

Clinical Report

Brachydactylic Multiple Delta Phalanges Plus Syndrome

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Delta phalanges are unusual, shortened bones of the hands and feet with abnormal epiphyses and diaphyses. Here, we report on a patient with a unique multiple congenital anomaly syndrome that includes brachydactyly consisting of multiple delta phalanges in several digits of the hands and feet. The patient, who was born to consanguineous parents, had several other congenital anomalies, including butterfly vertebrae, craniofacial dysmorphism, and coarctation of the aorta. We have called this distinctive condition “brachydactylic multiple delta phalanges plus syndrome.” Although no other member of the family had obvious hand or foot anomalies, several siblings had other malformations. Possible modes of inheritance in this family include variable expression of a recessive or de novo dominant condition.

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KEY WORDS: delta phalanx; brachydactyly; aortic coarctation; supernumerary nipples; syndactyly

INTRODUCTION

Delta phalanges are unusual, shortened bones of the hands and feet with epiphyseal and diaphyseal abnormalities. The defective epiphyses run the length of the phalanx instead of sitting at the ends, producing the unusual morphology. Delta bones were first described in 1921 [Pol, 1921], but until 1999, this congenital anomaly was never reported to occur more than once within the same digit [Wood and Rubinstein, 1999]. These abnormalities are clinically important because corrective surgery is often required for adequate function. When multiple delta phalanges exist in the same digit, brachydactyly occurs.

Here, we report on a patient with a unique constellation of congenital anomalies that includes brachydactyly consisting of multiple delta phalanges in several digits of the hands and feet. To our knowledge, this is the first description of such a case, which we have called “brachydactylic multiple delta phalanges plus syndrome,” based on its most distinctive feature. The patient, who was born to consanguineous parents, also had several other congenital anomalies, including butterfly vertebrae, craniofacial findings, and coarctation of the aorta. Several family members had disparate malformations, which may be caused by variable expression of an inherited condition.

CLINICAL REPORT

The proband is a 12-year-old Mexican female born after an uncomplicated, full-term pregnancy to a 26-year-old G6 P4 mother by spontaneous vaginal delivery. The parents are second cousins, and their first child, a male with no known malformations, died at 40 days of life of unknown causes. The mother then had a first trimester spontaneous abortion, followed by the birth of two normal females, a son who had dysplastic kidneys and renal failure, the proband, and a normal sixth male. A seventh male with vertebral anomalies and dextrocardia had dysmorphic features including hypertelorism, low-set ears with postauricular pits and epicanthal folds (Fig. 1). An eighth female was born with no anomalies. None of the other family members had hand malformations.

The proband's birth weight was 3.70 kg (>90th centile), length was 50 cm (50th centile), and head circumference was 36 cm (75th centile). She had respiratory distress at birth, and echocardiography showed coarctation of the aorta. The coarctation was repaired, and a patent ductus arteriosus was ligated. Other studies in the neonatal period included a normal female karyotype, 46, XX, a normal head sonogram, brain MRI, and a normal renal ultrasound. Tracheomalacia was identified during a fluoroscopic exam. Skeletal survey showed four sacral vertebrae, multiple butterfly vertebrae in the thoracic region, rhizomelic shortening of the humeri, bilateral soft tissue syndactyly in the hands, and soft tissue syndactyly in the right foot. Prior to presenting to our facility, the patient had undergone one surgery on her upper right extremity and three on her lower extremities to correct bony abnormalities.

On examination in our clinic at 12 years of age, the patient's weight was 50.9 kg (75th–90th centile), height was 136 cm (3rd centile), and head circumference was 51.5 cm (3rd–10th centile). Craniofacial anomalies consisted of a narrow forehead, upslanting palpebral fissures, high palate, and dental malocclusion (Fig. 2A). Cardiac examination showed a soft systolic murmur. She had accessory nipples in the milk line above the umbilicus bilaterally. Skeletal examination showed upper thoracic scoliosis secondary to the vertebral anomalies, and her elbows were markedly hyperextensible but without dislocation of the radial head. Neurological examination demonstrated an unusually wide based and slightly unsteady gait. Developmentally, the patient was delayed by approximately one grade level; she could read but required special education in all subjects. She had mild unilateral hearing loss on the right, and it is not known if this was sensorineural or conductive.

