Published in final edited form as:

Clin Dysmorphol. 2001 April ; 10(2): 95–99.

Total anomalous pulmonary venous connection and a constellation of craniofacial, skeletal, and urogenital anomalies in a newborn and similar features in his 36-year-old father

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Abstract

We report on a newborn male born to non-consanguineous parents with total anomalous pulmonary venous connection (TAPVC) and additional findings of malformed ears, hypertelorism, brachyphalangy in the hands, pterygium of the elbows, knees, and wrists, complex lower limb pre-axial polydactyly, tibial shortening, clubfeet, horseshoe kidney and a micropenis. He had a 46,XY karyotype. His 36-year-old father had similar craniofacial and limb anomalies suggesting an autosomal dominant syndrome with variable expression. Our patients may represent the 3rd and 4th examples of a newly-described syndrome by Baraitser *et al.* [(1997) *Clin Dysnorphol* 6:111–121] which is distinguished by malformed ears, complex pre-axial polydactyly and tibial aplasia in the lower limbs, severe brachyphalangy in the hands, and a micropenis.

Keywords

total anomalous pulmonary connection; craniofacial anomalies; preaxial polydactyly; tibial shortening; brachyphalangy; micropenis; autosomal dominant

CASE REPORTS

Proband (C.S.)

A 38-week-gestational-age white male weighing 2381 g was born in vertex position by spontaneous vaginal delivery to a G2P2, 21-year-old Caucasian mother. Despite visible

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multiple congenital anomalies noted at delivery, the proband was stable with Apgar scores of 8 and 10 at 1 and 5 mins, respectively. Dysmorphic features initially identified included: microphthalmia; blepharophimosis; hypertelorism; broad-nasal bridge; abnormal ear formation with marked over-folding of hairy helices; carp-shaped mouth; high-arched palate; mild micrognathia; torticollis; unusual splayed hand position with a broad thumb and nail hypoplasia bilaterally; brachydactyly; preaxial polydactyly of the feet with a central gap and triplication of the great toes bilaterally; clubfeet; contractures and pterygium of the elbows, knees and wrists; short underdeveloped limbs; prominent bony sacrum; cryptorchidism and micropenis with hypospadias (see Figures 1 and 2). A 2-year-old sister had a history of gastroesophageal reflux but was otherwise normal. The parents were non-consanguineous. The proband tolerated feeding and was discharged to home on the 2nd day of life. On the 6th day he was admitted to hospital because of temperature fluctuations, apneic episodes, feeding difficulties, and decreased urine output. On admission an echocardiogram revealed total anomalous pulmonary venous connection (TAPVC) of the infradiaphragmatic type with concurrent atrial septal defect (ASD) and mild tricuspid regurgitation. A skeletal survey demonstrated relative microcephaly, shortening of the radius and ulna bilaterally; abnormal appearing fingers and short metacarpals; shortening of the tibia bilaterally; six metatarsals and seven phalanges bilaterally with a rudimentary 7th distal metatarsal on the left foot; abnormal clavicles; pelvic flaring of the iliac wings; a prominent sacrum and delayed bone age (lack of tali/ calcanei calcification). A renal ultrasound revealed a horseshoe kidney with two ureters and one collection system. On the 9th day of life, an endotracheal intubation with ventilatory support was necessary after an episode of prolonged respiratory decompensation. On the 12th day of life, the TAPVC and ASD were successfully repaired but supra-systemic pulmonary hypertension and disseminated intravascular coagulopathy developed. Unfortunately, he died within hours of the surgical procedure.

Chromosome analysis revealed a normal 46,XY karyotype. At the time of death, he was small for gestational age weighing 2640 g (5th percentile) with a length of 46 cm (10th percentile) and a head circumference of 30 cm (< 3rd percentile).

The 36-year-old father displayed similar features including: blepharophimosis; hypertelorism; a broad-nasal bridge; abnormal ear formation with marked over-folding of hairy helices; a high-arched palate; mild micrognathia; torticollis; abnormal clavicles; unusual hand position; preaxial polydactyly of the feet with a central gap and triplication of the great toes bilaterally; clubfeet (the latter two features repaired in childhood); and a prominent bony sacrum (see Figures 3 and 4).

