Polycystic lipomembranous osteodysplasia with sclerosing leukoencephalopathy

Description

Polycystic lipomembranous osteodysplasia with sclerosing leukoencephalopathy, commonly known as PLOSL, is a progressive disorder that affects the bones and brain. "Polycystic lipomembranous osteodysplasia" refers to cyst-like bone changes that can be seen on x-rays. "Sclerosing leukoencephalopathy" describes specific changes in the brain that are found in people with this disorder.

The bone abnormalities associated with PLOSL usually become apparent in a person's twenties. In most affected individuals, pain and tenderness in the ankles and feet are the first symptoms of the disease. Several years later, broken bones (fractures) begin to occur frequently, particularly in the bones of the ankles, feet, wrists, and hands. Bone pain and fractures are caused by thinning of the bones (osteoporosis) and cysts in the bones. These abnormalities weaken bones and make them more likely to break.

The brain abnormalities characteristic of PLOSL typically appear in a person's thirties. Personality changes are among the first noticeable problems, followed by a loss of judgment, feelings of intense happiness (euphoria), a loss of inhibition, and poor concentration. These neurologic changes cause significant problems in an affected person's social and family life. As the disease progresses, it causes a severe decline in thinking and reasoning abilities (dementia). Affected people ultimately become unable to walk, speak, or care for themselves. People with this disease usually live only into their thirties or forties.

Frequency

PLOSL is a very rare condition. It was first reported in the Finnish population, where it has an estimated prevalence of 1 to 2 per million people. This condition has also been diagnosed in more than 100 people in the Japanese population. Although affected individuals have been reported worldwide, PLOSL appears to be less common in other countries.

Causes

Variants (also called mutations) in the *TREM2* gene or the *TYROBP* gene can cause PLOSL. The proteins produced from these two genes work together to activate certain

kinds of cells. These proteins appear to be particularly important in osteoclasts, which are specialized cells that break down and remove (resorb) bone tissue that is no longer needed. Osteoclasts are involved in bone remodeling, which is a normal process that replaces old bone tissue with new bone. The TREM2 and TYROBP proteins are also critical for the normal function of microglia, which are a type of immune cell in the brain and spinal cord (central nervous system). Although these proteins play essential roles in osteoclasts and microglia, their exact function in these cells is unclear.

Variants in the *TREM2* or *TYROBP* gene disrupt normal bone remodeling and lead to progressive brain abnormalities in people with PLOSL. Researchers believe that the bone changes seen in people with this disorder are related to malfunctioning osteoclasts, which are less able to resorb bone tissue during bone remodeling. In the central nervous system, *TREM2* or *TYROBP* gene variants cause widespread abnormalities of microglia. Researchers are working to determine how these abnormalities lead to the neurological problems associated with PLOSL.

Learn more about the genes associated with Polycystic lipomembranous osteodysplasia with sclerosing leukoencephalopathy

- TREM2
- TYROBP

Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell must have a variant to cause the disorder. The parents of an individual with an autosomal recessive condition each carry one copy of the altered gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- Nasu-Hakola disease
- NHD
- PLO-SL
- PLOSL
- Presenile dementia with bone cysts

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Polycystic lipomembranous osteodysplasia with sclerosing leukoencephalopathy 1 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C4721893/)

Genetic and Rare Diseases Information Center

- Nasu-Hakola disease (https://rarediseases.info.nih.gov/diseases/9921/index)

Patient Support and Advocacy Resources

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

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Polycystic lipomembranous osteodysplasia with sclerosing leukoencephalopathy%22)

Catalog of Genes and Diseases from OMIM

- POLYCYSTIC LIPOMEMBRANOUS OSTEODYSPLASIA WITH SCLEROSING LEUKOENCEPHALOPATHY 1; PLOSL1 (https://omim.org/entry/221770)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28membranous+lipodystrophy%5BTIAB%5D%29+OR+%28nasu-hakola+disease%5BTIAB%5D%29+OR+%28plosl%5BTIAB%5D%29+OR+%28plo-sl%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D)

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