Atelosteogenesis III

Authors: Professor David Sillence [1] and Professor Kazimierz Kozlowski
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[1]Academic Department of Medical Genetics, The Children's Hospital at Westmead, Westmead 2145, AUSTRALIA. DavidS@chw.edu.au

Abstract
*Atelosteogenesis III (AOIII, incomplete ossification) is a short limb skeletal dysplasia, with dysmorphic faces and diagnostic radiographic findings. Recurrent respiratory insufficiency (tracheo-broncho-malacia) and/or infections usually result in early death. The diagnosis is established after full skeletal survey is performed. Correct antenatal diagnosis possible can be achieved by prenatal sonography. Atelosteogenesis III results from heterozygous mutations in the gene encoding filamin B (*FLNB*). All cases of this autosomal dominant disorder are sporadic. This is a very infrequently described disorder.*

Keywords
Atelosteogenesis – Short limb skeletal dysplasia - filamin B encoding gene (*FLNB*)

Disease name/synonyms
Atelosteogenesis III

Definition/diagnostic criteria
Atelosteogenesis III is a rare short-limb skeletal dysplasia with dysmorphic face and diagnostic radiographic findings.

Differential diagnosis
In ***Atelosteogenesis I*** the face is more dysmorphic; there are no multiple joint dislocations, the long tubular bones are less well ossified and the short tubular bones are less well ossified and the short tubular bones of the hands and feet show severe hypoplastic/dysplastic changes.
Atelosteogenesis II is characterised by absence of large joint dislocations, hitchhiker thumbs and big toes, and equinovarus deformity of the feet. The short tubular bones are severely hypoplastic/dysplastic.
Multiple joint dislocations are a major feature of ***Larsen syndrome***, but supernumerary carpal/tarsal ossification centers, only slightly dysplastic short tubular bones, cervical kyphosis

and less severe clinical course differentiate it from Atelosteogenesis III.
Oto-Palato-Digital syndrome shows distinctive faces, spatulate thumb and very short big toe. Supernumerary carpal bones, dysplastic carpal bones and proximal ends of the short tubular bones are diagnostic radiographic features of the latter.

Etiology
Atelosteogenesis III is due to heterozygous mutations in the gene encoding filamin B.

Clinical description
Shortening of the trunk and of the extremities, multiple joint dislocations, unusual face (especially a broad forehead, widely spaced eyes, and hypoplastic nose), broad hands and feet with broad digits, syndactyly/camptodactyly of the digits, equinovarus deformity of the feet. Half of the patients have s cleft palate.

Diagnostic methods
Skeletal survey. DNA analysis of the *FLNB* gene.

Epidemiology
About a dozen cases have been reported. No geographical, community or racial preponderance.

Genetic counseling
Autosomal dominant inheritance. In an individual, sporadic case a recurrence risk should be given which recognises that the germinal cell mosaicism is possible with a (presumed) recurrence risk of about 5%.

Prenatal diagnosis
Prenatal sonography documents bone dysplasia. Correct diagnosis is possible because of multiple joints dislocations and well ossified, large phalanges. Although not yet reported prenatal diagnosis should also be possible by DNA analysis of chorionic villi.

Management including treatment
Respiratory problems with recurrent tract infections, secondary to laryngo-tracheo-bronchomalacia. Orthopaedic supervision.

Unresolved questions
Atelosteogenesis I, Atelosteogenesis III, and Larsen syndrome constitute a continuous spectrum of disorders ("family") which have been demonstrated in some cases to be due to allelic heterozygous mutations in filamin B. These disorders may be expressions of allelic mutations of a single gene.

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