Catel–Manzke syndrome: A case report of a female with severely malformed hands and feet. An extension of the phenotype or a new syndrome?

J.H.W. Clarkson[a], T. Homfray[b], C.W. Heron[c] and A.L. Moss[a]

An unusual case of a female infant with Catel–Manzke syndrome is presented. Additional features not previously reported include three accessory ossicles at the bases or associated with the proximal phalanx of the index, middle, ring and little fingers bilaterally. There are also numerous bony abnormalities in both feet. Previous cases have shown no more than 2 accessory ossicles in the hand and these usually involve the index alone. The foot abnormalities are more extensive than any previously seen in this syndrome. This is only the 8th female case out of a total of 27 reported cases. ***Clin Dysmorphol*** **13:237–240 © 2004 Lippincott Williams & Wilkins.**

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Departments of [a]Paediatric Plastic Surgery, [b]Clinical Genetics and [c]Radiology, St Georges Hospital and St Georges Hospital Medical School, London, UK.

Correspondence and requests for reprints to James Clarkson, Flat 9 Berkswell Hall, Meriden Road, West Midlands, CV7 7BG, UK.
e-mail: jhwclarkson@hotmail.com

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Introduction

Catel–Manzke syndrome comprises the association of Pierre Robin sequence (micrognathia and cleft palate) with digital abnormalities, classically an extra delta phalanx in the second digit. Although originally described briefly in German by Catel in 1961, Manzke later presented the same case in more detail (Manzke, 1966). The mode of inheritance is unknown; recurrences within a family have been noted suggesting this is a genetic syndrome (Brude, 1984; Dignan *et al.*, 1986; Lipson *et al.*, 1984). Although the majority of reported patients have been male the increasing number of females now reported (8/27) suggests that X-linked inheritance is unlikely. Catel–Manzke syndrome is also known as Digitopalatal syndrome.

Case report

NG was the first child of healthy first cousin parents from Pakistan. Her mother was nineteen and her father twenty-eight at the time of her birth. She has two paternal first cousins whose parents were also both consanguineous, one apparently died of congenital heart disease and the other of multiple congenital abnormalities, cause unspecified in Pakistan. NG was a full term normal delivery weighing 3.52 kg; she was noted at birth to have a cleft palate and abnormal hands and feet.

Examination at three months of age showed a healthy female infant who had reached her appropriate developmental milestones, head circumference and length were on the 25th centile and her limbs were proportionate. She had micrognathia (Figure 1) and a midline cleft palate. Sensorineural hearing loss was noted on follow up.

Examination of her hands (Figures 2, 3) showed radial deviation at the metacarpophalangeal joints of fingers 2 and 3 bilaterally and 4 on the left with ulna deviation from the metacarpophalangeal joints of the 5th fingers with further abnormalities at the distal interphalangeal joints.

Radiographs of the hands aged 2 months (Figure 4) revealed normal metacarpals. Both hands had ulna deviation of the 5th fingers. The proximal phalanges of the index and middle fingers were hypoplastic and deformed. There was either duplication or triplication and deformity of the proximal phalanx of both thumbs. Hypoplasia of the left proximal phalanx and right middle phalanx of the 5th fingers was noted. There was a supernumerary delta phalanx between the middle and ring fingers on the right hand.

Radiographs of the hands aged 4.5 years (Figure 5) showed in both hands that there was ulnar deviation of the 5th finger and radial deviation of the index and middle fingers. Both thumbs were short demonstrating abnormally shaped proximal phalanges with accessory ossicles at either side of them. In the index and middle fingers of both hands, and the left ring and little fingers, there were accessory proximal phalanges with a delta shape associated with a further accessory bone next to them. In the left index it was partially fused to the proximal phalanx. In the right index there was hypoplasia of the middle phalanx, which was fused to a shortened proximal phalanx. The left middle finger had a very hypoplastic middle phalanx, the right side having a short proximal phalanx. In addition, the right little finger

