Mirror hands and feet: a further case of Laurin-Sandrow syndrome

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Abstract

We report a girl with mirror hands and feet and associated groove of the nasal columella. She represents only the sixth reported case of this spectrum of congenital anomalies, first reported by Laurin and Sandrow.

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Key words: polysyndactyly; mirror hands and feet; columellar groove.

Polydactyly is a common malformation in man, occurring both as an isolated defect or as part of a syndrome. The presence of "mirror" polydactyly, however, is rare. Laurin *et al*¹ reported a boy with polysyndactyly of the hands and mirror polydactyly of both feet in association with bilateral fibular and ulnar dimelia. Subsequent reports by Sandrow *et al*² and others³⁻⁵ have highlighted the association between polysyndactyly of the hands, mirror polydactyly of the feet, and nasal defects, particularly involving the columella.

This report describes a girl with complete cup shaped syndactyly of the hands and mirror polysyndactyly of the feet in association with a columellar groove.

Case report

The girl was born to a 28 year old mother and 29 year old father. The parents were healthy and non-consanguineous. The pregnancy was normal; the mother smoked until she was aware of the pregnancy. The mother had two urinary tract infections in pregnancy but otherwise remained healthy. The baby was born at term by normal delivery and there were no neonatal problems. Birth weight was 3820 g, OFC 34 cm, and length 51 cm.

Examination at birth showed the presence of five digits on the hands, with no discernible thumb. Syndactyly of the fingers extended to their tips (figs 1 and 2). Polysyndactyly was present in the feet, with eight digits on the right foot and seven on the left (fig 1). There was a marked talipes equinovarus deformity of the right foot (fig 1). There was no facial dysmorphism but a groove was apparent in the nasal columella (fig 3).

Figure 1 Appearance of the hands and feet shortly after birth; note complete syndactyly of the hands, mirror polydactyly of the feet, and right talipes equinovarus deformity.

Figure 2 Syndactyly of all fingers and mirror polydactyly of both feet.

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Figure 3 Patient aged 20 months showing a columellar groove. The patient was not otherwise dysmorphic.

Radiological examination confirmed the presence of five digits bilaterally in the hands, and of mirror image polydactyly in the feet (fig 4). The right tibia and fibula did not appear well differentiated (fig 5) but other long bones were within normal limits. The karyotype was normal (46,XX).

The father's family from Cyprus were reported as having polydactyly. The nearest

affected relative, however, was the father's maternal grandmother, the father being unaffected. The reported polydactyly was not of the type described in this girl and is likely to be coincidental.

Discussion

We believe that our patient warrants inclusion in the diagnostic category of Laurin-Sandrow syndrome. Significant differences, however, exist between our patient and those described by Laurin *et al*¹ and Sandrow *et al*.² Firstly, although the right tibia and fibula did not appear well differentiated in our patient, there was no evidence of fibular dimelia on the left or of ulnar dimelia in the upper limbs. Secondly, the nasal defect in our patient is different from the nasal clefts in the father and daughter described by Sandrow *et al*.² These nasal anomalies may, however, all belong to the same spectrum of defects (that is, incomplete fusion of nasal folds).

In a recent case report, Martinez-Frias *et al*⁵ reviewed the reported cases of Laurin-Sandrow syndrome and concluded that all the cases warrant inclusion under the same diagnostic heading, despite some obvious phenotypic variability. They also felt that, although not mentioned explicitly in the case report by Laurin *et al*,¹ nasal anomalies may have been evident in the published photograph.

It is likely that Laurin-Sandrow syndrome is an autosomal dominant disorder, there having been two cases of transmission from father to daughter^{2,4}; X linkage, however, cannot yet be excluded as no male-male transmission has been reported. The existence of "sporadic" cases probably reflects new dominant mutations. Autosomal recessive inheritance cannot be discounted in these cases; however, there are no reports of affected sibs born to unaffected parents or of parental consanguinity.

The report by Viljoen and Kidson⁶ of an infant with mirror polydactyly of the left foot in association with left fibular dimelia and a left sided sacrococcygeal tumour raises the possibility of a new dominant mutation arising postzygotically. Segmental involvement in this child may thus be the result of genetic mosaicism for the mutation which gives rise to Laurin-Sandrow syndrome when present constitutionally, although there have been no reports of sacrococcygeal tumours in this syndrome. The authors of this report, however, suggested that the sacrococcygeal tumour may have interfered with migration of predetermined polarising cells, resulting in inappropriate anterior positioning of these cells (see below).

The presence of nasal defects in Laurin-Sandrow syndrome serves to differentiate this condition from others in which similar hand defects have been reported. Bilateral complete syndactyly of the hands, as described by Haas in 1940,⁷ is not associated with other congenital defects. Rambaud-Cousson *et al*⁸ reported on an autosomal dominant family with syndactyly type VI of the hands (Haas type hexadactyly), hexadactyly of the feet, and variable tibial hemi-

Figure 4 Radiograph of right foot showing the presence of eight digits and rays.

