The tricho-rhino-phalangeal syndrome*

Summary. The tricho-rhino-phalangeal syndrome is characterized by sparse fine hair, bulbous nose, and brachydactyly. The clinical and radiological findings of four affected family members, a father and his three children, are presented. Cardiovascular anomalies, previously unreported in this syndrome, were present in one of the children. Psychological and immunological evaluations were found to be essentially normal. The genetics of this condition and suggested counselling are presented.

The most striking features of the tricho-rhino-phalangeal syndrome, first reported by Giedion (1966), are sparse fine hair, bulbous nose with tented nares, cone-shaped epiphyses in the hands

FIG. 1. Pedigree. II.2 appears to represent a fresh autosomal dominant mutation from unaffected parents.

Received 7 January 1974.

* This work was supported by: Maternal and Child Health Service, Health Services and Mental Administration. Department of Health, Education and Welfare, Project 913; United States Public Health Service Career Development Award No. K04 DE40648-02; National Institutes of Health Grant No. HD 05961; The National Foundation—March of Dimes; United States Public Health Service Fellowship No. 1 F03 GM 54160-01.

and feet, and, in some cases, short stature. This paper sets forth the clinical findings in an affected adult and his three children, as summarized in Table I and illustrated in Figs. 1–4.

One of the patients (III.3) was found to have an atrial septal defect and total anomalous venous return, representing the first reported association of cardiovascular anomaly in this syndrome. Although increased susceptibility to upper respiratory infections has been noted in several reports (Klingmüller, 1956; Hobolth and Mune, 1963; Giedion, 1966), the frequency and severity of infections has not been unusual in this family. In addition, their serum immunoglobulin A, G, and M levels were found to be either normal or only slightly elevated.

In the tricho-rhino-phalangeal syndrome, scalp hair is sparse from early infancy, especially in the fronto-temporal areas. It grows slowly and is of fine texture. These hair characteristics are also present in this family. Baldness occurred by the age of 21 years for the father (II.2). Cone-shaped epiphyses usually do not become evident until after early childhood. Subsequent to their appearance,

TABLE I
PHYSICAL FEATURES

	Father II.2	Offspring		
		III.1	III.2	III.3
Age (yr)	35	9	8	6
<i>Craniofacial</i>				
Sparse, slow growing blond scalp hair	+	+	+	+
Medial up sweep, eyebrows	+	+	+	+
Tented nares	+	+	+	+
Prominent ears	+	+	+/-	+
Prominent elongated philtrum	+	+	+	+
Mild micrognathia	+	+	+	+
Narrow palate	?	+	+	+
'Bridged' sella turcica	+	+	+	+
<i>Hands</i>				
Brachydactyly, especially 5th finger	+	+	-	+/-
Clinodactyly, 3rd and 4th fingers	+	+	-	-
Broad thumbs	+	+	+	-
Cone-shaped epiphyses	+	+	+	+
Short terminal phalanges and nails	+	+/-	-	-
Broad middle interphalangeal joints with tapered fingers	+	+	+	+
Short metacarpals	+	+	+	+/-
Triangular distal ulnar epiphyses	+	+	+/-	?
<i>Feet</i>				
Short hallux with cone-shaped epiphyses	+	+	+	+/-
Short metatarsals and proximal phalanges	+	+	+	+/-
Thin, fragile, chronically infected large toenails	+	-	-	-
<i>Others</i>				
Winged scapulae	+	+	+	+
Coxa valga	?	+	+	+
Short stature	-	-	-	+/-
Atrial septal defect and total anomalous venous return	-	-	-	+

+ = present; +/- = borderline; - = absent; ? = unknown.

FIG. 2. Affected family members: 35-year-old father (A) and his 9-, 8-, and 6-year-old offspring (B, C, D). Note the prominent ears in the individuals in (A) and (D). Each has hypoplasia of the alae nasi and a long philtrum.

FIG. 3. Right hands of affected individuals: father (A) 9-, 8-, and 6-year-old offspring (B, C, D). Note the brachydactyly, especially of the fifth fingers, short nails, fusiform fingers, and clinodactyly (in B only). The index fingers are disproportionately shortened, an unusual anomaly.

FIG. 4. X-rays of the right hands of the affected individuals: father (A) and his 9-, 8-, and 6-year-old-offspring (B, C, D). Cone-shaped epiphyses are present in the proximal ends of the first, second, and fifth proximal and the second, third, and fourth middle phalanges in all persons. These epiphyses are fused in the father.

metaphyseal growth in the long bones of the hands and feet is slowed and the metaphyses may be distorted. Thus, brachydactyly and, less commonly, clinodactyly may develop postnatally. These changes tend to progress slowly during childhood. Linear growth deficiency is a variable feature and is present in only one of our patients (III.3). However, his short stature may be related to his cardiovascular anomalies. Intellectual and psychological evaluations were within the normal range in the proposita and her sibs.

Discussion

Autosomal dominant inheritance (Giedion, 1969; Langer, 1969; Murdoch, 1969; Fontaine *et al*, 1970) has been clearly established in the majority of families with the tricho-rhino-phalangeal syndrome, as in the present report. Instances of affected sibs with this disorder (Klingmüller, 1956; Giedion, 1969; Hussels, 1971) from presumably normal parentage have raised the question of autosomal recessive inheritance in some cases. Until this question of possible genetic heterogeneity for the tricho-rhino-phalangeal syndrome is resolved, it is difficult to provide sound genetic counselling for the family in which there is a sporadic occurrence of this disorder. This syndrome should be differentiated from the oral-facial-digital syndrome (Smith, 1970) in which similar nasal, hair, and digital anomalies may occur. However, patients with the latter condition usually have clefting of their upper lip, tongue, and palate and presumably it is inherited as an X-linked dominant, lethal in the males. The Langer-Giedion syndrome (Hall *et al*, 1974) shares many features in common with the tricho-rhino-phalangeal syndrome, but has in addition multiple exostoses, redundant and/or loose skin during infancy, laxity or hypermobility of joints, mild microcephaly, mental deficiency with significantly delayed onset of speech, and skin naevi. To date all cases of the Langer-Giedion syndrome have been sporadic.

It is of interest to speculate that the autosomal dominant type of the tricho-rhino-phalangeal syndrome and the Langer-Giedion syndrome form a constellation of disorders, which may be the result of different mutations within the same genetic locus or system.

DAVID D. WEAVER, M. MICHAEL COHEN, and
DAVID W. SMITH

*Dysmorphology Unit, Department of Pediatrics,
University of Washington, School of Medicine,
Seattle, Washington 98195, USA*

We thank Dr W. Morrison for the referral of this family, Dr N. Wiltz for his psychological evaluation of the children, Mr D. Aragon for the photographs, and Mrs M. A. Harvey and Mrs C. Hansen for their editorial assistance.

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