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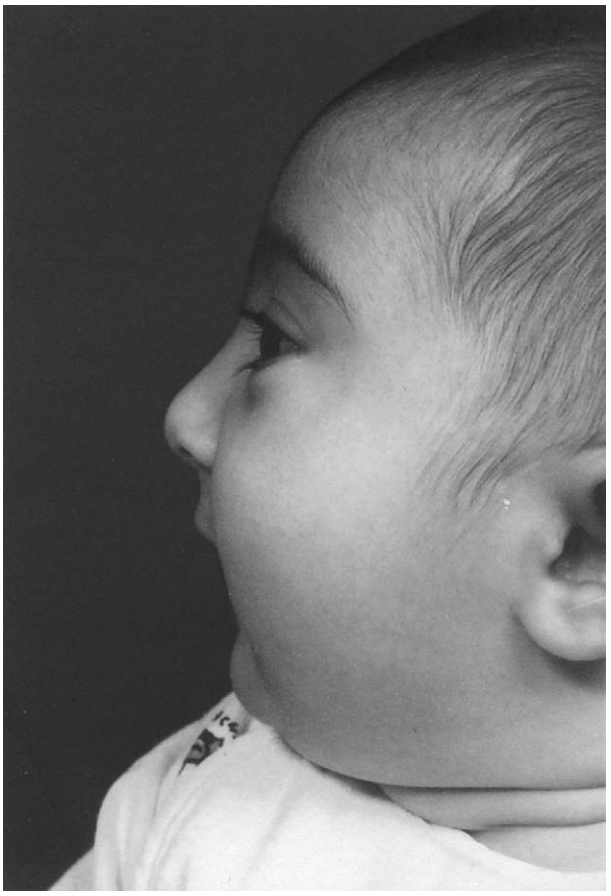
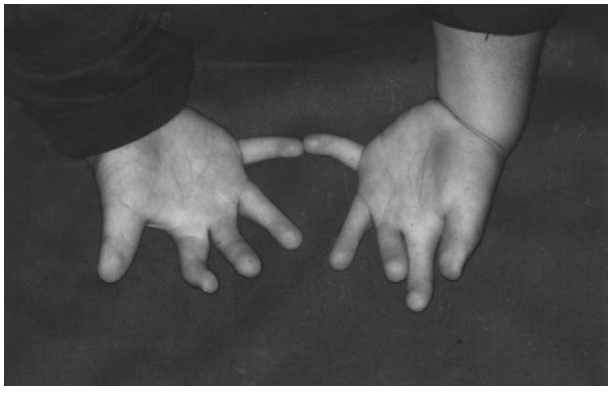
Fig. 1



Side view face age 6 months.

Fig. 2



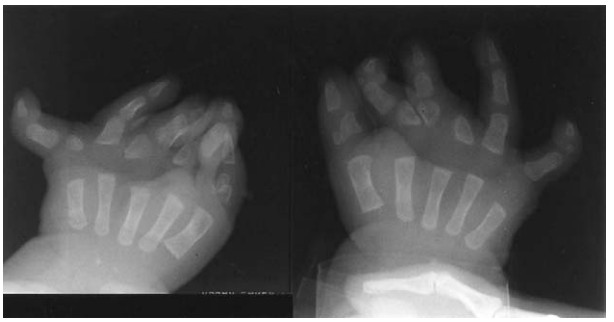
Ventral view hand age 5 years.

demonstrated an accessory proximal phalanx and a hypoplastic middle phalanx with no accessory ossicles seen next to it.

Fig. 3

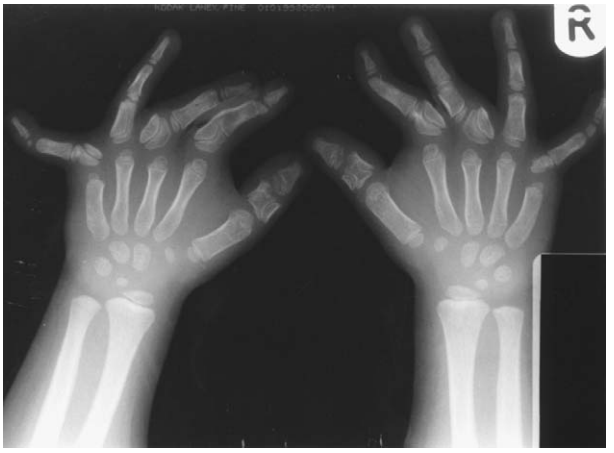
Dorsal view hand age 5 years.