Our physical examination of the hands showed that the middle digits appeared relatively normal, but the thumbs were short and broad with excess thenar webbing (Fig. 2B,C). The unoperated left hand had brachyphalanges on digit 2 and 4 and soft tissue syndactyly of digit 3 and 4. There was camptodactyly of digit 3 and 4 with possible absence of the 3rd finger PIP joint. Abnormal palmar creasing, likely a secondary effect of the digit abnormalities, was noted. The surgically repaired right hand showed multiple soft tissue syndactyly and brachyphalanges with clinodactyly and camp-

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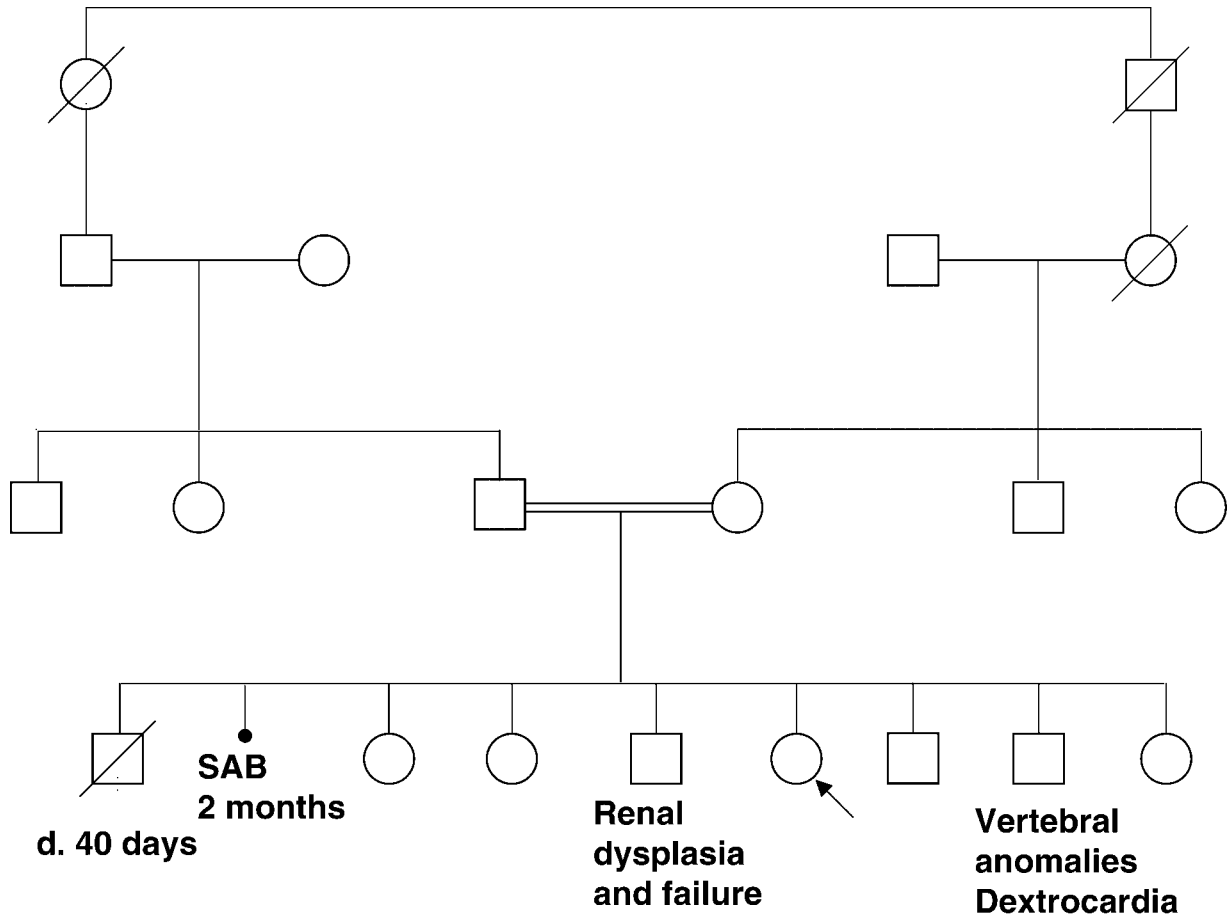


Fig. 1. Pedigree. Distinct malformations were seen in several members of the sibship, as described in the text.

todactyly. The left foot had a wide sandal gap, 2–4 toe syndactyly, and nail hypoplasia on digit 4 and 5 (Fig. 2D). The right foot had 2–3 toe syndactyly, hypoplastic nails on toe 4 and 5, and short toes 1, 4, and 5.

