



Niemann-Pick Disease– A Rare Case Report

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Abstract

Introduction: *The lysosomal lipid storage diseases are diverse disorders, each caused by an inherited deficiency of a specific lysosomal hydrolases leading to the intralysosomal accumulation of the enzyme's particular substrate. Niemann-Pick Disease results from the deficient activity of acid sphingomyelinase (ASM), a lysosomal enzyme encoded by a gene on chromosome 11. It is inherited as autosomal recessive trait. The enzymatic defect results in the pathologic accumulation of sphingomyelin, a ceramide phospholipid, and other lipids in the monocyte-macrophage system, the primary pathologic site. The progressive deposition of sphingomyelin in the CNS results in neurodegenerative course seen in type A & in non-neural tissue in the systemic disease manifestation of type B, including progressive lung disease in some patients.*

Case Report: *A 14-month Fch presented to OPD with history of not gaining weight & height, not achieving milestones as per his age with its peers of same age for last 7 month and abdominal distension for last 6 month. Patient is 2nd order child born out of consanguineous marriage (2nd degree) with uneventful perinatal history. Elder siblings doing well. After complete workup the child was found to have deficient in sphingomyelinase activity suggesting Niemann pick disease. Prognosis & course of the disease explained, counselling done to the parents.*

Conclusion: *There is no specific treatment for Niemann pick disease. Orthotopic liver transplantation in an infant with Type A disease & cord blood transplantation in several type B NPD patients have been attempted with little or no success. BMT in a small number of patients with type B has been successful. ERT with recombinant human ASM is currently in clinical trials for the type B patients.*

Keywords: *Lysosomal, sphingomyelinase, autosomal recessive trait, Orthotopic.*

Introduction

The lysosomal lipid storage diseases are diverse disorders each caused by an inherited deficiency of a specific lysosomal hydrolase leading to the intralysosomal accumulation of the enzyme's particular substrate. Sphingolipids are essential components of all cell membranes, the inability to degrade these substances and their subsequent accumulation results in the physiologic and morphologic alterations and characteristic clinical

manifestations of the lipid storage disorders. Progressive lysosomal accumulation of glycosphingolipids in the central nervous system leads to neurodegeneration, whereas storage in visceral cells can lead to organomegaly, skeletal abnormalities, pulmonary infiltration, and other manifestations. The storage of a substrate in a specific tissue is dependent on its normal distribution in the body. Diagnostic assays for the identification of affected individuals rely on the

measurement of the specific enzymatic activity in isolated leukocytes or cultured fibroblasts or lymphoblasts.

Case Report

A 14-month Fch with uneventful perinatal history presented to OPD with complaints of not gaining weight & height, not achieving appropriate milestone as per her age with her peers of same age for last 7 to 8 months. She also had complaints of gradual swelling of abdomen for last 6 month. This patient is a 2nd order child, born out of consanguineous marriage (2nd degree), through vaginal route with no history of birth asphyxia & SNCU hospitalisation, birth weight of 2.9 kg. She was gaining weight & length up to 6 month of age. Thereafter no significant increase in weight & length. Also, the patient didn't attain any milestone as per her age. Elder sibling is doing well. There is no history of any antenatal maternal infection or abortion or sibling death. And a provisional diagnosis of lipid storage disorder was made. The patient was vitally stable. Anthropometry showed Weight 6.4 kg, Length 73.5 cm, Head circumference 43 cm, MUAC 9.3 cm, wt/age <-3SD, ht/age between -2SD to -1SD, wt/ht -2SD indicating severe acute malnutrition. During the hospital stay all the routine investigations was carried out. CBC showed microcytic hypochromic anaemia, LFT, RFT, electrolytes, ICTC of both mother & child were normal. Ophthalmological examination revealed cherry red spot in both fundus. Lipid storage enzymatic panel revealed deficiency of sphingomyelinase activity (Patient value – 1.10 nmol/hr/mg, < 1.5 indicates deficient activity). Then a final diagnosis of Niemann-Pick Disease was confirmed. Thereafter parents are explained about the disease prognosis & was discharged with regular follow-up in OPD.



Fig. 1: Showing Hepatosplenomegaly of a NPD patient

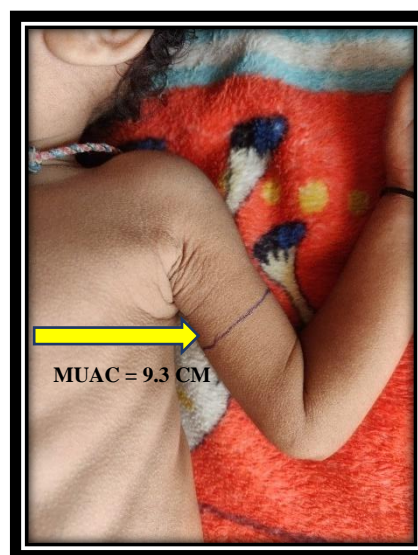


Fig. 2: Showing measured MUAC 9.3 cm over left upper arm of a NPD patient (Severe acute malnutrition)

Discussion

Lysosomal lipid storage disorder or lipidoses are group of inherited metabolic disorders in which lipids accumulate in monocytes-macrophages of various organs like liver, spleen, bone marrow, lymph node, brain, nerves and kidney and causes permanent damage to that organ. They are caused by complete absence or deficiency of enzyme

which is needed to metabolise lipids. Niemann pick disease, Tay sachs disease, Fabry disease, Farber disease etc. are examples of lipidoses. Niemann-Pick Disease is an autosomal recessive disorder. The original description of Niemann-Pick disease (NPD) was what is now known as **Type A** NPD, a fatal disorder of infancy characterized by failure to thrive, hepatosplenomegaly, and a rapidly progressive neurodegenerative course that leads to death by 2-3 yr of age. **Type B** disease is a nonneuronopathic form Observed in children and adults. **Type C** disease is a neuronopathic form that results from defective cholesterol transport. The name Niemann Pickis derived from two German paediatricians – Albert Niemann, who first described it in 1914, and Ludwick Pick who showed tissue deposition of sphingomyelin in 1927. In 1980, Crocker classified NPD into 4 types-

- Acute neuropathic infantile
- Chronic non-neuropathic/visceral
- Sub-acute neuropathic/juvenile
- Nova scotia

Conclusion

There is no specific treatment for NPD. Orthotopic liver transplantation in an infant with type A disease & cord blood transplantation in severe type B NPD patients have been attempted with little or no success. Clinical trials of miglustat have been performed, & the drug has been approved in Europe for the treatment of Type C disease. Many case of neuroregression in early stages confuse with cerebral palsy. Presence of hepatosplenomegaly & neuroregression will give a thought towards possibility of storage disease. !st half of infancy being normal, no early infancy convulsion, hepatosplenomegaly. Failure to thrive, thereafter neuroregression will start that clinch towards possibility of LIPIDOSIS. Eye examination reveals cherry red spot seen in NPD,

Tay-sachs disease, Gaucher disease, GM1 gangliosidoses. Final diagnosis remains with lipid storage enzyme panel assay, that helps in prognosticate the outcome.

References

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