There was hearing loss on the left side. Clinical and ultrasound study showed no cardiac or urogenital problems.

DISCUSSION

The constellation of craniofacial, skeletal, cardiac, and urogenital anomalies identified in this newborn male infant and similar features in his father suggest an autosomal dominant syndrome. Baraitser *et al.* (1997) reported two unrelated children with complex lower limb

pre-axial polydactyly, tibial aplasia, severe finger brachydactyly, overlapping craniofacial features, and a micropenis (see Table 1). There were no cardiac or renal problems or a positive family history in either case. Our patients may be the third and fourth examples of this newly documented dysmorphic syndrome. Our patients share many of the distinctive features described by Baraitser *et al.* (1997) including a similar craniofacial appearance (malformed ears, short neck, small chin), limb anomalies (pre-axial polydactyly, short abnormal fingers, tibial shortening, nail hypoplasia) and urogenital abnormalities. The finding of TAPVC and horseshoe kidney in our proband, but not in his affected father or patients reported by Baraitser *et al.* (1997) emphasizes the variable expressivity of this condition. In summary, the findings in our proband and his father are very similar to those reported by Baraitser *et al.* (1997) and suggest that this newly described dysmorphic syndrome is inherited as an autosomal dominant condition.

REFERENCE

Baraitser M, Stewart F, Winter RM, Hall CM, Herman S, Nevin NC (1997). A syndrome of brachyphalangy, polydactyly and absent tibiae. Clin Dysmorphol 6:111–121. [PubMed: 9134290]

