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APERT SYNDROME WITH PARTIAL POLYSYNDACTYLY: A PROPOSAL ON THE CLASSIFICATION OF ACROCEPHALOSYNDACTYLY

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Summary A newborn girl is reported with seemingly typical Apert syndrome with preaxial polysyndactyly of the feet. As a result of reevaluation of familial cases of acrocephalosyndactyly with polysyndactyly, acrocephalosyndactyly is suggested to be divided into two major groups. Apert-Pfeiffer type (acrocephalosyndactyly type I) is characterized by Crouzon-like facies, hallux varus and severe syndactyly. Saethre-Chotzen/Robinow-Sorauf type (acrocephalosyndactyly type II) is characterized by Saethre-Chotzen facies, hallux valgus and mild syndactyly. Each type should have atypical forms with polysyndactyly due to pleiotropic effect of a dominant gene.

Key Words Apert syndrome, acrocephalosyndactyly, polydactyly

INTRODUCTION

Apert syndrome is characterized by syndactyly of the hands and the feet, and peculiar facies due to premature closure of the coronal sutures. It is classified as acrocephalosyndactyly (ACS) type I (McKusick No. *10120, 1988). A similar syndrome, acrocephalopolysyndactyly (ACPS), is discerned from ACS by recessive inheritance, association of polysyndactyly and other clinical features. We present a patient with seemingly typical Apert syndrome associated with partial preaxial polysyndactyly of the feet.

CASE REPORT

The propositus, a female newborn, is the third child born to healthy and unrelated parents, both 32 years of age. The pregnancy was complicated with genital

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bleeding at 4th month, and toxemia since 7th month of gestation. She was delivered by cesarean section at 36 weeks. Apgar score was 9 at both 1 and 5 min. Birth weight was 3,024 g. She was referred to us soon after birth, when peculiar facies, syndactyly and inspiratory disturbance were noted.

Her length was 50.0 cm, weight 2,988 g, and head circumference 34.5 cm. The head was brachyacrocephalic with a widely patent anterior fontanel (4.5 × 4.5 cm). Complete premature closure of left coronal suture was noted as well as partial closure of the right. Her facies was characteristic with frontal bossing, prominent eyes with shallow orbits, beaked nose, facial asymmetry, narrow palate and bifid uvula (Fig. 1A).

The hands showed complete syndactyly of all fingers except the broad thumbs. Nails of 3rd and 4th fingers were fused (Fig. 1B). The feet showed complete syn-

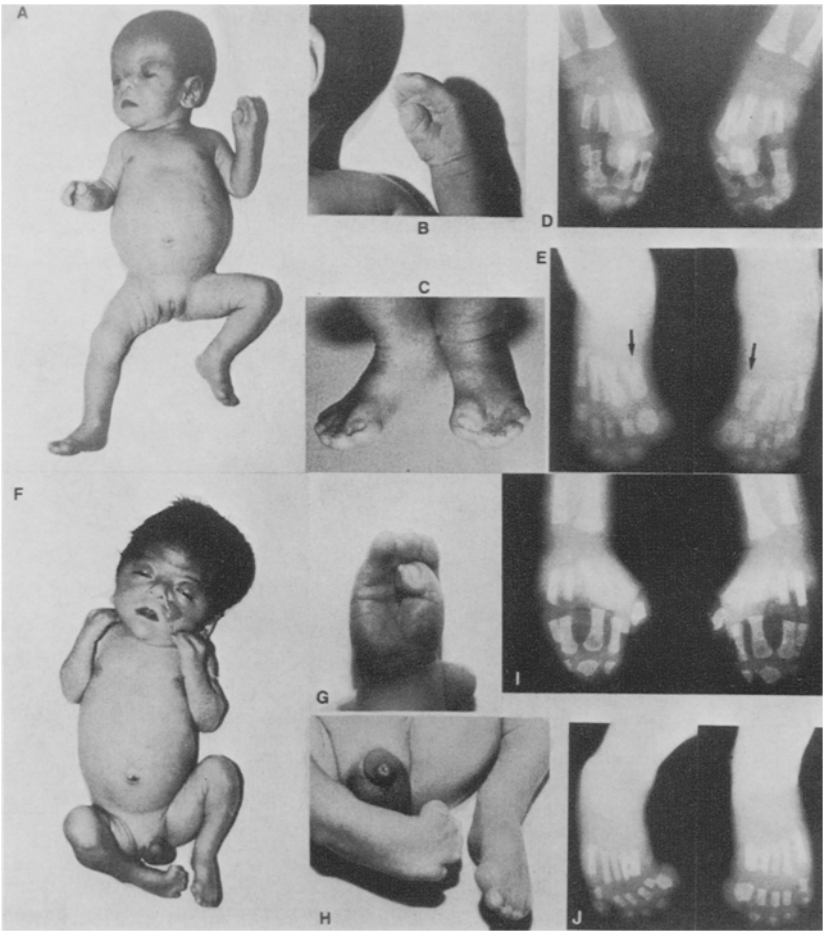

Fig. 1. A to E: The propositus at 1 month of age. F to J: Typical Apert syndrome. Arrows indicate bifid 1st metatarsals.

