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Olipudase alfa enzyme replacement therapy. One-year outcomes in an adult patient with acid sphingomyelinase deficiency type B

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Introduction: Acid Sphingomyelinase Deficiency (ASMD) is a rare autosomal recessive lysosomal storage disorder caused by variants in the SMPD1 gene, leading to a deficiency in the activity of sphingomyelinase (ASM) that catabolizes sphingomyelin (SPM). ASMD Type B is a late-onset, severe disease characterized by progressive hepatosplenomegaly, gradual deterioration of liver and pulmonary function, osteopenia and an atherogenic lipid profile. Olipudase alfa is a recombinant human ASM enzyme replacement therapy indicated for the treatment of non-CNS manifestations of ASMD (1).

Methods: We report the 1-year outcome of an adult patient with ASMD Type B, confirmed by enzymatic assay and genotyping, treated with olipudase alfa. The drug was administered intravenously every 2 weeks, with the recommended gradual dose escalation over 14 weeks to 3 mg/kg, maintaining the dose afterword.

Results/Case report: We present the case of a 53 years old man diagnosed at the age of 37, when he complained of fertility problems and thrombocytopenia (76 to 145×109/L) and splenomegaly were found. A myelogram and bone biopsy revealed foam cells and the diagnosis was confirmed by a homozygous mutation c.1426C>T; p.R476W in the SMPD1 gene. He also presented interstitial lung disease with impaired diffusion capacity for carbon monoxide (DLco), bone involvement (BMS score 5 on MRI), osteopenia and dyslipidemia. At age 49, biclonal gammopathy was diagnosed IgG K e IgA k.
After one year treatment, there is near normalization of plasma lyso-sphingomyelin (from 300 to 17,2 MoM; ref:0,5--2,7), platelet counts normalization, reduction in spleen volume (from 900 to 529 mL), DLco normalization (from 57% to 78%), and a decrease in monoclonal free light K chains from 5.16 to 3.69 mg/dL. No adverse events were observed.

Conclusion: Treatment with olipudase resulted in clinical improvement: the patient no longer experienced gingival bleeding or epistaxis, feeling of abdominal fullness, began tolerating facial masks and noticed urodynamic improvement, incomplete bladder emptying sensation and pollakiuria resolved. The efficacy of olipudase alfa was evidenced by lyso SM509 reduction, improved DLco and decreased spleen volume. There were no variations in bone scores on MRI or densitometry. Chitotriosidase, was a low-sensitivity biomarker, remaining within normal values. Treatment with olipudase alfa was well tolerated.

References:

(1) Geberhiwot T, Wasserstein M, Wanninayake S, Christopher Bolton S,Dardis A, Lehman A, Lidove O, Dawson C, Giugliani R, Imrie J, Hopkin J, Green J, Vicente Corbeira D, Madathil S, Mengel E, Ezgü F, Pettazzoni M, Sjouke B, Hollak C, Vanier M, McGovern M, Schuchman E. Consensus clinical management guidelines for acid sphingomyelinase deficiency (Niemann–Pick disease types A,B and A/B). Orphanet Journal of Rare Diseases. 2023;18:85.