Familial crossed polysyndactyly in four generations of an Indian family

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Background: **Polydactyly is the most common malformation of the limbs. "Crossed" polydactyly of hands and feet, i.e., preaxial in one and postaxial in the other, is extremely rare. It has not been included in the standard classification of hand and feet anomalies.**

Methods: **We report an Indian family with 7 affected members across 4 generations who had "crossed polysyndactyly". All but one affected member had involvement of all four limbs. There were no other congenital anomalies in any of the family members.**

Results: **Familial crossed polysyndactyly appeared to follow an autosomal dominant transmission. This is probably the first case of familial crossed polysyndactyly without any associated anomalies.**

Conclusion: **Familial crossed polysyndactyly is a rare malformation and all family members should be screened for other congenital malformations.**

World J Pediatr 2010;6(2):177-180

Key words: **familial; polysyndactyly**

Introduction

In 1978, Temtamy and McKusick proposed the classification of hand and feet anomalies which are inherited as Mendelian traits.[1] Polysyndactyly of bilateral hands and feet is unusual in an individual. It is even rarer to have "crossed" involvement of hands and feet, i.e., preaxial in one and postaxial involvement in the other.[2] In 1994, Goldstein et al[3] reported a family across 6 generations with 5 affected members, with preaxial polydactyly in the feet and postaxial polydactyly in hands in all affected members. They labelled this entity as "familial crossed polysyndactyly". But this entity has not been described in the classification by Temtamy and McKusick. We report in this paper an Indian pedigree across 4 generations including 7 members affected by crossed polysyndactyly.

Case report

Patient 1

Fig. 1 is the pedigree of the four generations. The family was ascertained through the youngest affected member (propositus, IV-2), a 3.1 kg female baby delivered at term gestation to a 26-year-old lady. The baby was found to have bilateral postaxial polydactyly of hands with webbing of the 4th and 5th fingers (cutaneous syndactyly). There was also bilateral preaxial polydactyly of feet with cutaneous syndactyly of the great toe and an extra toe on both feet. Her anthropometry was appropriate for gestation and the rest of her clinical examination was unremarkable. Ultrasonograms of her abdomen and head were normal. A detailed history from the mother revealed a similar affliction of hands and feet in other family members, which was confirmed clinically in 5 members of over 3 generations, and in another 2 members by history.

Patient 2

The mother of the patient (III 1) had bilateral postaxial polydactyly of both hands, which had been removed surgically 5 years before, and cutaneous syndactyly between the 3rd and 4th fingers of both hands. There was also preaxial polydactyly of both feet and the extra toe had been removed surgically. Examination revealed cutaneous syndactyly between the 1st and 2nd toes.

Patient 3

The maternal aunt (III 2) had been operated on for bilateral postaxial polydactyly of both hands and preaxial polydactyly of both feet. There was cutaneous syndactyly between the 3rd and 4th fingers of the left hand and

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doi:10.1007/s12519-010-0020-7

syndactyly of the 1st, 2nd and 3rd toes of both feet.

Patient 4

The maternal uncle (III 3) was also found to have been operated upon for bilateral postaxial polydactyly of hands and preaxial polydactyly of both feet. He was found to have symmetrical syndactyly of both feet involving the 1st, 2nd, and 3rd toes, and syndactyly of the 1st, 2nd, 3rd and 4th fingers of the right hand, which had also been separated surgically.

Patient 5

The maternal grandfather (II 3) had heptadactyly (postaxial) of both hands and feet. One extra postaxial finger from both hands was removed surgically, as was the case of one preaxial polydactylous toe of both feet. Examination revealed bilateral symmetrical syndactyly of the extra digit, 1st and 2nd toes of feet.

Another two family members (II 2 and I 1) were described to be affected by crossed polysyndactyly on history. All available family members were evaluated clinically to rule out other congenital malformations. Ultrasonography of the abdomen and a karyotype from all affected members showed nothing abnormal. Photographs of the affected members (Fig. 2) were taken after informed consent was obtained. Table shows the phenotypic pattern seen in the available family members.

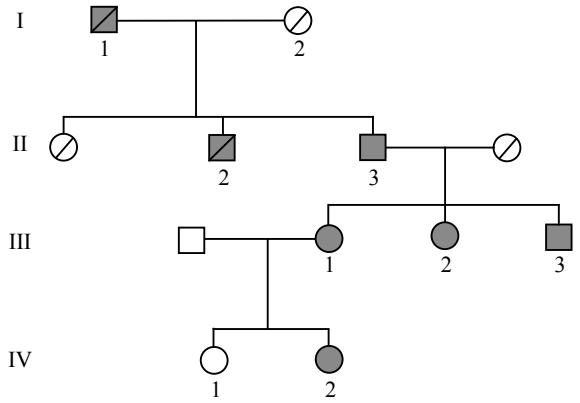

Fig. 1. Pedigree showing affected members (grey) over four generations.