dactyly of all toes. The great toes were broad with hallux varus (Fig. 1C). Mobility of the elbow joints and abduction of the hip joints were limited. Though a Levine II/VI systolic murmur was noted, no cardiac anomaly was detected by echocardiography. Diastasis recti abdomini and bilateral inguinal herniae were noted as well. Routine laboratory findings were all within the normal ranges except hyperbilirubinemia due to ABO blood group incompatibility. Her chromosomal karyotype was normal.

On radiographs of the hands, fusion of distal phalanges and symphalangism between middle and proximal phalanges were noted on 3rd and 4th fingers (Fig. 1D). Distal and proximal phalanges of the great toes were broad and fused. Moreover, 1st metatarsals were broad and bifid in its proximal part, indicating preaxial polysyndactyly (Fig. 1E).

DISCUSSION

Typical Apert syndrome shows syndactyly of the hands and the feet (Fig. 1, F, G and H). The hand has been compared to a spoon hand or an obstetric hand. On radiographs, variable degrees of symphalangism or fusion of the phalanges are seen, but polydactyly (Fig. 1, I and J). Recently, Maroteaux and Fonfria (1987) have reported typical Apert type ACS with postaxial polydactyly of the hands and preaxial polydactyly of the feet. They discussed that it may be pleiotropic effect of a dominant gene or a new clinical syndrome.

Association of polysyndactyly has been reported in other types of ACS as well. Kopyść *et al.* (1980) have reported a family with Saethre-Chotzen type ACS (ACS type III), in which involved three cases with bifid distal phalanges of the great toes. Similar cases have been reported by Robinow and Sorauf (1975), Carter *et al.* (1982) and Young and Harper (1982). Carter *et al.* (1982) proposed that ACS with Saethre-Chotzen facies, duplication of distal phalanges of the great toes and hallux valgus should be called Robinow-Sorauf syndrome (Robinow-Sorauf type ACS, McKusick No. 18075, 1988). In the four reports of Robinow-Sorauf type ACS, three were familial (Robinow and Sorauf, 1975; Kopyść *et al.*, 1980; Young and Harper, 1982). The pedigrees were illustrated in the figure (Fig. 2). The case, which showed Saethre-Chotzen facies, bifid terminal phalanges of the great toes and hallux valgus was considered to be Robinow-Sorauf type ACS. As shown in the figure, most cases without bifid terminal phalanges were considered to be Saethre-Chotzen type ACS, and it was always seen in the family with Robinow-Sorauf type ACS. Thus, it may be possible that these two types are due to a same dominant gene. Polysyndactyly seen in Robinow-Sorauf type ACS may be considered as pleiotropic effect.

Association of preaxial polydactyly has also been reported in Pfeiffer type ACS. The cases reported by Noack *et al.* (1959) were initially classified as ACPS type I (Noack syndrome). However, later it was considered to be same as Pfeiffer type ACS (Pfeiffer, 1969; Temtamy, 1976 cited by McKusick, 1988).

