyly (IV.4). All five individuals showed craniosynostosis, hip dysplasia, and pes planus, and had pain on walking. The least affected family member is IV.4 who had symphalangism and clinodactyly, but lacked brachydactyly, had normal nails, and showed partial craniosynostosis. Hip dysplasia in II.7 caused a severe joint dislocation. The stature, weight, and intelligence are normal in all subjects. III.1 and his daughter IV.1 showed strabismus, but there was no defect of vision or hearing.

Laboratory data were normal including serum calcium, serum phosphorus, and serum phosphatase. The

FIG. 1.

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FIG. 2.

electroencephalogram was also normal, as were the pattern of the sensitive organs. A normal karyotype was seen on two affected individuals (II.7 and III.1) by banding techniques. The following genetic markers were examined: adenylate kinase, malate dehydrogenase, phosphohexose isomerase, phosphoglucomutase, adenosine deaminase, phosphoenolpyruvate, aspartate transaminase, alanine transaminase, diaphorase. Unfortunately, no information regarding linkage was obtained from these data.

Dermatoglyphic patterns showed some unusual features, including: absence of some digital triradii and an increase in the axial triradius angle; a type 'epsilon' configuration by D-line exit in III.3; characteristic patterns on the brachydactylic fingers; the absence of flexion creases at interphalangeal joints; the presence of triradius in some of these areas; and the high incidence of whorls. There were no patterns in the thenar or hypothenar areas.

Discussion

The only syndrome in which symphalangism and brachydactyly occur together is that described by Haws (1963), classified by McKusick (1975) as type C brachydactyly; in that instance affected individuals showed deformity of the middle and proximal phalanges of the second and third fingers, hyperphalangy (hypersegmentation of the proximal phalanx), brachymetapody, and symphalangism; they lacked anomalies of the hips and cranium.

Robinson *et al* (1968) reported a kindred considered by the authors to show type C brachydactyly, in which affected individuals had brachydactyly and Legg-Perthes disease of the hip, but no symphalangism or craniosynostosis.

The syndrome described here shows more widespread bony anomalies than others of this general

FIG. 3.

FIG. 4.

FIG. 5.

type reported previously. The disorder is located both in hands and feet, though the thumbs and

great toes are unaffected. To our knowledge, strabismus and craniosynostosis have not been described before in connexion with symphalangism and/or brachydactyly. As for the dysplasia of hip joints, it is noteworthy that the femoral heads appeared to be normal; the anomaly involved the acetabular structure (osteochondritis). The hip abnormality is, therefore, distinct from that described by Robinson *et al*, in which the changes were similar to those of Perthes' disease (osteochondritis of the capital femoral epiphysis).

The distribution in the pedigree is consistent with an autosomal dominant trait, with some variation in gene expressivity. It may have arisen as a new mutation in generation I.

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Appendix overleaf.

APPENDIX CLINICAL-RADIOLOGICAL FEATURES OF FAMILY

Case	Phalanges											
	Fingers					Toes						
	Digits	Proximal Phalanges	1st inter-phal. joint	Middle Phalanges	2nd interphal. joint	Distal Phalanges	Proximal Phalanges	1st inter-phal. joint	Middle Phalanges	2nd inter-phal. joint	Distal Phalanges	Fingernails
II.7	1		Symphal.	Absent		Absent	Brachy.	Symphal.	Absent		Absent	Absence of 3rd, 4th, 5th; dysplasia of 2nd
	2		Symphal.	Absent		Absent		Symphal.	Absent		Absent	
	3			Absent					Absent			
	4			Absent					Absent			
	5			Absent					Absent			
III.1	1		Symphal. (R)	Absent		Hypopl.	Brachy.		Absent		Absent	Absence of 4th, 5th, dysplasia of 2nd
	2		Symphal.	Absent					Absent		Absent	
	3		Symphal.	Absent					Absent		Absent	
	4		Symphal.	Absent					Absent		Absent	
	5		Symphal.	Absent					Absent		Absent	
III.3	1		Symphal.	Absent				Symphal.	Absent		Absent	Absence of 4th, 5th (L); dysplasia of 5th (R)
	2		Symphal.	Absent				Symphal.	Absent		Absent	
	3		Symphal.	Absent				Symphal.	Absent		Absent	
	4		Symphal.	Absent				Symphal.	Absent		Absent	
	5		Symphal.	Absent				Symphal.	Absent		Absent	
IV.1	1	Hypopl.	Symphal.	Absent		Absent (R); Hypopl. (L)	Brachy.		Absent		Hypopl.	Absence of 3rd (R), 4th, 5th; dysplasia of 2nd
	2		Symphal.	Absent		Absent (R)			Absent		Absent	
	3		Symphal.	Absent		Absent			Absent		Absent	
	4		Symphal.	Absent		Absent			Absent		Absent	
	5		Symphal.	Absent		Absent			Absent		Absent	
IV.4	1	Brachy.	Symphal. (R)	Hypopl.			Brachy.	Symphal.	Hypopl.		Absent (L)	Normal
	2		Symphal.	Hypopl.				Symphal.	Absent			
	3		Symphal.	Hypopl.								
	4		Symphal.	Hypopl.								
	5	Clinodactyly	Symphal.	Hypopl.								
	Metatarsals											
	Metatarsals					Hip						
	Carpals	Metacarpals	Radius and Ulna	Tarsals	Brachymetapod (1st)	Osteochondritis acetabular roof	Neocotile (R) dislocation	capitulum femur	Synostosis	Cranium		
II.7	Fusion: trapezium-trapezoid-capitate hamate-lunate	Deformed Brachymetapod (1st)	Absence of nuclei of styloid apoph. Hypopl. distal epiph.	Fusion: 2nd-3rd cuneiform; deformed scaphoid	Brachymetapod (1st)	Osteochondritis acetabular roof	Neocotile (R) dislocation	capitulum femur	Synostosis	Cranium		
III.1	Normal	Deformed: 2nd, 3rd Brachymetapod (1st)	Hypopl. distal epiph.	Deformed: cuboid, scaphoid	Brachymetapod (1st)	Osteochondritis acetabular roof; bilateral coxa valga; angle of femoral neck with shaft			Synostosis			
III.3	Fusion: trapezium-scapoid hamate-lunate trapezoid-capitate	Deformed: 1st, 2nd, 3rd	Absence of nucleus of ulnar styloid apoph. Hypopl. distal epiph.	Deformed: lateral 1st cuneiform scaphoid Fusion: 2nd-3rd cuneiform	Normal	Osteochondritis acetabular roof; angle of femoral neck with shaft			Synostosis			
IV.1	Fusion: hamate-capitate	Deformed	Normal	Fusion: calcaneus-cuboid; 2nd cuneiform; 2nd metatarsal; deformed scaphoid; absence of 3rd cuneiform	Two ossification centres of 1st metatarsal basal epiphysis	Sclerositis acetabular roof; angle of femoral neck with shaft			Synostosis			
IV.4	Normal	Brachymetapod (1st)	Normal	Absence of 2nd, 3rd cuneiform	Normal	Sclerositis acetabular roof; angle of femoral neck with shaft			Partial synostosis			