Discussion

Polydactyly, syndactyly, and polysyndactyly are common malformations of the limbs.[4] Of these, polydactyly is the most common anomaly.[5] According to location, polydactyly can be subdivided into preaxial, postaxial or central polydactyly. Preaxial polydactyly is defined as a supernumerary digit on the medial aspect of the foot or hand. Postaxial polydactyly involves the lateral aspect of the foot or hand. Central ray polydactyly involves duplication of the second, third, or fourth digits. Preaxial forms are less common than postaxial forms. Another unusual form of polydactyly proposed by Nathan and Keniston is that of mixed polydactyly where preaxial and postaxial polydactyly exist in the same extremity.[6,7] Polydactyly may occur

Table. Phenotypic characteristics of polysyndactyly in the affected family members

Pedigree	Sex	Left hand	Right hand	Left foot	Right foot
IV 2	F	Hexadactyly, postaxial polydactyly, syndactyly, cutaneous, 4th and 5th fingers	Hexadactyly, postaxial polydactyly, syndactyly, cutaneous, 4th and 5th fingers	Hexadactyly, preaxial polydactyly, syndactyly, cutaneous, 1st and extra toes	Hexadactyly, preaxial polydactyly, syndactyly, cutaneous, 1st and extra toes
III 1	F	Hexadactyly, postaxial polydactyly (operated), syndactyly, cutaneous, 3rd and 4th fingers	Hexadactyly, postaxial polydactyly (operated), syndactyly, cutaneous, 3rd and 4th fingers	Hexadactyly, preaxial polydactyly (operated), syndactyly, cutaneous, 1st and 2nd toes	Hexadactyly, preaxial polydactyly (operated), syndactyly, cutaneous, 1st and 2nd toes
III 2	F	Hexadactyly, postaxial polydactyly (operated), syndactyly, cutaneous, 3rd and 4th fingers	Hexadactyly, postaxial polydactyly (operated)	Hexadactyly, preaxial polydactyly (operated), syndactyly, cutaneous, 1st and 2nd toes and 2nd and 3rd toes	Hexadactyly, preaxial polydactyly (operated), syndactyly, cutaneous, 1st and 2nd toes and 2nd and 3rd toes
III 3	M	Hexadactyly, postaxial polydactyly (operated), syndactyly, cutaneous, 1st and 2nd, and 3rd and 4th fingers	Hexadactyly, postaxial polydactyly (operated), syndactyly, cutaneous, 1st and 2nd (operated), and 3rd and 4th (operated) fingers	Hexadactyly, preaxial polydactyly (operated), syndactyly, cutaneous, 1st and 2nd toes, and 2nd and 3rd toes	Hexadactyly, preaxial polydactyly (operated), syndactyly, cutaneous, 1st and 2nd toes, and 2nd and 3rd toes
II 3	M	Hexadactyly, postaxial polydactyly, syndactyly, cutaneous, 1st and 2nd fingers	Hexadactyly, postaxial polydactyly, syndactyly, cutaneous, 4th and 5th fingers	Heptadactyly, preaxial polydactyly (operative removal of one toe), syndactyly, cutaneous, 1st and 2nd, and 2nd and 3rd toes	Heptadactyly, preaxial polydactyly (operative removal of one toe), syndactyly, cutaneous, 1st and 2nd, and 2nd and 3rd toes

F: female; M: male.

