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 propositus, 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
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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
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Fig. 3.

Fig. 4.
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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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REFERENCES


Appendix overleaf.
## APPENDIX

### CLINICAL-RADIOLOGICAL FEATURES OF FAMILY

<table>
<thead>
<tr>
<th>Case</th>
<th>Fingers</th>
<th>Phalanges</th>
<th>Toes</th>
<th>Fingernails</th>
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<tr>
<td></td>
<td>Digits</td>
<td>Proximal</td>
<td>1st inter-</td>
<td>Middle</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Phalanges</td>
<td>phal. joint</td>
<td>Phalanges</td>
</tr>
<tr>
<td>II.7</td>
<td>1 2 3 4 5</td>
<td>Symphal.</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>III.1</td>
<td>1 2 3 4 5</td>
<td>Symphal. (R)</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>III.3</td>
<td>1 2 3 4 5</td>
<td>Symphal.</td>
<td>Absent</td>
<td></td>
</tr>
<tr>
<td>IV.1</td>
<td>1 2 3 4 5</td>
<td>Hypopl.</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>IV.4</td>
<td>1 2 3 4 5</td>
<td>Brachy.</td>
<td>Absent</td>
<td>Absent</td>
</tr>
</tbody>
</table>

### Details

<table>
<thead>
<tr>
<th>Carpals</th>
<th>Metacarpals</th>
<th>Radius and Ulna</th>
<th>Tarsals</th>
<th>Metatarsals</th>
<th>Hip</th>
<th>Cranium</th>
</tr>
</thead>
<tbody>
<tr>
<td>II.7</td>
<td>Fusion: trapezium-trapezoid-capitate hamate-lunate</td>
<td>Deformed</td>
<td>Absence of nuclei of styloid apophysis; Hypopl. distal epiphysis</td>
<td>Brachymetapody (1st)</td>
<td>Osteochondritis acutabular roof</td>
<td>Synostosis</td>
</tr>
<tr>
<td>III.1</td>
<td>Normal</td>
<td>Deformed: 2nd, 3rd</td>
<td>Hypopl. distal epiphysis</td>
<td>Deformed: cuboid, scaphoid</td>
<td>Brachymetapody (1st)</td>
<td>Osteochondritis acutabular roof; bilateral coxa valga; angle of femoral neck with shaft</td>
</tr>
<tr>
<td>III.3</td>
<td>Fusion: trapezium-scaphoid hamate-lunate trapezoid-capitate</td>
<td>Deformed: 1st, 2nd, 3rd</td>
<td>Absence of nucleus of ulnar styloid apophysis; Hypopl. distal epiphysis</td>
<td>Deformed: lateral 1st cuneiform scaphoid</td>
<td>Normal</td>
<td>Osteochondritis acutabular roof; bilateral coxa valga; angle of femoral neck with shaft</td>
</tr>
<tr>
<td>IV.1</td>
<td>Fusion: hamate-capitate</td>
<td>Deformed</td>
<td>Normal</td>
<td>Fusion: calcaneus-cuboid; 2nd cuneiform-2nd metatarsal; deformed scaphoid; absence of 3rd cuneiform</td>
<td>Two ossification centres of 1st metatarsal basal epiphysis</td>
<td>Sclerosis acutabular roof; angle of femoral neck with shaft</td>
</tr>
<tr>
<td>IV.4</td>
<td>Normal</td>
<td>Brachymetapody (1st)</td>
<td>Normal</td>
<td>Absence of 2nd, 3rd cuneiform</td>
<td>Normal</td>
<td>Sclerosis acutabular roof; angle of femoral neck with shaft</td>
</tr>
</tbody>
</table>
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