Hand radiographs, performed prior to corrective surgery at the age of 8, showed reasonably symmetrical bilateral involvement (Fig. 3). Carpal abnormalities included non-ossification of the lunate as well as hypoplastic ossification and unusual shape of other carpal bones. The metacarpals were unremarkable except for a short 2nd metacarpal. Proximal phalanges 2–5 had multiple delta phalanges. Both “kissing”—in which a duplicated longitudinal bracketed epiphysis is found—and isolated delta bones were noted. The proximal phalangeal region of the 2nd digit had an extra delta phalanx ossification similar to that seen in Catel–Manzke syndrome [Taybi and Lachman, 1996b]. The 3rd proximal phalanx on the right had a kissing delta phalanx, while on the left there was a small metaphyseal divot and pseudoepiphysis on this phalanx. The middle phalanges (2–5) were essentially normally shaped, but 2 and 5 were somewhat small bilaterally. The distal phalanges were normal bilaterally except for several minor irregular epiphyses on the right. Some beginning symphalangism was seen in digit 1–3 on the right, and 2 and 5 on the left.

Radiographs of the feet revealed that the right foot had a delta phalanx of the first metatarsal encompassing the medial aspect and both ends of this bone (Fig. 4). This metatarsal was also quite short. The medial cuneiform on the right had an unusual small distal indentation. There were hypo-

plastic phalanges in both feet and other delta-like phalanges bilaterally.

DISCUSSION

Delta phalanges are rare anomalies in which the triangular or trapezoidal bone has an abnormal epiphysis, which is oriented along the proximal to distal axis. Commonly, only a single delta phalanx is seen. The patient we describe here has involvement of multiple phalanges in several digits in both the hands and feet, producing a previously undescribed brachydactyly.

Triangular phalanges were first reported in 1921 [Pol, 1921], and the term “delta phalanx” was first used in 1964 [Jones, 1964]. Over time, several designations have been used to describe these abnormal bony structures, including “longitudinally bracketed diaphysis,” “longitudinal epiphyseal bracket,” “brachybasophalangism,” “kissing delta phalanx,” and “wedge-shaped phalanx” [Wood and Flatt, 1977; Shea et al., 2001]. In addition to the phalanges, this anomaly can also be seen in the metacarpal and metatarsal bones [Calif and Stahl, 2002]. The presence of a delta phalanx has been associated with syndactyly, polydactyly, symphalangism, brachydactyly, cleft hand, and triphalangeal thumb [Wood and Flatt, 1977]. Delta phalanges have been reported in a variety of conditions, including Apert syndrome [Neil and Conacher, 1984], Poland sequence [Wood and Flatt, 1977], Down syndrome [Taybi and Lachman, 1996a], Klinefelter

