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OPINION ARTICLE

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Signs and Symptoms of Niemann–Pick disease

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Description

Sphingomyelin builds up in cell lysosomes in a spectrum of severe genetic metabolic illnesses known as Niemann-Pick disease. Sphingolipids, which are fats, found in cell membranes, have a faulty metabolism that contributes to several diseases. They can be thought of as a specific type of sphingolipidosis, one of the many lysosomal storage diseases. Sphingomyelin builds up in specific organs, which is associated to the symptoms. Hepatosplenomegaly, an enlargement of the liver and spleen, can result in pain, discomfort, and decreased appetite. Low amounts of platelets in the blood may also result from spleen enlargement.

Ataxia, dysarthria, and difficulties swallowing are all symptoms of sphingomyelin buildup in the central nervous system, which includes the cerebellum. The limbs, trunk, and face adopt aberrant postures as a result of basal ganglia dysfunction. Impairment of voluntary, fast eye movements is caused by upper brainstem illness. A more pervasive condition that affects the cerebral cortex and subcortical regions results in a progressive decline in mental capacity, dementia, and seizures. Additionally, the condition may affect the bones, thinning the cortical bone, distorting the hip bone, or producing larger bone marrow cavities. The disease is also accompanied by sleep-related disorders, such as sleep inversion, daytime sleepiness, and nighttime wakefulness. When a patient experiences gelastic cataplexy, they also experience an abrupt loss of muscle tone when they laugh [1,2].

Causes

SMPD1 gene mutations lead to types A and B of Niemann-Pick disease. The lysosomal enzyme acid sphingomyelinase, which breaks down the lipid sphingomyelin, is less active as a result of their presence. Niemann-Pick disease, type C (NPC), results from mutations in the lipid-transporting NPC1 or NPC2 protein.

To distinguish a group of patients with apparently identical illnesses who had a common lineage from Nova Scotia, type D was first split off from type C. NPC is utilised for both groups because it is known that patients in this category have a certain mutation in the NPC1 gene in common. The labels "Niemann-Pick type I" and "Niemann-Pick type II" were proposed to distinguish the high- and low-sphingomyelin types of the illness in the early 1980s before the molecular flaws were explained [3,4].

Niemann-Pick disease is inherited in an autosomal recessive fashion, which means that for the disease to manifest, both of the gene's copies, or both of its alleles, must be damaged. "Defective" refers to an alteration that prevents them from performing as intended. The parents of a kid who has an autosomal recessive condition are frequently carriers; they carry one mutated copy of the gene but are unaffected since the other copy generates the enzyme. Each pregnancy has a 25% risk of generating an afflicted child if both parents are carriers. For families who might be disease carriers, genetic counselling and testing are advised [5,6].

Pathophysiology

Sphingolipidoses, a subclass of lipid storage disorders, include Niemann-Pick diseases, in which dangerous lipid accumulations occur in the spleen, liver, lungs, bone marrow, and brain [7]. A missense mutation in the classic infantile type-A variation results in a total lack of sphingomyelinase. Since sphingomyelin is a component of many cell membranes, including the organellar membrane, an enzyme deficit prevents lipid from being broken down, which causes sphingomyelin to accumulate in lysosomes in the macrophage-monocyte phagocyte lineage [8].

Diagnosis

Sphingomylinase levels for types A and B can be determined from a blood sample. A skin sample can be used in the Filipin test, which uses fluorescent staining to de-

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tect the accumulation of unesterified cholesterol, to assist diagnose type C if the transporter is compromised.

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