X-linked spondyloepiphyseal dysplasia tarda

X-linked spondyloepiphyseal dysplasia tarda is a condition that impairs bone growth and occurs almost exclusively in males. The name of the condition indicates that it affects the bones of the spine (spondylo-) and the ends of long bones (epiphyses) in the arms and legs. "Tarda" indicates that signs and symptoms of this condition are not present at birth, but appear later in childhood, typically between ages 6 and 10.

Males with X-linked spondyloepiphyseal dysplasia tarda have skeletal abnormalities and short stature. Affected boys grow steadily until late childhood, when their growth slows. Their adult height ranges from 4 feet 6 inches (137 cm) to 5 feet 4 inches (163 cm). Impaired growth of the spinal bones (vertebrae) primarily causes the short stature. Spinal abnormalities include flattened vertebrae (platyspondyly) with hump-shaped bulges, progressive thinning of the discs between vertebrae, and an abnormal curvature of the spine (scoliosis or kyphosis). These spinal problems also cause back pain in people with this condition. Individuals with X-linked spondyloepiphyseal dysplasia tarda have a short torso and neck, and their arms are disproportionately long compared to their height.

Other skeletal features of X-linked spondyloepiphyseal dysplasia tarda include an abnormality of the hip joint that causes the upper leg bones to turn inward (coxa vara); multiple abnormalities of the epiphyses, including a short upper end of the thigh bone (femoral neck); and a broad, barrel-shaped chest. A painful joint condition called osteoarthritis that typically occurs in older adults often develops in early adulthood in people with X-linked spondyloepiphyseal dysplasia tarda and worsens over time, most often affecting the hips, knees, and shoulders.

Frequency

The prevalence of X-linked spondyloepiphyseal dysplasia tarda is estimated to be 1 in 150,000 to 200,000 people worldwide.

Causes

Mutations in the TRAPPC2 gene cause X-linked spondyloepiphyseal dysplasia tarda. The TRAPPC2 gene provides instructions for producing the protein sedlin. Sedlin is part of a large group of proteins called the trafficking protein particle (TRAPP) complex, which plays a role in the transport of proteins between various cell compartments (organelles). Research shows that sedlin is required for transporting large proteins out of the endoplasmic reticulum, which is an organelle that is involved in protein processing and transport. For example, sedlin is needed to move large molecules called procollagens out of the endoplasmic reticulum so they can be processed by
enzymes to create smaller mature collagen proteins, which strengthen and support connective tissues, such as skin, bone, cartilage, tendons, and ligaments.

Almost all TRAPPC2 gene mutations that cause X-linked spondyloepiphyseal dysplasia tarda result in a nonfunctional sedlin protein. As a result, large proteins, including procollagen, cannot be transported out of the endoplasmic reticulum. A lack of procollagen transport results in a decrease in mature collagen in cells and impairs the development of bones, cartilage, and other connective tissues. It is likely that this disruption in bone development leads to many of the signs and symptoms of X-linked spondyloepiphyseal dysplasia tarda, although it is unclear why the skeletal problems do not appear until later in childhood.

In about 10 percent of affected males, an identified mutation in the TRAPPC2 gene is not found. The cause of the condition in these individuals is unknown.

Inheritance Pattern

X-linked spondyloepiphyseal dysplasia tarda is inherited in an X-linked recessive pattern. The TRAPPC2 gene is located on the X chromosome, which is one of the two sex chromosomes. In males (who have only one X chromosome), one altered copy of the gene in each cell is sufficient to cause the condition. In females (who have two X chromosomes), a mutation must be present in both copies of the gene to cause the disorder. Males are affected by X-linked recessive disorders much more frequently than females. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

In X-linked recessive inheritance, a female with one mutated copy of the gene in each cell is called a carrier. She can pass on the altered gene, but usually does not experience signs and symptoms of the disorder. In rare cases, however, females who carry a TRAPPC2 gene mutation may develop osteoarthritis in early adulthood.

Other Names for This Condition

• late onset spondyloepiphyseal dysplasia  
• SED tarda  
• X-linked SED  
• X-linked SEDT  

Diagnosis & Management

Genetic Testing Information

• What is genetic testing?  
/primer/testing/genetictesting  
• Genetic Testing Registry: Spondyloepiphyseal dysplasia tarda  
Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22X-linked+spondyloepiphyseal+dysplasia+tarda%22+OR+%22Spondyloepiphyseal+Dysplasia%22+OR+%22Dysplasias%22+Spondyloepiphyseal%22+OR+%22Dysplasia%22+Spondyloepiphyseal%22

Other Diagnosis and Management Resources

- GeneReview: X-Linked Spondyloepiphyseal Dysplasia Tarda
  https://www.ncbi.nlm.nih.gov/books/NBK1145

Additional Information & Resources

Health Information from MedlinePlus

- Health Topic: Bone Diseases
  https://medlineplus.gov/bonediseases.html
- Health Topic: Growth Disorders
  https://medlineplus.gov/growthdisorders.html
- Health Topic: Osteoarthritis
  https://medlineplus.gov/osteoarthritis.html
- Health Topic: Scoliosis
  https://medlineplus.gov/scoliosis.html

Genetic and Rare Diseases Information Center

- Spondyloepiphyseal dysplasia tarda X-linked
  https://rarediseases.info.nih.gov/diseases/4985/spondyloepiphyseal-dysplasia-tarda-x-linked

Additional NIH Resources

- National Institute of Arthritis and Musculoskeletal and Skin Diseases: Osteoarthritis
  https://www.niams.nih.gov/health-topics/osteoarthritis
- National Institute of Arthritis and Musculoskeletal and Skin Diseases: Scoliosis
  https://www.niams.nih.gov/health-topics/scoliosis

Educational Resources

- Cincinnati Children’s Hospital: Coxa Vera
  https://www.cincinnatichildrens.org/health/c/coxavera
- Johns Hopkins Medicine
  https://www.hopkinsmedicine.org/health/conditions-and-diseases/spondyloepiphyseal-dysplasia-tarda

• MalaCards: spondyloepiphyseal dysplasia tarda, x-linked https://www.malacards.org/card/spondyloepiphyseal_dysplasia_tarda_x_linked

• Orphanet: Spondyloepiphyseal dysplasia tarda https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=93284

Patient Support and Advocacy Resources

• International Skeletal Dysplasia Registry, UCLA https://www.uclahealth.org/ortho/isdr

• Little People UK https://littlepeopleuk.org/

• National Organization for Rare Disorders (NORD) https://rarediseases.org/rare-diseases/spondyloepiphyseal-dysplasia-tarda/

• The Human Growth Foundation https://www.hgfoundation.org/

• The MAGIC Foundation https://www.magicfoundation.org/

Clinical Information from GeneReviews

• X-Linked Spondyloepiphyseal Dysplasia Tarda https://www.ncbi.nlm.nih.gov/books/NBK1145

Scientific Articles on PubMed

• PubMed https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28x-linked+spondyloepiphyseal+dysplasia+tarda%5BTIAB%5D%29+OR+%28SEDT%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

• SPONDYLOEPIPHYSEAL DYSPLASIA TARDA, X-LINKED http://omim.org/entry/313400
Sources for This Summary

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15221797

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