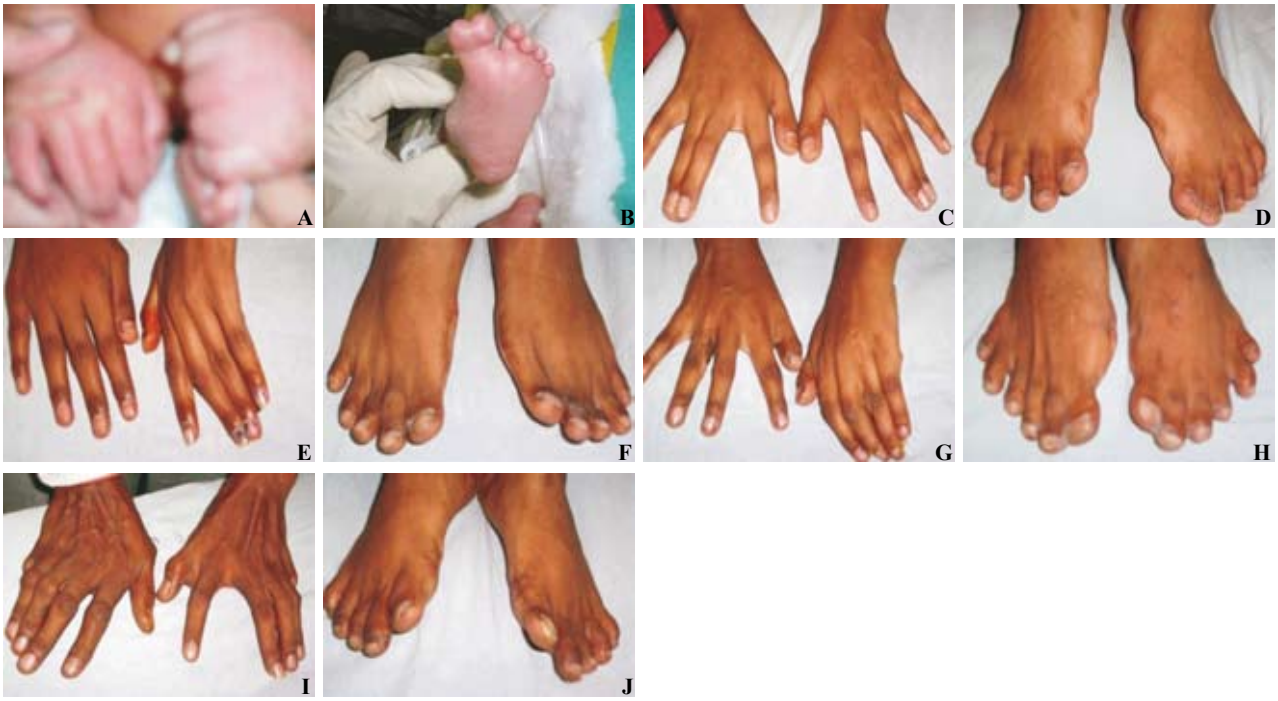

Fig. 2. Hands and feet of the affected family members (pedigree), dorsal aspect. **A & B:** IV 2 (proband), **C & D:** III 1 (mother), **E & F:** III 2 (maternal aunt), **G & H:** III 3 (maternal uncle), **I & J:** II 3 (maternal grandfather). Note: visible scars at previously operated areas.

as an isolated malformation or it may be associated with other birth defects. The latter presentation may be further labelled as "combined" if another limb defect (syndactyly, deficiency, deformity) is present, "syndromic" if some other non-limb defects are seen, or as "multiple congenital anomaly" when other birth defects are seen in addition to polydactyly.[8] Postaxial polydactyly has been described to be significantly associated with cephalocele, microcephaly, anophthalmia, cleft lip, polycystic kidney, and cyclopia. Preaxial polydactyly has been found to be significantly associated with esophageal atresia.[8]

In 1978, Temtamy and McKusick[1] at present proposed a classification of polydactyly which has been widely accepted. Over the years several complex associations with polydactyly have been observed which do not fit into this simple classification. In our patients, a rare form of polysyndactyly was seen, i.e., postaxial polydactyly in hands and preaxial polysyndactyly in feet. It was described as "crossed polydactyly" in the modified Temtamy and McKusick classification by Goldstein et al.[3] Since it was seen across generations and associated with syndactyly, it was named as familial crossed polysyndactyly. This form of polydactyly has been reported previously.[9-11] Most cases of polysyndactyly were reported to have multiple congenital anomalies to be associated with certain syndromes. Goldstein et al[3] found one case was affected with micropenis, abnormal ears, poorly defined philtrum, and down-slanting palpebral fissures and strabismus. Greig's syndrome is characterized by crossed polysyndactyly, i.e., preaxial polysyndactyly of feet and postaxial polydactyly of hands, along with craniofacial anomalies such as macrocephaly and hypertelorism.[12] However, none of our cases had any other non-limb deformities or dysmorphism suggestive of any particular syndrome.

In the modified classification,[6] type A polydactyly would be preaxial or postaxial, and could be unilateral or bilateral in hands or feet. Type B would indicate the polydactyly of the upper and lower extremities, either preaxial or postaxial. Type C would represent the involvement of the upper and lower extremity with opposite orientation (crossed), which is further subdivided into C1 and C2. C1 is upper extremity postaxial with lower extremity preaxial polydactyly (as seen in our cases). C2 is the upper extremity preaxial and the lower extremity postaxial. Type D has preaxial and postaxial polydactyly on the same extremity, previously referred as mixed. Type E is type D polydactyly of the upper or lower extremities along with type A polydactyly in the other set of extremities. All subtypes could be unilateral or bilateral.

The pedigree of affected family members is depicted in Fig. 1, with male to male transmission suggesting an autosomal dominant inheritance. Since some family members were not affected (I 2, II 1, IV 1), this genetic condition has a variable penetrance.

The phenotypic variation seen among the family members also indicates variable expressivity. A single gene may be incriminated for the condition due to the concordance among family members. However, we did not analyze a genetic linkage in our patients. Normal karyotyping was found in all members.

Future identification and characterization of the gene responsible for these phenotypes can explain phenotype variability, and elucidate the embryology of limb formation.

Funding: None.
Ethical approval: Not needed.
Competing interest: None.
Contributors: Dewan P, Batta V and Agarwal N drafted the manuscript. Dewan Pr and Batta V provided critical comments. All authors approved the final draft. Dewan P is the guarantor.

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Received December 23, 2008
Accepted after revision March 25, 2009