Second case of inherited Laurin-Sandrow Syndrome (LSS)?

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Case report

Phenotype

We report a father and son with almost identical features:

- Upper limbs: Preaxial/postaxial polydactyly, triphalangeal thumb, mal formed middle/distal phalanges, fused distal phalanges, total syndactyly.
- Lower limbs: Two identical long bones were observed, morphologically most appearing like fibula. Calcaneus and cuboideum were dulicated in cluding two shortened achilles tendons. The anterior and posterior tibial arteries were duplicated ending in two sets of dorsal and plantar arcades, respectively. There occurred 7/8 metatarsals, 9/10 toes, distal phalangeal splitting, and syndactyly.
- Nose: Nasal stenosis, septal deviation.
- Cranium/cerebrum/psychomotoric development: Normal

Genotype

G-band chromosomal staining showed that the father had a normal karyotype. No screening of candidate genes have been performed yet.

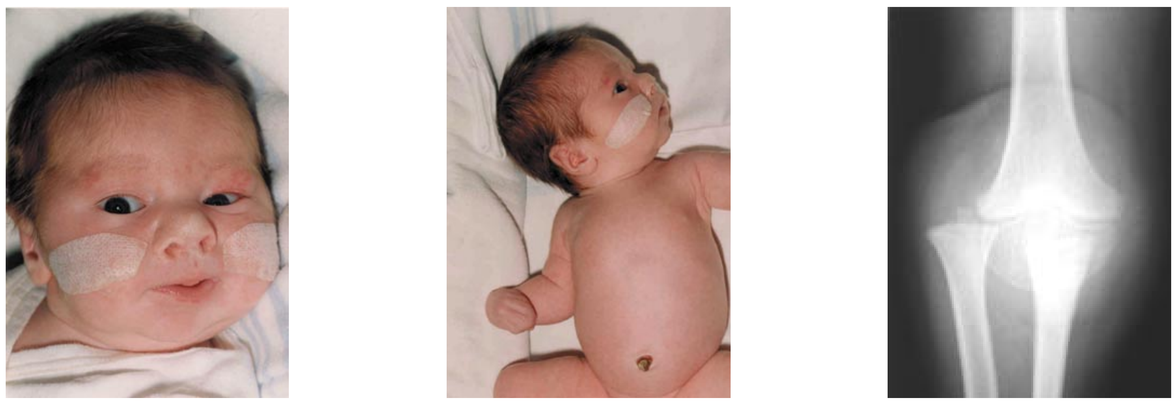

Fig. 1*. Left and middle: Face and whole body of the affected son. Note nasal anomalies, complete hand syndactyly, and deformity of lower limbs. Right: Duplicated fibula of son.*

Discussion

To our knowledge this is the first case of LSS transmitted from male to male which excludes X-linked inheritance. Out of 9 previously reported cases 7 were sporadic. The syndrome shows varying expressivity: Nasal anomalies, total hand syndactyly, mirror foot and interphalangeal joint deformity are the most consistent findings whereas ulna/fibula duplication do not occur in all patients (reviewed by Kantaputra, 2001).

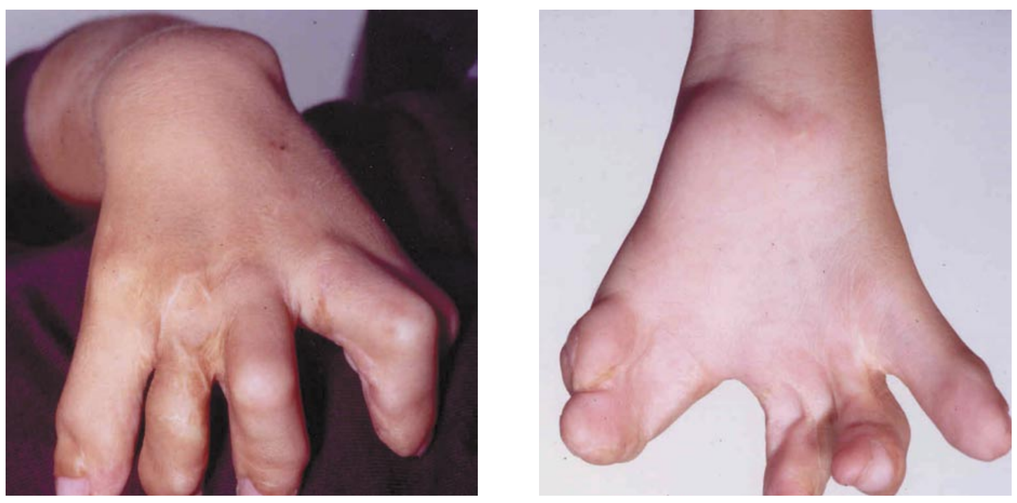

Fig. 2 *The hand of the son after surgery. Dorsal and palmar view.*

References

• Charité J et al. 1994. Ectopic expression of Hoxb-8 causes duplication of the ZPA in the forelimb and homeotic transformation of axial structures. Cell 78(4):589-601. • Kantaputra PN. 2001. Laurin-Sandrow Syndrome With Additional Associated Manifestations. AJMG 98:210-215. • Kondo S et al. 2002. A novel gene is disrupted at a 14q13 breakpoint of t(2;14) in a patient with mirror-image polydactyly of hands and feet. J Hum Genet 47:136-139. • Tanaka M et al. 2000. Distribution of polarizing activity and potential for limb formation in mouse and chick embryos and possible relationships to polydactyly. Development 127(18):4011-21.

