Diastrophic Dysplasia

Genetics

-Gene: SLC26A2 (Sulfate transporter; 5q32-q33.1)

-AR

Clinical findings/Dysmorphic features

-Short limbs, normal-sized skull, hitchhiker thumbs, small chest, large joint contracture, cleft palate, cystic ears (cauliflower ears), ulnar deviation of fingers, clubfoot, low tone, early osteoarthritis; spinal (scoliosis, exaggerated lumbar lordosis, cervical kyphosis); normal IQ

Etiology

-Approximately 1:100,000

Pathogenesis

-Impaired activity of the sulfate transporter in chondrocytes and fibroblasts --> synthesis of unsulfated proteoglycans due to intracellular sulfate depletion --> affects composition of the extracellular matrix and leads to impaired proteoglycan deposition --> necessary for proper enchondral bone formation

Genetic testing/diagnosis

-SLC26A2 only gene; targeted testing --> then sequencing --> then InDel

-Most common variants: p.Arg279Trp (37% of the disease alleles), p.Arg178Ter (13%), c.-26+2T>C (8%), p.Cys653Ser (6%); most cases of DTD (97%) are due to com-het variants

Others

-Incorporation of sulfate into macromolecules can be studied in cultured chondrocytes and/or skin fibroblasts through double labeling with 3H-glycine and 35S-sodium sulfate