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, tripalangeal thumb, malformed 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 duplicated 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.

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).

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 malinterpretation of signals at the zeugopodial level prior to the condensation process.

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).

Related conditions

Complete syndactyly of fingers is associated with tibial-hemimelia-polydactyly-triphalangeal-thumb syndrome (THPTTS) and tripalangeal-thumb-polydactyly syndrome (TPPS). Furthermore, LSS-like phenotypes have been reported in THPTTS/TPPS families suggesting a causal relationship (Kantaputra, 2001). THPTTS/TPPS has been mapped to 14q36.


References