Anonychia and absence/hypoplasia of distal phalanges (Cooks syndrome): report of a second family

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Abstract

We describe a second family with four affected members in three successive generations with a rare nail dysplasia syndrome. The syndrome, which was first reported by Cooks *et al* in 1985, is characterised by bilateral nail hypoplasia of digits 1-3, with absence of nails of digits 4-5 of the hands, and total absence of all toe nails. In addition, there is absence/hypoplasia of the distal phalanges of the hands and feet. Our family confirms this syndrome as a distinct entity with autosomal dominant inheritance.

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In 1985, Cooks *et al*¹ described a rare and previously unrecognised form of nail dysplasia

with bone abnormalities in seven affected members of a family. The nail lesion was characterised by progressive bilateral nail hypoplasia of digits 1-3, with complete absence of the nails of fingers 4-5. There was total absence of all toe nails. Radiologically there was hypoplasia of the distal phalanges in digits 2-4 with absence of the distal phalanx of digit 5. In the feet, there was absence of all distal phalanges of digits 2-5 with hypoplasia of the distal phalanx of digit 1. As seven people (four males and three females) were affected in two generations with male to male transmission, the authors concluded that inheritance was autosomal dominant. We present a second family with anonychia and absence/hypoplasia of the distal phalanges in four people in three generations.

Case report

The proband (fig 1, IV.2) was a 4 month old male born at 37 weeks' gestation weighing 3232 g. The parents, who were aged 21 years (mother) and 33 years (father) at the birth, were unrelated. Clinical examination was unremarkable except for the appearance of the hands and feet. Both hands showed progressive hypoplasia of the nails of digits 1-3 with absence of the nails of digits 4-5. The fifth digit was shortened (fig 2A). The terminal creases were absent on both hands. The first digits were bulbous. There was total absence of all nails and hypoplasia of the terminal portion of the toes (fig 3A). All available members of the family were examined. The proband's mother (III.5), a maternal uncle (III.4), and maternal grandfather (II.3) were similarly affected. The mother (III.5), showed almost identical features in her hands and feet (fig 2B, fig 3B) as those observed in her son. In both hands, there was progressive nail hypoplasia of digits 1-5 and the fifth digits were shortened. The thumbs were long and bulbous (fig 2B). There were no nails on any of the toes and the big toes were bulbous (fig 3B). The maternal uncle (III.4) and the maternal grandfather (II.3) had similar changes in the fingers and toes (fig 2C, D, fig 3C, D). The clinical findings of the four affected members are summarised in the table.

RADIOLOGICAL STUDIES

In the proband (IV.2) at the age of 4 months, the terminal phalanges (TPs) of digits 1, 3, and 4 were small with increased soft tissue bulk at the tips. There were only tiny bony elements

Figure 1 Pedigree of the family.

Figure 2 (A) The left hand of IV.2 showing hypoplasia and absence of the nails and shortening of the fifth digits. (B) Similar changes in III.5. There is progressive hypoplasia of the nails on digits 1-3 with absence of nails on digits 4-5. (C-D) The hands of II.3 showing almost identical changes to his daughter, III.5, in (B).

Figure 3 (A) The left foot of IV-2, (B) the feet of III-5, (C, D) the feet of II-3 showing total absence of all nails and hypoplasia of the terminal portions of the digits.

Figure 4 (A, B) X rays of the hands of the proband (IV-2) showing small terminal phalanges of digits 1, 3, and 4. The terminal phalanx of the second digit is represented as only a tiny bony element. (C) The feet of IV-2 show first digits which are short and broad with only small terminal phalanges. The terminal phalanges of digits 2-5 are absent.

for the TPs of the second digits while the bony TPs of the fifth digits were absent. The middle phalanges (MPs) of the fifth digits were shorter than normal and tapered distally (fig 4A, B).

The first digits of the feet were short and broad with small, short TPs. The TPs of the other digits were absent; there was increased soft tissue bulk at the tips of the fifth digits (fig 4C). In the three adults (III-5, III-4, II-3) the bony changes in the hands and feet were similar. The TPs of the third digit of the hands had a characteristic shape with a rectangular basal section which extended for between 5 and 8 mm distally and then became a normally shaped tapering terminal phalanx with a clearly defined terminal tuft. This appearance was suggestive of an additional small phalanx at the terminal IP joint which had united with the TP (fig 5A-D). The TP of the left first digit of the mother was longer than that of the right and appeared to have an additional fused bony phalanx at the base (fig 6). In all four affected subjects, the TPs of the fifth digits of the hand were absent and the distal ends of the MPs were bulbous (fig 5B-D). The other middle phalanges and all the proximal phalanges and metacarpals were normal. In the feet, the first digits of all the adults have long PPs and abnormally shaped TPs with rectangular bases which were rounded distally and did not have normal tufts. All the other toes had only two phalanges (fig 7A-B).