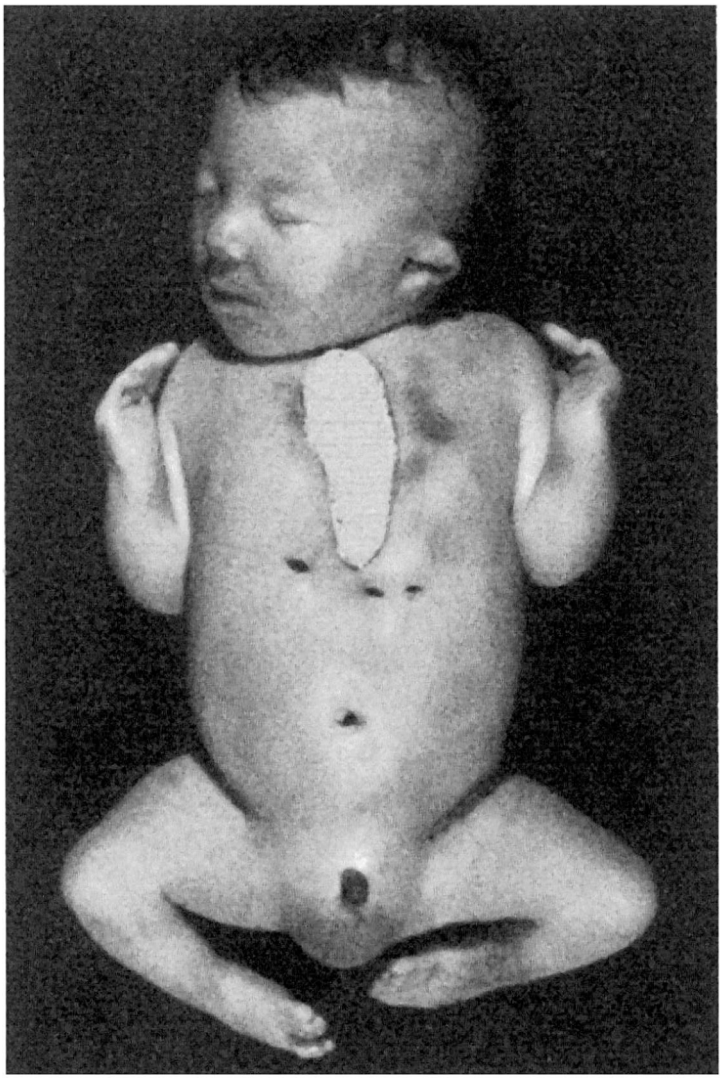


FIGURE 1.
The 12-day-old proband at autopsy

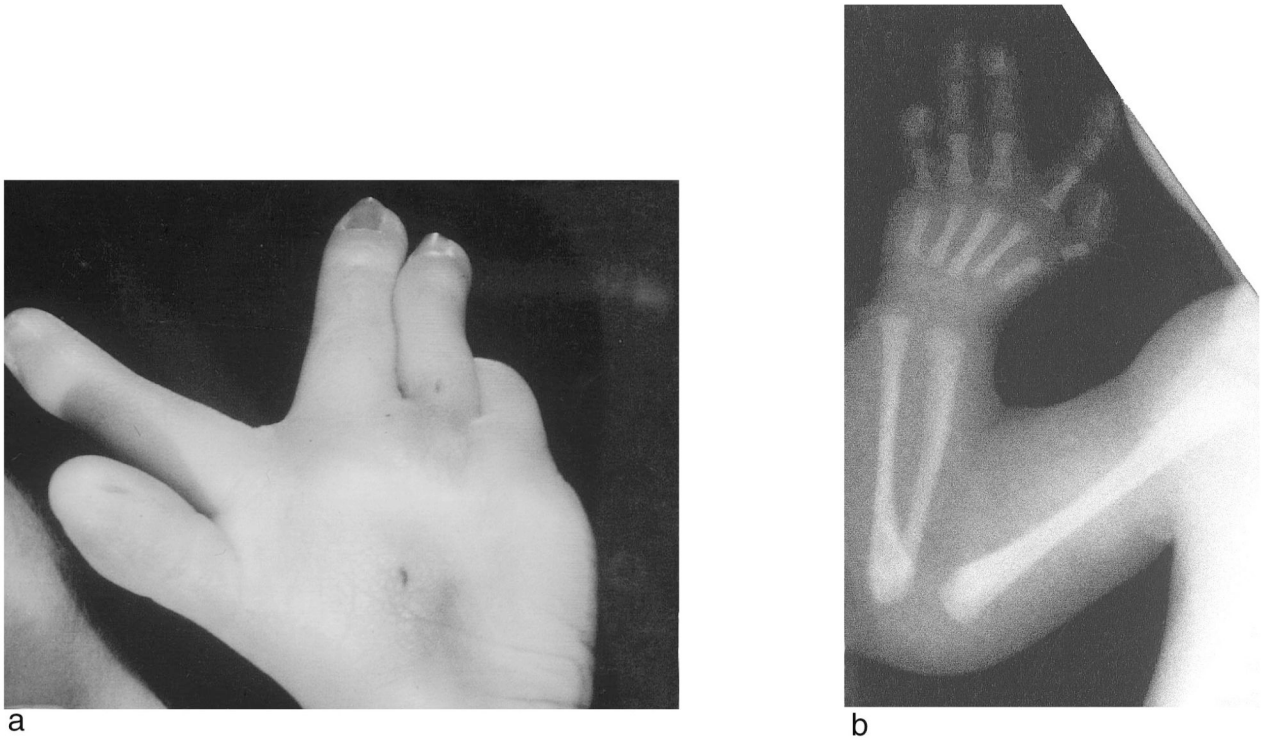


FIGURE 2.

The proband. (a) Splayed 2nd and 3rd digits with broad thumbs and nail hypoplasia; (b) An AP radiograph of the left arm shows relative shortening of the radius and ulna, abnormal fingers and short metacarpals

