Atelosteogenesis II

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 II is a perinatally short-limb skeletal dysplasia with dysmorphic features and diagnostic skeletal radiographic appearances. The patients are stillborn or die soon after birth. Diagnosis can be established if a full skeletal survey is performed. Atelosteogenesis II results from mutations in the diastrophic dysplasia sulfate transporter gene (*DTDST*) and is pathogenetically related to the phenotypically milder Diastrophic Dysplasia and phenotypically more severe Achondrogenesis IB. The disorder is infrequently described. It shows autosomal recessive inheritance with a 25% recurrence risk for future offspring. DNA molecular prenatal diagnosis on first trimester chorionic villus sampling is feasible in instances where there characterized* DTDST *gene mutations are known.*

Keywords
Atelosteogenesis - DTD sulfate transporter - Achondrogenesis type IB - diastrophic dysplasia sulfate transporter gene (*DTDST*)

Disease name/synonyms
Atelosteogenesis II
Neonatal osseous dysplasia I
De la Chapelle dysplasia

Differential diagnosis
Diastrophic dysplasia: less severe clinical course, cystic masses of the external ears, similar but less severe pattern of skeletal changes.

Atelosteogenesis I severe dysmorphic face, more marked distal tapering of humerus and femur, discordant ossification of the short tubular bones.
Atelosteogenesis III: less dysmorphic face, well ossified dysplastic short tubular bones.

Etiology
Atelosteogenesis II results from homozygous or compound heterozygous mutations in the *DTDST* gene.

Clinical description
The major clinical abnormalities are short limbs and a short trunk, somewhat unusual face (frontal bossing, flat nasal bridge, short neck) plus or minus cleft palate, and hitch-hiker thumbs and toes with talipes equinovarus. The skeletal survey shows short tubular bones with distal tapering of the humeri and femora, prominent lesser trochanter, and dysplastic radius and ulna. Fibulae are present but dysplastic. The short tubular bones of the hands and feet are hypoplastic/dysplastic with a proximally placed and short first metacarpal and metatarsal. This accounts for the hitch-hiker position of the thumbs and big toes.

Diagnostic methods
Newborn or fetal skeletal radiographs should include views of hands and feet, upper and lower limbs and lateral spine. Perinatal autopsy with study of chondro-osseous histopathology will give a definitive diagnosis. Cultured skin fibroblasts can be used for DNA testing and/or study of the DTD sulfate transporter.

Epidemiology
About 25 cases have been observed in various populations.
There is interfamilial variability.

Genetic counseling
Atelosteogenesis II and related disorders show autosomal recessive inheritance with a 25% recurrence risk for future offspring. Carrier detection of a characterized *DTDST* mutation is possible.

Prenatal diagnosis
Prenatal sonography can detect short limbs at 18-20 weeks of gestation. DNA molecular prenatal diagnosis on first trimester chorionic villus sampling is feasible in instances where there are characterized *DTDST* gene mutations.

Management including treatment
In most cases, infants die at birth or in the perinatal period due to respiratory insufficiency. Long term survival is not possible.

Unresolved questions
The similar pattern of phenotypic features including hitchhiker thumbs, cleft palate, skeletal anomalies, and homozygous or compound heterozygous mutations in the same gene, *DTDST*, confirms that Atelosteogenesis II, Achondrogenesis IB and Diastrophic dysplasia are allelic disorders.

References
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