Fig. 4



X-ray Hand age 2 months.

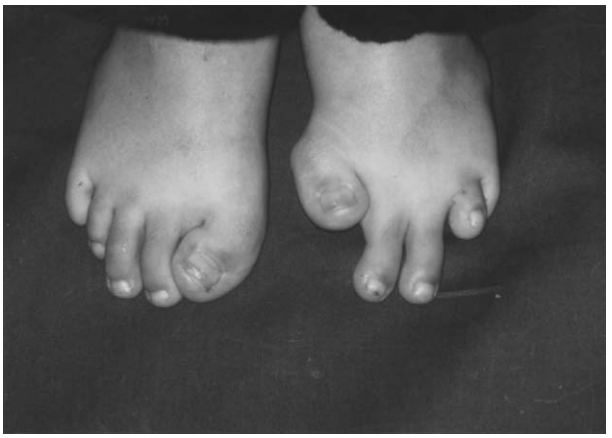
Fig. 5



X-ray Hand age 4 year 6 months.

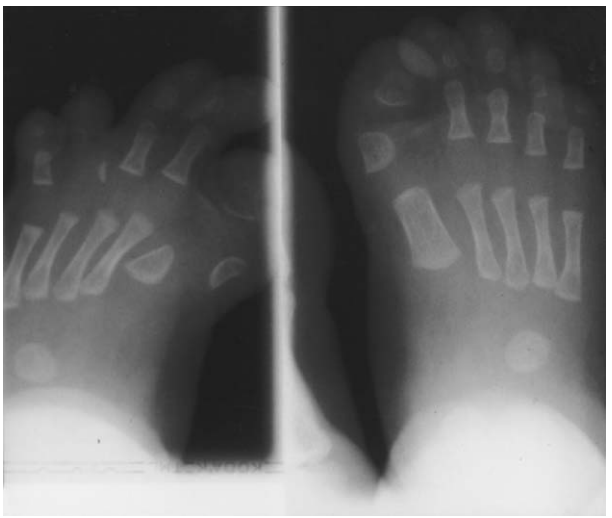
Examination of her feet (Figure 6) showed short halluces and a short 4th toe on the left. In addition there was medial deviation of most toes (Figure 7). Radiographs of the left foot aged two months revealed a short wide first metatarsal associated with short phalanges of the great toe, the proximal phalanx being medially displaced. The middle phalanx of the 5th toe was absent. In the right foot the metatarsal of the great toe was small and misshapen. The proximal phalanx of the great toe was small and medially displaced, as was the corresponding 4th toe phalanx. The terminal phalanx of the great toe was slightly short and widened. The 4th toe had a small and deformed middle phalanx. The middle phalanx of the little toe was absent.

Fig. 6



Dorsal view foot age 5 years.

Fig. 7



X-ray foot age less than 1 year.

Her karyotype was 46,XX at the 550 band level. At the age of 2 years 6 months she developed a severe pyrexial illness associated with diarrhoea. Full blood count and bone marrow examination on two occasions suggested myelodysplasia. In view of the digital abnormalities chromosome breakage studies were undertaken using mitomycin C. No excessive chromosome breakage was noted. She recovered from this illness and 7 years later there has been no suggestion of further haematological abnormalities.

Discussion

There are now 26 reported cases of Catel–Manzke syndrome (all references, Table 1). Skeletal anomalies of the toes are an unusual feature of this syndrome but 5 cases with toe involvement have been reported. Features include a short hallux (Dudin *et al.*, 1995; Gorlin *et al.*, 1975), short toes (Dignan *et al.*, 1986; Wilson *et al.*, 1993) and a bifid metatarsal (Holthusen, 1972).

Only seven out of the 26 cases published to date have been female (Manzke, 1966; Dignan *et al.*, 1986; Gorlin *et al.*, 1975; Kant *et al.*, 1998; Klug *et al.*, 1983; Petit *et al.*, 1994). The rarity of female cases initially suggested an X-linked pattern of inheritance however, the number of girls now reported including a pair of siblings reported by Dignan *et al.* (1986), make this very unlikely. Autosomal dominant inheritance with reduced penetrance is suggested by the pedigree of Stevenson *et al.* (1980), in their case report the proband and the grandfather's X-rays were examined by the author although the other two cases within the family were not examined. In view of the consanguinity in the case reported here and the siblings reported by Dignan *et al.* (1986) autosomal recessive inheritance is possible although germinal mosaicism cannot be discounted.