Discussion

The onychodystrophy/anonychia with abnormalities of the distal phalanges in our family appears to be similar to the family reported by Cooks *et al.*¹ These authors described a family in which there were three affected people in two generations. In the hands, there was progressive hypoplasia of the nails of digits 1-3 with absence of both nails of digits 4 and 5. The fifth digits were shortened and some subjects showed lengthening of the first digit. There was complete absence of all toe nails. The table shows the comparison of the clinical features of the family of Cooks *et al.*¹ with our family. The main finding was hypoplasia of the distal phalanges in digits 2-4 of the hands with absence of the distal phalanges in the fifth digits. The mother (III-5) showed a possible extra phalanx in the first digit (fig 6). In the feet there was total absence of all the distal phalanges of digits 2-5 and hypoplasia of the distal phalanx of the first digit.

The shortening of the fifth digit of the hands

Clinical findings in hands and feet of affected subjects

Clinical findings	Cooks <i>et al.</i> ¹	Affected relatives			
		IV-2 (M, 4 mth)	III-5 (F, 21 y)	III-4 (M, 22 y)	III-3 (M, 57 y)
Hands					
Bulbous thumbs	3/3	0	+	+	+
Long thumbs	2/3	0	+	+	0
Hypoplasia nails 1-3	3/3	+	+	+	+
Shortened fifth digit	3/3	+	+	+	+
Absent nails 4-5	3/3	+	+	+	+
Absence of terminal creases 2-5	3/3	+	+	+	+
Feet					
Absent toe nails 1-5	3/3	+	+	+	+
Hypoplasia of distal part of toes	3/3	+	+	+	+
Hallux valgus	2/3	0	+	0	0

+ = present, 0 = absent, M = male, F = female

Figure 5 (A-D) X rays of hands of III-5 (A,B), II-3 (C), and III-4 (D) showing hypoplasia of distal phalanges of digits 2-4 and total absence of the distal phalanges of digit 5. The terminal phalanx of the third digit has a characteristic shape with a rectangular basal section and then becomes a normally shaped tapering terminal phalanx.

Figure 7 (A, B) X rays of left foot of the mother (III-5) and the maternal uncle (III-4).

Figure 6 The first digit of the left hand of the mother (III-5) showing a terminal phalanx with an appearance of an additional fused phalanx at the base.

is most likely because of absence of the terminal phalanx. With regard to the toes, it is not quite clear cut. The bony TPs of digits 2-4 of the mother and digits 2-5 of the uncle appear like MPs with rounded ends, but those of the grandfather are quite similar to the usual TP. With regard to the fifth toes, it is a fairly common normal anatomical variant to have only two phalanges in these toes. When this occurs the shape of the long TP is similar to that seen in the TPs of digits 3 and 4 of the hands of the mother and grandfather suggesting that there may have been a small additional phalanx at the base of the TP which had fused with it.

The findings in our family and in that of Cooks *et al*¹ differ from other genetic disorders involving nail and bone dysplasia of the hands and feet.² Hobbs³ described an autosomal dominant nail dysplasia which was most marked in the first digit of the hands and feet. There were 11 affected family members with male to male transmission. Affected members showed an unusual tapering of the distal phalanx with a spatulate tip. The family described by Verbov,⁴ in addition to congenital anonychia, had hyper- and hypopigmentation of the axillae and groins. The patient, a 26 year old female, her mother, brother, and maternal uncle were similarly affected. In the autosomal dominant anonychia and onychodystrophy described by Timmerman *et al*,⁵ there is a progressive nail hypoplasia from the fifth to the first digits, with anonychia often present in the second and third digits. Our family and that of Cooks *et al*¹ show nail hypoplasia of the first digit progressing to absence of the nails on the fourth and fifth digits. In autosomal dominant anonychia and onychodystrophy, no bony changes have been reported. The family described by Kumar and

Levick,⁶ in addition to the anonychia/onychodystrophy, showed hypoplasia of the metacarpals, metatarsals, and distal phalanges. In several genetic syndromes of anonychia/onychodystrophy, other major clinical features co-exist such as deafness,⁷ mental retardation,⁸ hair and teeth anomalies,⁹ joint contractures,¹⁰ eye defects,¹¹ and ectrodactyly.¹² Neither the family of Cooks *et al*¹ nor the present one had any associated clinical features.

Cooks *et al*¹ concluded that inheritance was probably autosomal dominant despite the fact that both parents in generation I were unaffected (the father was examined, the mother was unavailable). Four of 12 children of these parents were affected. X linked inheritance was excluded as there was male to male transmission. Our family confirms the autosomal dominant mode of inheritance, as the disorder occurred in three generations with male to male transmission. The grandfather (III-3) was the only one of five sibs affected. Presumably the condition in him was the result of a new mutation.

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