Schimke immuno-osseous dysplasia

Description

Schimke immuno-osseous dysplasia is a condition characterized by short stature, kidney disease, and a weakened immune system. In people with this condition, short stature is caused by flattened spinal bones (vertebrae), resulting in a shortened neck and trunk. Adult height is typically between 3 and 5 feet. Kidney (renal) disease often leads to life-threatening renal failure and end-stage renal disease (ESRD). Affected individuals also have a shortage of certain immune system cells called T cells. T cells identify foreign substances and defend the body against infection. A shortage of T cells causes a person to be more susceptible to illness.

Other features frequently seen in people with this condition include an exaggerated curvature of the lower back (lordosis); darkened patches of skin (hyperpigmentation), typically on the chest and back; and a broad nasal bridge with a rounded tip of the nose.

Less common signs and symptoms of Schimke immuno-osseous dysplasia include an accumulation of fatty deposits and scar-like tissue in the lining of the arteries (atherosclerosis), reduced blood flow to the brain (cerebral ischemia), migraine-like headaches, an underactive thyroid gland (hypothyroidism), decreased numbers of white blood cells (lymphopenia), underdeveloped hip bones (hypoplastic pelvis), abnormally small head size (microcephaly), a lack of sperm (azoospermia) in males, and irregular menstruation in females.

In severe cases, many signs of Schimke immuno-osseous dysplasia can be present at birth. People with mild cases of this disorder may not develop signs or symptoms until late childhood.

Frequency

Schimke immuno-osseous dysplasia is a very rare condition. The prevalence in North America is estimated to be one in 1 million to 3 million people.

Causes

Mutations in the *SMARCAL1* gene increase the risk of Schimke immuno-osseous dysplasia. The *SMARCAL1* gene provides instructions for producing a protein whose specific function is unknown. The SMARCAL1 protein can attach (bind) to chromatin, which is the complex of DNA and protein that packages DNA into chromosomes. Based

on the function of similar proteins, SMARCAL1 is thought to influence the activity (expression) of other genes through a process known as chromatin remodeling. The structure of chromatin can be changed (remodeled) to alter how tightly DNA is packaged. Chromatin remodeling is one way gene expression is regulated during development. When DNA is tightly packed, gene expression is lower than when DNA is loosely packed.

Mutations in the *SMARCAL1* gene are thought to lead to disease by affecting protein activity, protein stability, or the protein's ability to bind to chromatin. It is not clear if mutations in the *SMARCAL1* gene interfere with chromatin remodeling and the expression of other genes.

The mutations associated with Schimke immuno-osseous dysplasia disrupt the usual functions of the SMARCAL1 protein or prevent the production of any functional protein. People who have mutations that cause a complete lack of functional protein tend to have a more severe form of this disorder than those who have mutations that lead to an active but malfunctioning protein. However, in order for people with *SMARCAL1* gene mutations to develop Schimke immuno-osseous dysplasia, other currently unknown genetic or environmental factors must also be present.

Approximately half of all people with Schimke immuno-osseous dysplasia do not have identified mutations in the *SMARCAL1* gene. In these cases, the cause of the disease is unknown.

Learn more about the gene associated with Schimke immuno-osseous dysplasia

- SMARCAL1

Inheritance

Mutations in the *SMARCAL1* gene are inherited in an autosomal recessive pattern, which means that an increased risk of Schimke immuno-osseous dysplasia results from mutations in both copies of the *SMARCAL1* gene in each cell. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- Immunoosseous dysplasia, Schimke type
- Schimke immunoosseous dysplasia
- SIOD

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Schimke immuno-osseous dysplasia (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0877024/)

Genetic and Rare Diseases Information Center

- Schimke immuno-osseous dysplasia (https://rarediseases.info.nih.gov/diseases/4984/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Catalog of Genes and Diseases from OMIM

- SCHIMKE IMMUNOOSSEOUS DYSPLASIA; SIOD (https://omim.org/entry/242900)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28schimke+immunoosseous+dysplasia%5BTIAB%5D%29+OR+%28schimke+immuno-osseous+dysplasia%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

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Last updated November 1, 2008