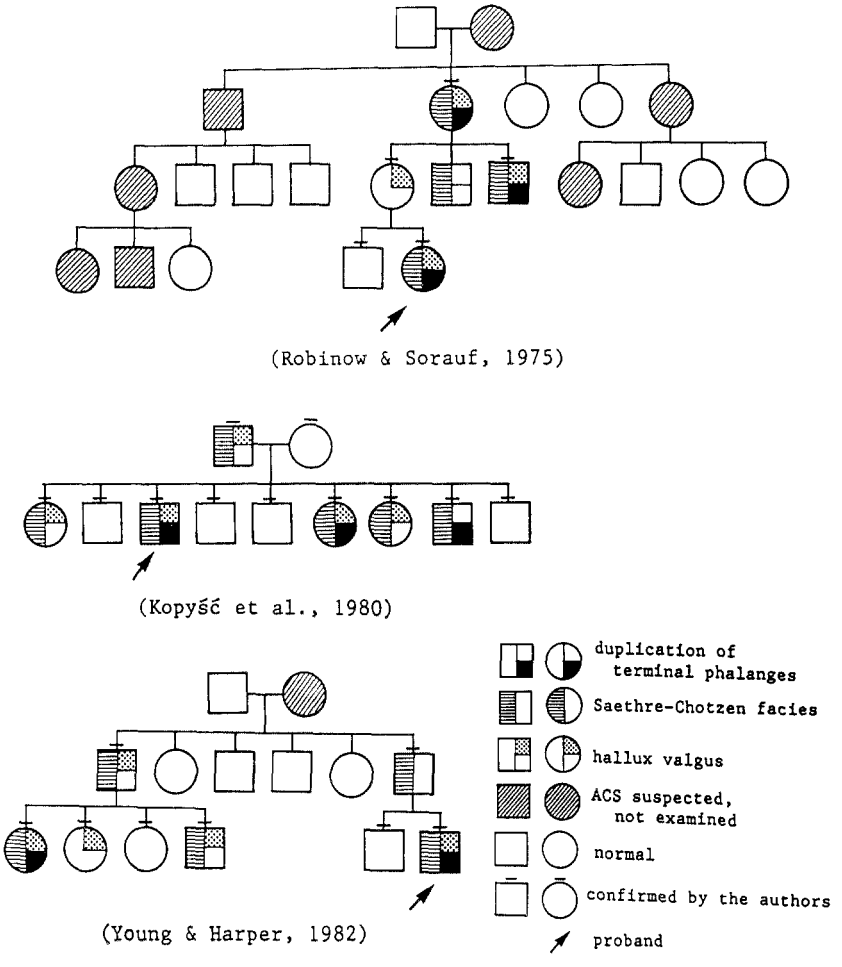

Fig. 2. Pedigrees with Robinow-Sorauf type ACS.

Apert type ACS is discerned from Saethre-Chotzen type ACS by several features. Apert type ACS shows hallux varus, severe syndactyly and Crouzon-like facies. On the contrary, Saethre-Chotzen type ACS shows hallux valgus, mild syndactyly and distinct Saethre-Chotzen facies with downward slanting of the palpebral fissures. Preaxial polysyndactyly is occasionally seen in both types. However, the type of polysyndactyly is different. In Apert type ACS, it is duplication from metatarsal to distal phalanx, compared with duplication of distal phalanx in Saethre-Chotzen type ACS, as seen in Robinow-Sorauf type.

The difference between Apert type and Pfeiffer type ACSs seems to be reflected mainly by the degree of syndactyly. Moreover, these two types of ACS have been identified within the same family (Escobar and Bixler, 1977). Thus, it may be

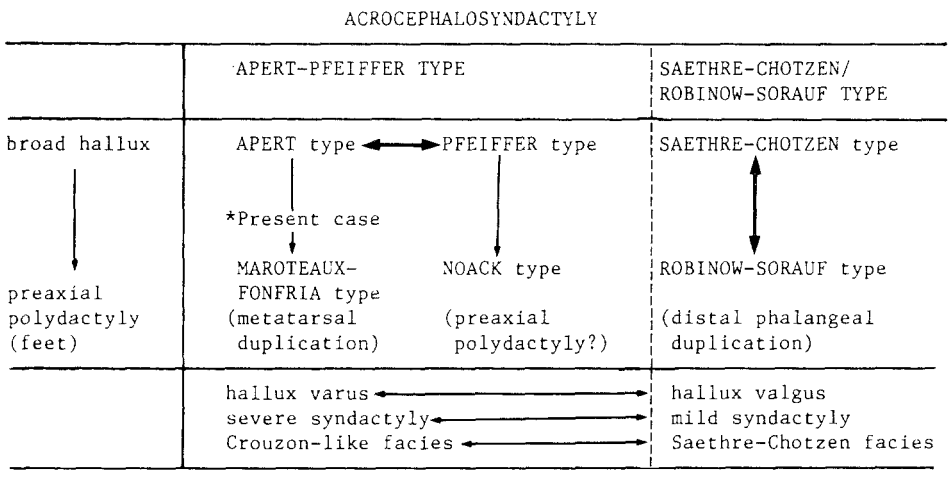

Fig. 3. Proposed classification of autosomal dominant ACS. Broad arrows indicate the types identified within the same family.

possible that these two types were discerned by the degree of phenotypic expression of the same dominant gene.

Summarization of the reports of ACS with polysyndactyly leads us to a new idea of classification for ACS (Fig. 3). Autosomal dominant ACS is suggested to be divided into two major groups. One is Apert-Pfeiffer type (ACS type I), and the other is Saethre-Chotzen/Robinow-Sorauf type (ACS type II). Each type should have atypical forms with polysyndactyly due to pleiotropic effect of a dominant gene. The present case and the cases reported by Maroteaux and Fonfria (1987) are considered to be the examples.

Carpenter type ACPS (ACPS type II, McKusick No. *20100, 1988) may be confused with atypical ACS forms with polysyndactyly. However, it is characterized by mild polysyndactyly, oxycephaly, obesity, clinodactyly and, most importantly, autosomal recessive inheritance. Though Goodman syndrome and Summitt syndrome are known to be autosomal recessive ACPS, these two types have been considered to be same as Carpenter type ACPS (Cohen *et al.*, 1987).

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