The hand anomalies in this case are very complex when compared to the published literature, with accessory ossicles in the 2nd, 3rd/4th and 5th digits and abnormal proximal phalanges of the thumb. In the literature, there are no reports of supernumerary ossicles at the base of the 5th phalanx, although ossicles are reported at the base of the 3rd phalanx (Petit *et al.*, 1994; Sundaram *et al.*, 1982). Abnormalities of the proximal phalanx of the thumb are not reported.

Otopalatodigital syndrome (OPDS, MIM 311300) is an X-linked semi-dominant condition due to mutations in the filamin A gene (Robertson *et al.*, 2003). In this disorder cleft palate as well as mixed sensorineural and conductive hearing losses are associated with foot abnormalities similar to our case. However, we feel that OPDS is an unlikely diagnosis because such a high degree of deformity would be unlikely to be expressed in a girl. The facial features of OPDS consisting of a large forehead

Table 1 Summary of published hand and foot skeletal abnormalities found in Catel–Manzke syndrome

Case	Sex	Index delta phalanx	Other hand abnormalities	Metatarsal/Toe abnormalities
Manzke (1966)	Female	Yes	No	No
Farnsworth and Pacik (1971)	Male	Yes	No	No
Gorlin *et al.* (1971)	Unknown	Yes	Unknown	Unknown
Holthusen (1972)	Male	Yes	No	Bifurcation 1st metatarsal
Holthusen (1972)	Male	Yes	Clinodactyly 5th	No
Gorlin *et al.* (1975)	Female	Yes	Clinodactyly 5th	Hypoplastic proximal phalanx hallux
Silengo *et al.* (1977)	Male	Yes	No	No
Gewitz *et al.* (1978)	Male	Yes	Clinodactyly 5th	No
Stevenson *et al.* (1980)	Male	Yes	No	No
Sundaram *et al.* (1982)	Male	Yes	Clinodactyly 5th, delta phalanx base of 3rd	No
Klug *et al.* (1983)	Female	Yes	No	No
Brude (1984) [historical]	Male (brother)	Unknown	Clinodactyly 5th	No
Lipson *et al.* (1984)	Unknown (siblings)	Yes	No	No
Lipson *et al.* (1984)	Unknown (siblings)	Index clinodactyly	No	No
Thompson *et al.* (1986)	Male	Yes	Clinodactyly 5th	No
Dignan *et al.* (1986)	Female (sister)	Yes	Clinodactyly 5th	Short toes
Dignan *et al.* (1986)	Female (sister)	Yes	No	No
Skinner *et al.* (1989)	Male	Yes	Syndactyly 3/4	No
Skinner *et al.* (1989)	Male	Yes	Clinodactyly 5th	No
Bernd *et al.* (1990)	Unknown	Yes	Clinodactyly 5th	No
Bernd *et al.* (1990)	Unknown	Yes	No	No
Wilson *et al.* (1993)	Male	Yes	Clinodactyly V, short fingers	Short toes
Petit *et al.* (1994)	Female	Yes	Delta phalanx base 3rd, missing 1st ray	No
Dudin *et al.* (1995)	Male	Yes	No	Short 1st metatarsal
Kant *et al.* (1998)	Female	Yes	Clinodactyly 5th	No

and pugilistic nose are strikingly different from ours. Although clinodactyly is a common feature in OPDS, there are no reported accessory ossicles.

There are also some similarities to the diseases caused by mutations in the CDMP1 gene including acromesomelic chondrodysplasia, Grebe chondrodysplasia, autosomal dominant brachydactyly type C and DuPan (fibula hypoplasia and complex brachydactyly) syndromes. We think mutations in this gene are unlikely, as extra phalanges are not recorded in any of the described phenotypes.

Our case is more severe than previously reported cases of Catel–Manzke syndrome; it therefore represents either an extension of the phenotype or a new syndrome not previously described. The consanguinity would support autosomal recessive inheritance.