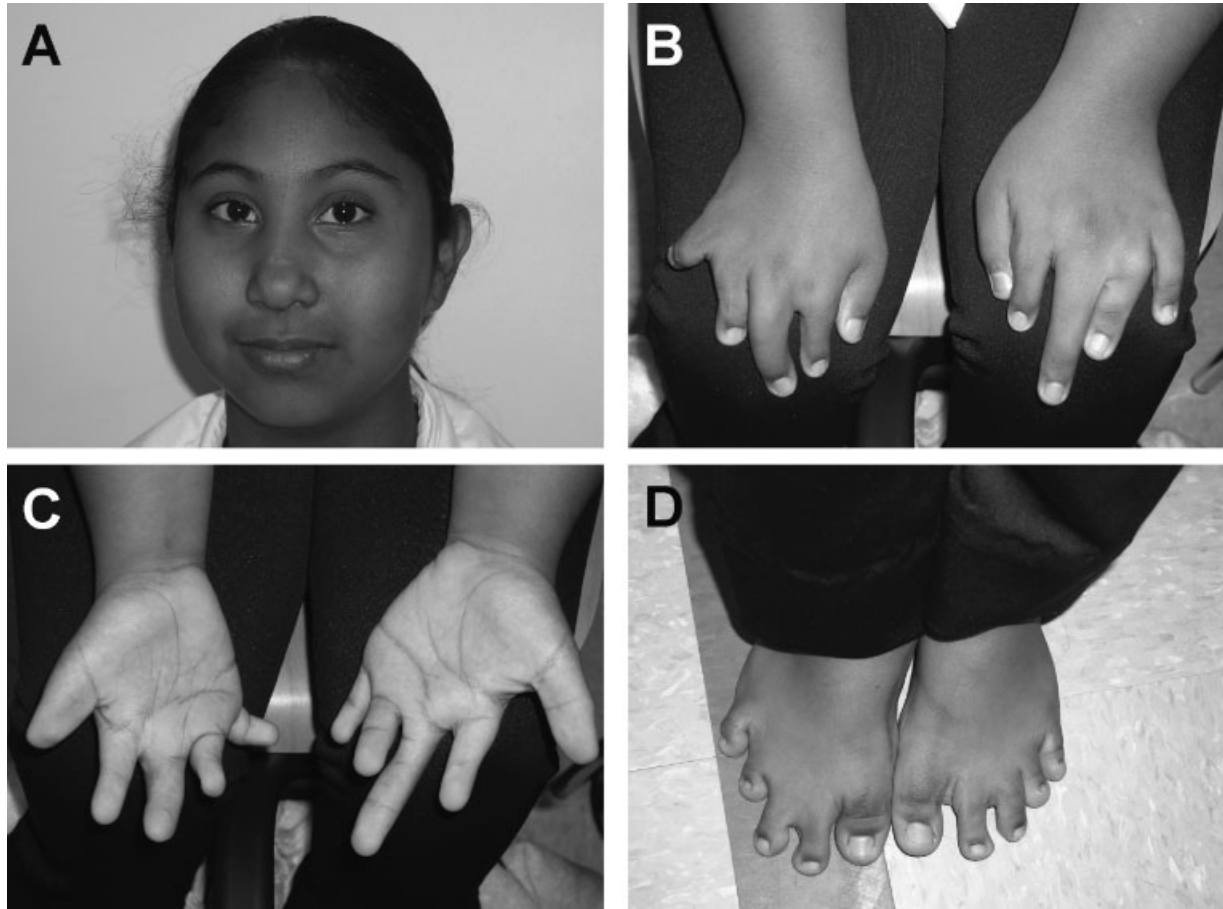


Fig. 2. Proband at 12 years of age. Clinical details are provided in the text.

syndrome [Lai et al., 1991], Antley–Bixler syndrome [Kitoh et al., 1996], and diastrophic and Desbuquois dysplasias [Faivre et al., 2004].

The presence of multiple delta bones within a single digit was first described in 1999 in patients with Rubinstein–Taybi syndrome (RTS) [Wood and Rubinstein, 1999]. The

presence of two delta phalanges that faced each other and were enclosed by a longitudinal epiphyseal bracket was termed “kissing delta phalanx.” Kissing delta phalanx was later observed in both Carpenter syndrome and Cenani–Lenz syndrome (CLS) [Wood and Shuren, 2002; Elliott et al., 2004a]. Early imaging is necessary in these cases as separated kissing

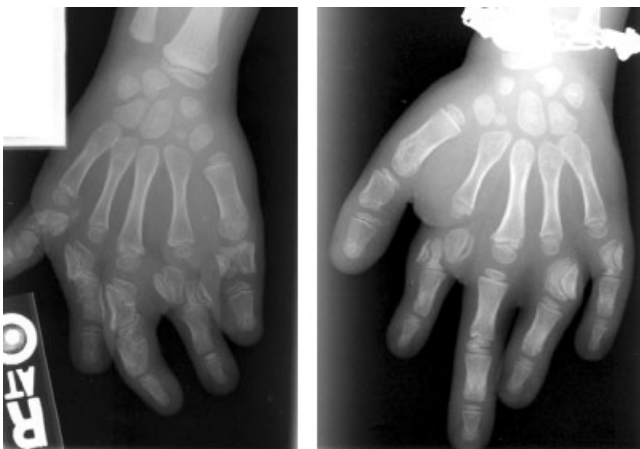


Fig. 3. Radiographs of proband's hands showing multiple delta phalanges bilaterally in proximal phalanges 2–5 and other anomalies. Both “kissing” (duplicated longitudinal bracketed epiphysis) and isolated delta phalanges are seen. Carpal abnormalities include hypoplastic ossification and unusual shapes of carpal bones.