Figure 5 Radiograph of both lower limbs showing the relative lack of differentiation between the tibia and fibula on the right.

melia. No mention was made of nasal defects and the polydactyly of the feet was not of the mirror type. It is likely that this syndrome is distinct from Laurin-Sandrow syndrome but the possibility of variable expression of the Laurin-Sandrow gene should not be excluded.

Mirror image digit duplications in chicks were first produced experimentally by Saunders and Gasseling⁹ in 1968, who grafted a small piece of the posterior border mesoderm into an anterior site in the limb bud. The resulting limbs had digit patterns 432234 or 43234. Retinoic acid is known to mimic the effects of the polarising zone of cells responsible for the formation of digital patterns.^{10,11} The distribution of endogenous retinoic acid parallels the anterior-posterior gradient hypothesised to result from the presence of the polarising zone anteriorly in the limb bud, and retinoic acid has thus been proposed as the morphogen synthesised by the polarising cells and responsible for this gradient.¹² In addition to the digit duplications in chicks, other limb anomalies have been noted including fibular dimelia with absent tibia, two normal fibulae with a normal tibia, or only a solitary fibula present in the affected limb.¹³

Recently, similar abnormalities of limb formation have been induced in transgenic chicks who have ectopic expression of Hoxb-8.¹⁴ In

the most extreme case, a 5432345 mirror image pattern in the forelimb digits was accompanied by ulnar dimelia and mirror image duplication of posterior carpal bones. In addition, other midline defects were noted, including vertebral anomalies (splitting of the posterior arch of the atlas) and neural tube closure defects. It is likely that Hoxb-8 is important in the specification of the position of the cells of the zone of polarising activity (ZPA), which is normally anteriorly placed in the limb bud, but is not required for maintenance of the ZPA.¹⁴ Thus, while there are likely to be many genes that influence the anterior-posterior patterning in the developing limb bud, Hoxb-8 should be considered in any future list of possible candidate genes for Laurin-Sandrow syndrome; in particular, activating mutations of the human Hoxb-8 homologue might result in ectopic activity of this gene and concomitant interference with the normal anterior-posterior gradient.

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- 1 Laurin CA, Favreau JC, Labelle P. Bilateral absence of the radius and tibia with bilateral reduplication of the ulna and fibula. *J Bone Joint Surg [Am]* 1964;46:137-42.
- 2 Sandrow RE, Sullivan PD, Steel HH. Hereditary ulnar and fibular dimelia with peculiar facies. A case report. *J Bone Joint Surg [Am]* 1970;52:367-70.
- 3 Kogekar N, Teebi AS, Vockley J. Sandrow syndrome of mirror hands and feet and facial abnormalities. *Am J Med Genet* 1993;46:126-8.
- 4 Martin RA, Jones MC, Jones KL. Mirror hands and feet with a distinct nasal defect, an autosomal dominant condition. *Am J Med Genet* 1993;46:129-31.
- 5 Martínez-Frías ML, Alcaraz M, Espejo P, Gómez MA, García de Leon R, González Moro L. Laurin-Sandrow syndrome (mirror hands and feet and nasal defects): description of a new case. *J Med Genet* 1994;31:410-2.
- 6 Viljoen DL, Kidson SH. Mirror polydactyly: pathogenesis based on a morphogen gradient theory. *Am J Med Genet* 1990;35:229-35.
- 7 Haas SL. Bilateral complete syndactylism of all fingers. *Am J Surg* 1940;50:365-6.
- 8 Rambaud-Cousson A, Dudin AA, Zuaire AS, Thalji A. Syndactyly type IV/ hexadactyly of feet associated with unilateral absence of the tibia. *Am J Med Genet* 1991;40:144-5.
- 9 Saunders JW, Gasseling MT. Ectodermal-mesenchymal interactions in the origin of limb symmetry. In: Fleischmajer R, Billingham RE, eds. *Epithelial-mesenchymal interactions*. Baltimore: Williams and Wilkins, 1968:78-97.
- 10 Tickle C, Lee J, Eichele G. A quantitative analysis of the effect of all-trans-retinoic acid on the pattern of chick wing development. *Dev Biol* 1985;109:82-95.
- 11 Tickle C, Alberts B, Wolpert L, Lee J. Local application of retinoic acid to the limb bud mimics the action of the polarizing region. *Nature* 1982;296:564-6.
- 12 Thaller C, Eichele G. Identification and spatial distribution of retinoids in the developing chick limb bud. *Nature* 1987;327:625-8.
- 13 Wilde SM, Wedden SE, Tickle C. Retinoids reprogramme pre-bud mesenchyme to give changes in limb pattern. *Development* 1987;100:723-33.
- 14 Charité J, De GW, Shen S, Deschamps J. Ectopic expression of Hoxb-8 causes duplication of the ZPA in the forelimb and homeotic transformation of axial structures. *Cell* 1994; 78:589-601.