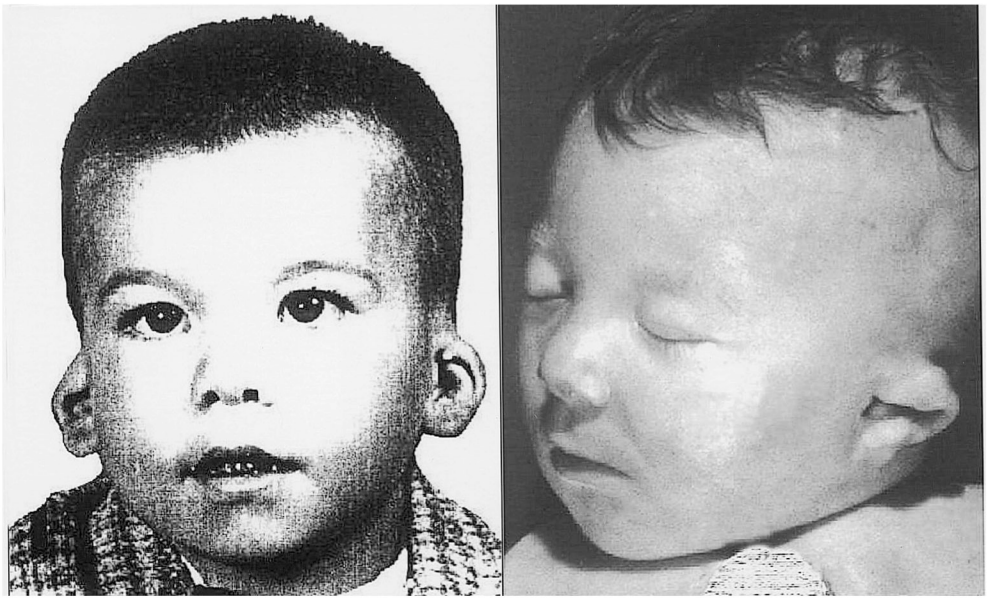
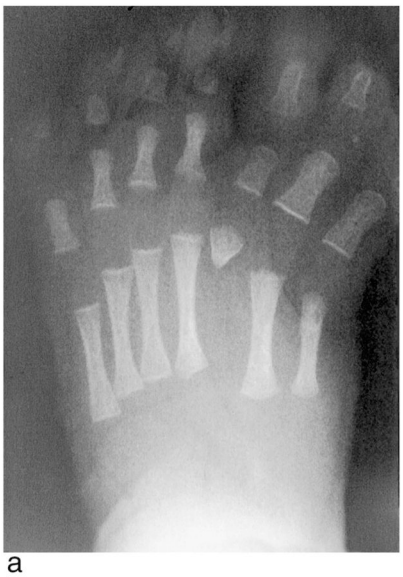


FIGURE 3.
Similar facial features were evident in the father (left) at 5 years of age and the proband (right) at the age of 12 days



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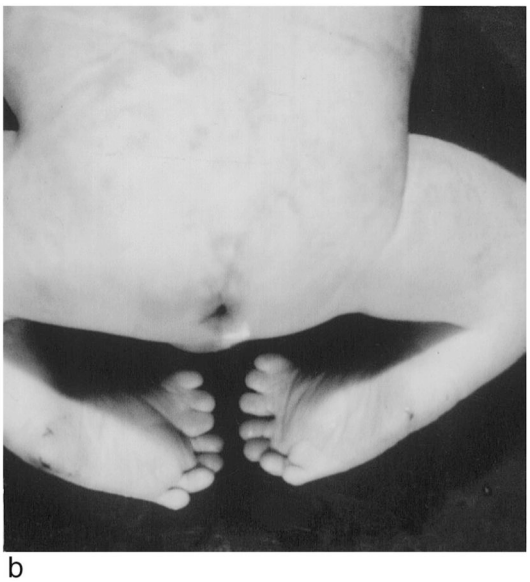

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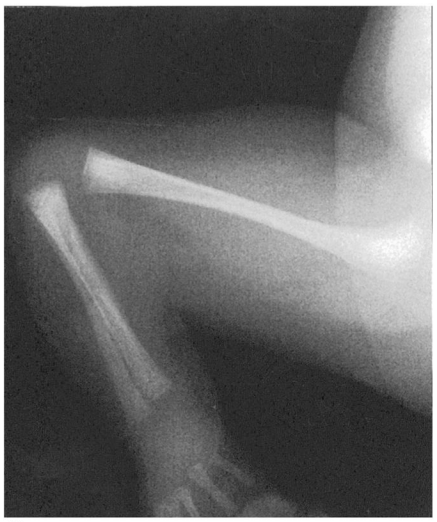