References

Bernd L, Martini AK, Schiltenwolf M (1990). Catel–Manzke syndrome. *Klin Padiatr* **202**:60–63.

Brude E (1984). Pierre Robin sequence and hyperphalangy, a genetic entity (Catel Manzke syndrome). *Eur J Pediatr* **142**:222–223.

Dignan PSJ, Martin LW, Zenni EJ (1986). Pierre Robin anomaly with an accessory metacarpal of the index finger: the Catel–Manzke Syndrome. *Clin Genet* **29**:168–173.

Dudin A, Abdelshafi M, Rambaud-Cousson A (1995). Choledochal cyst associated with rare hand malformation. *Am J Med Genet* **56**:161–163.

Farnsworth PB, Pacik PT (1971). Glossoptotic hypoxia and micrognathia-the Pierre Robin syndrome reviewed. *Clin Pediatr* **10**:600–606.

Gewitz M, Dinwiddie R, Yuille T, Hill E, Carter CO (1978). Cleft palate and accessory metacarpal of index finger syndrome: possible familial occurrence. *J Med Genet* **15**:162–164.

Gorlin RJ, Cervenka J, Moller K, Horrobin M, Witkop CJ (1975). A selected miscellany. *Birth Defects Orig Artic Ser* **11**:39–50.

Gorlin RJ, Cervenka J, Pruzansky S (1971). Facial clefting and its syndromes. *Birth Defects Orig Artic Ser* **7**:3–49.

Holthusen W (1972). The Pierre Robin unusual associated developmental defects. *Ann Radiol (Paris)* **15**:253–262.

Kant SG, Oudshoorn A, Tjon Pian Gi CV, Zonderland HM, Van Haeringen A (1998). The Catel Mannzke syndrome in a female infant. *Genet Couns* **9**:187–190.

Klug MS, Ketchum LD, Lipsey JH (1983). Symmetric hyperphalangism of the index finger in the Palatodigital syndrome: a case report. *J Hand Surg* **8**: 599–603.

Lipson A, Beulher B, Bartley J, Walsh D, Yu J, O'Halloran M *et al.* (1984). Maternal hyperphenylalaninemia fetal effects. *J Pediatr* **104**:216–220.

Manzke VH (1966). Symmetrische Hyperphalangie des zweiten Fingers durch ein akzessorisches Metacarpale. *Fortschr Geb Rontgenstr Nuklearmed* **105**:425–427.

Petit P, Moerman P, Legius E, Fryns JP (1994). Catel–Manzke palatodigital syndrome in a second trimester female foetus with nuchal oedema, costovertebral anomalies and radial ray defect. *Genet Couns* **5**:381–385.

Robertson SP, Twigg SRF, Sutherland-Smith A, Biancalana V, Gorlin RJ, Horn D *et al.* (2003). OPD-spectrum Disorders Clinical Collaborative Group: Localized mutations in the gene encoding the cytoskeletal protein filamin A cause diverse malformations in humans. *Nat Genet* **33**:487–491.

Silengo MC, Franceschini P, Cerutti A, Fabris C (1977). Pierre Robin syndrome with hyperphalangism-clinodactylism of the index finger: a possible new Palato-Digital syndrome. *Pediatr Radiol* **6**:178–180.

Skinner SA, Flannery DB, Stevenson RE (1989). Catel Manzke syndrome. *Proceedings of the Greenwood Genetic LEFT* **8**:60–63.

Stevenson RE, Taylor HA, Burton OM, Hearn HBIII (1980). A digitopalatal syndrome with associated anomalies of the heart, face and skeleton. *J Med Genet* **17**:238–242.

Sundaram V, Taysi K, Hartmann AF Jr, Shackelford GD, Keating JP (1982). Hyperphalangy and clinodactyly of the index finger with Pierre Robin anomaly: Catel–Manzke syndrome. A case report and review of the literature. *Clin Genet* **21**:407–410.

Thompson EM, Winter RM, Williams MJH (1986). A male infant with the Catel–Manzke syndrome and dislocatable knees. *J Med Genet* **23**:271–274.

Wilson GN, King TE, Brookshire GS (1993). Index finger hyperphalangy and multiple anomalies: Catel–Manzke syndrome? *Am J Med Genet* **46**: 176–179.