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Letter to the Editor

Xenpozyme: a revelation for Neiman-Pick disease

Sir,

Nieman-Pick disease (NPD) also known as acid sphingomyelinase deficiency (ASMD) is a rare autosomal recessive disorder of lysosomal storage which affects 1 in 250,000 individuals mainly belonging to the Ashkenazi Jew population. The prevalence varies across the three main subtypes where type A and B affects 1 in 40,000 and type C affects 1 in 150,000 individuals, being more prevalent in the French-Acadian descent in the region of Nova Scotia.[1] NPD type A and B is caused by mutations in sphingomyelin phosphodiesterase (SMPD1) gene that causes decreased activity of acid sphingomyelinase (ASM) which is found in lysosome and produces ceramide and phosphocholine from sphingomyelin breakdown.[2] The lack of enzyme causes buildup of sphingomyelin and other lipids in the bone marrow, lungs, lymph nodes, and liver giving rise to symptoms.[3] The four broad categories: A, B, C, and E vary significantly in their severity and symptoms. Type A, also called infantile neurovisceral form which is fatal in early childhood causes neurological manifestations and impaired growth. Type B is usually less severe and causes minimal neurological manifestation with lesser extent of visceral involvement. The NPD type C, is a heterogeneous disorder having multi system manifestations and usually can affect in any phase of life but is more profound in adults. The lesser-known type E is a less common type that develops in adulthood.[4]

There is no cure for NPD, and management almost entirely comprises supportive therapies. Until recently, multiple drug regimens have been used such as: anticholinergics, antidepressants, and antiepileptics to treat certain symptoms i.e., tremor, dystonia and seizure.[5] On 31 August 2022 FDA granted an approval to the first ever medication for treatment of ASMD called "Olidupase Alfa" due to the profound results of ASCEND (NCT02004691) and ASCEND-Peds (NCT02292654) trials. These trials investigated Olidupase Alfa, an enzyme replacement therapy created by Genzyme/Sanofi in 36 adults and 20 children respectively and showed a remarkable reduction in levels of sphingomyelin and ceramide.[6,7] Most importantly, it resulted in an increase in lung diffusion capacity with improvement in gaseous exchange which is indeed crucial as patients with chronic ASMD often die of lung infections and respiratory failure. Profound improvement was also seen in lipid levels, hepatomegaly, and splenomegaly, and thrombocyte count. Among participants, 50% adults and 75% children suffered side effects such as headaches, nausea, and vomiting. There were also reports of 2 patients suffering from anaphylactic reaction. Regardless of these adverse effects, the Olipudase alfa was linked with a significant difference in the burden of disease in patients with chronic ASMD aging 1.5-7.5 years.[3]

After the approval, xenpozyme has garnered significant attention of the medical world due to an unprecedented effectiveness and ability to ameliorate the multisystem symptoms of NPD. The main limitation of Olidpudase Alfa is that it cannot penetrate the blood brain barrier and hence it does not have any effect on neurological symptoms which requires further research to create therapies that do so. Moreover, xenpozyme is currently only approved for type A and B NPD. Finally, the high cost is also a drawback which would make it unreachable to populations of lower socioeconomic status.

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