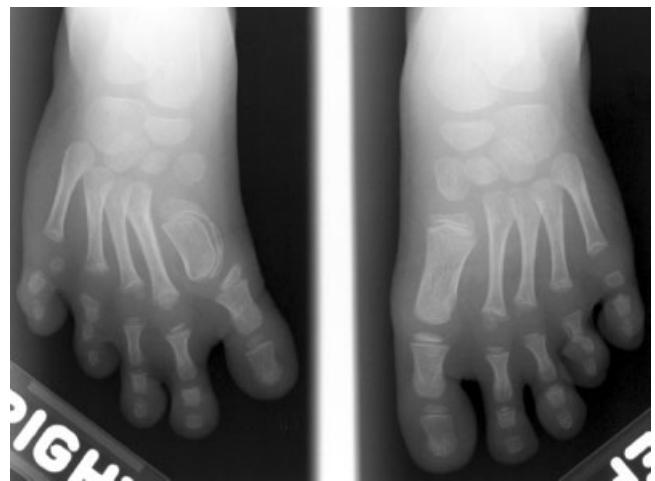


Fig. 4. Radiographs of proband's feet. Right foot has a delta phalanx of the first metatarsal. See text for details.

delta phalanges can fuse, thus obscuring an important radiological clue in the diagnosis of rare disorders [Elliott et al., 2004a]. Another compound manifestation of delta phalanx that has been described is the longitudinal terracing of three delta phalanges in a single digit, causing brachydactyly [Calif and Stahl, 2002]. The syndromes with a known genetic etiology in which delta phalanges are seen are caused by mutations in various genes, including *CREBBP*, *P63*, *POR*, and *FGFR2*, indicating that several pathogenic mechanisms can lead to this condition [Wilkie et al., 1995; Elliott et al., 2004a].

The dysmorphic craniofacial features in the proband are largely different from those that have been reported for patients with CLS, which can include a prominent forehead, hypertelorism, depressed nasal bridge, downslanting palpebral fissures, large ears, malar hypoplasia, and hypodontia [Temtamy et al., 2003; Elliott et al., 2004b]. However, CLS patients can have supernumerary nipples, as did our patient [Dodinval, 1979]. The proband also did not have facial features typical of RTS, such as a prominent nose with columella below the alae nasi, malpositioned and dysplastic ears, and hypoplastic maxillae [Wiley et al., 2003].

Several of the proband's family members were seen in our clinic, and none had obvious hand or foot deformities on physical examination. Interestingly, the parents' first child died at 40 days of age of unknown causes. Two children other than the proband were born with anomalies, one with renal dysplasia and the other with vertebral anomalies, facial dysmorphism, and dextrocardia. The presence of other anomalies in several siblings may be due to an inherited genetic aberration. Possible causes include variable expression of a recessive allele, in light of the parental consanguinity, as well as a new dominant mutation in the germline of one of the parents or a familial submicroscopic chromosomal rearrangement. Although the siblings' anomalies differ significantly from those of the proband, the reuse of signaling and gene regulatory cassettes in multiple organ systems during development may explain the pleiotropic findings [Schneider et al., 1999; Wang and Wynshaw-Boris, 2004].

In conclusion, we report a unique patient with multiple delta phalanges and several other anomalies, including butterfly vertebrae, craniofacial dysmorphism, and aortic coarctation. We have named this unusual constellation of anomalies the "brachydactylic multiple delta phalanges plus syndrome," based on its most unusual feature. We speculate, based on the consanguineous pedigree, that this condition may be caused by recessive inheritance, although other modes of inheritance cannot be discounted, and it is possible that variable expressivity of the mutant allele(s) may contribute to the distinct manifestations in the sibship.

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