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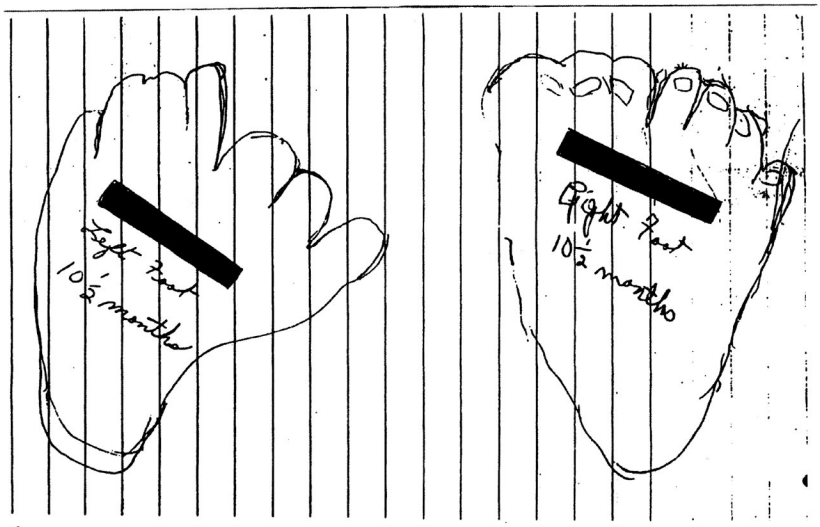

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FIGURE 4.

(a) An AP radiograph of the proband's left foot (see text for details); (b) view of proband's feet; (c) an AP radiograph of the proband's leg; normal femur but tibial shortening. The talus and calcaneus are not ossified; (d) a tracing of the father's feet made by his mother prior to surgical repair in childhood

Clin Dysmorphol. Author manuscript; available in PMC 2019 October 07.

TABLE 1.

Features identified in our proband, his father and two reported unrelated patients

Feature	Probound	Father	Patient 1[a]	Patient 2[a]
CRANIOFACIAL				
Microcephaly	+	−	+	?
Microphthalmia	+	−	?	+/−
Blepharophimosis	+	+	?	+
Hypertelorism	+	+	?	+
Malformed ears	+	+	+	+
Carp-shaped mouth	+	+	+	+
High-arched palate	+	+	?	?
Micrognathia	+	+	+	+
Torticollis	+	+	?	+
Short neck	+	+	+	+
SKELETAL				
Short/abnormal fingers	+	−	+	+
Cutaneous syndactyly	+/−	−	+	+
Shortening of the radius and ulna	+	−	−	+
Absent nails	+	−	+	+
Lower limb preaxial polydactyly	+	+	+	+
Mesomelic shortening	+	−	+	+
Clubfeet	+	−	+	+
Pterygium of the elbows, knees and wrists	+	−	+/−	+/−
Prominent bony sacrum	+	+	?	?
CARDIAC				
Structural defects	+	?	?	?
UROGENITAL				
Horseshoe kidney	+	−	−	−
Cryptorchidism	+	−	+	?
Micropenis	+	?	+	+
OTHER				

Feature	Proband	Father	Patient 1[a]	Patient 2[a]
Family history	+	+	–	–
Early death	+	–	–	–
Developmental delay/learning impaired	?	+/–	+/–	+
Hearing loss	?	+	?	+
RADIOLOGIC EVALUATION				
Abnormal renal ultrasound	Yes	No	?	?
Radius	Shortened	?	Not seen	Shortened
Ulna	Shortened	?	Not seen	Shortened
Metacarpals	Shortened	?	Shortened	Shortened
Short abnormal phalanges	Yes	?	Yes	Yes
Dislocated hips	No	?	Yes	Yes
Tibiae	Shortened	?	Absent	Absent
Fibulae	Present	?	Shortened	Present
Short metatarsals	No	?	Yes	Yes
Short toe phalanges	No	?	Yes	Yes (middle)
Preaxial polydactyly with a central gap	Yes	Yes	Yes	Yes
Abnormal clavicles	Yes	Yes	?	Yes
Ischiae	Present	?	Present (vertical)	Present (hypoplastic)
Acetabulae	Present	?	Present (shallow pseudoacetabulae)	Present (dysplastic)
Pubic rami	Present	?	Present (hypoplastic)	Present (dysplastic)

[a]Adapted from Tables 1 and 2, Baraitser *et al.* (1997). A skeletal survey of the proband's father was not available.