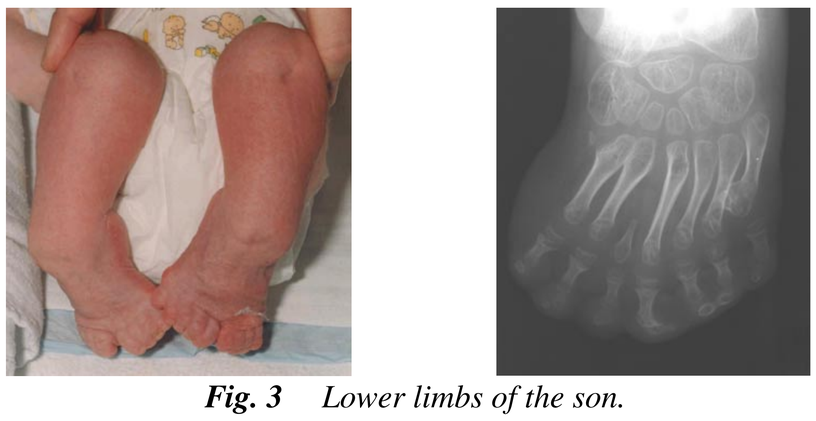

Fig. 3 *Lower limbs of the son.*

Pathogenetic considerations

What, where and when? Two zeugopod bones were formed but they both developed into an identical morphology that looks most like fibula. Thus either this is a tibial patterning defect, or it is a duplication defect already at the zeugopodial segment. The latter is supported by the occurrence of duplicated anterior and posterior tibial arteries. A true duplication will generate duplication of more distal structures, which is also seen in this case. Thus the first pathogenetic mechanism elicited by the responsible gene mutation is probably a duplication defect that lead to malinterpretion of signals at the zeugopodial level prior to the condensation proces.

Animal models

No animal models are known for LSS but limb duplication has been studied extensively. Ectopic expression of several genes in the flank mesoderm can lead to formation of an extra limb. Preaxial duplications starting at levels between stylopods and autopods have been produced by grafting experiments inducing a second anterior polarizing zone, via direct Shh-signalling or by increasing the number of anterior cells migrating into the limb bud (Tanaka et al., 2000). The most exact transgenic mouse model had duplicated ulna with mirror-image polydactyly induced by anterior ectopic expression of *Hoxb8* (Charité et al., 1994).

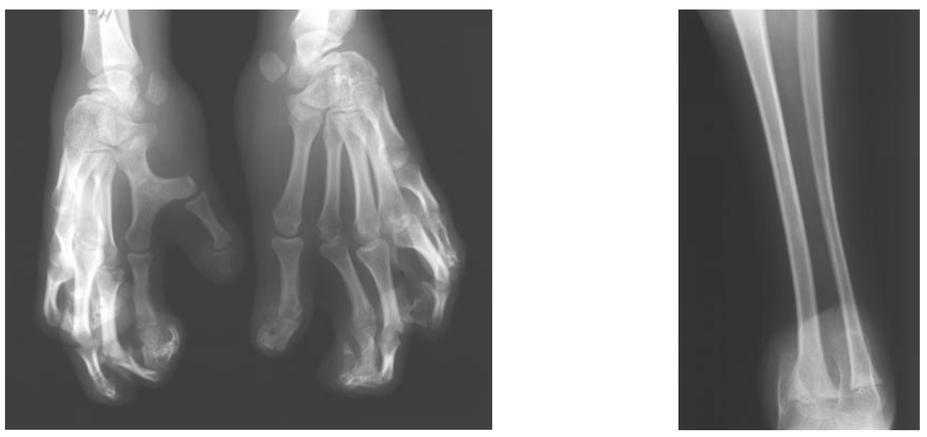

Fig. 4 *Left: Hand of the father. Right: duplicated fibula of the father*

Related conditions

Complete syndactyly of fingers is associated with tibial-hemimelia-polysyndactyly-triphalangeal-thumb syndrome (THPTTS) and triphalangeal-thumb-polysyndactyly syndrome (TTPS). Furthermore, LSS-like phenotypes have been reported in THPTTS/TTPS families suggesting a causal relationship (Kantaputra, 2001). THPTTS/TTPS has been mapped to 7q36.

In a Japanese boy with mirror-image polydactyly Kondo et al. (2002) identified a novel gene, *MIPOL1* at 14q13, that was disrupted by a break point. In spite of the lacking nasal and long bone anomalies they suggested a causal relation between this condition and LSS.

Acknowledgement

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