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A case report of ASMD Niemann pick disease

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***Abstract*---**Niemann Pick Disease is a rare disorder of lysosomal storage of the lipid sphingomyelin and foam cell infiltration of tissues presenting with varying degrees of severity. metabolic abnormalities of two types responsible for causing NPD. acid sphingomyelinase deficiency is the first metabolic abnormality causing NPD type A and B and and second is defect in cholesterol transport causing NPD type C disease. Herewith reporting a case of Acid Sphingomyelinase Deficient (ASMD) NPD Type A.

Keywords---Niemann pick disease, acid sphingomyelinase, sphingomyelin.

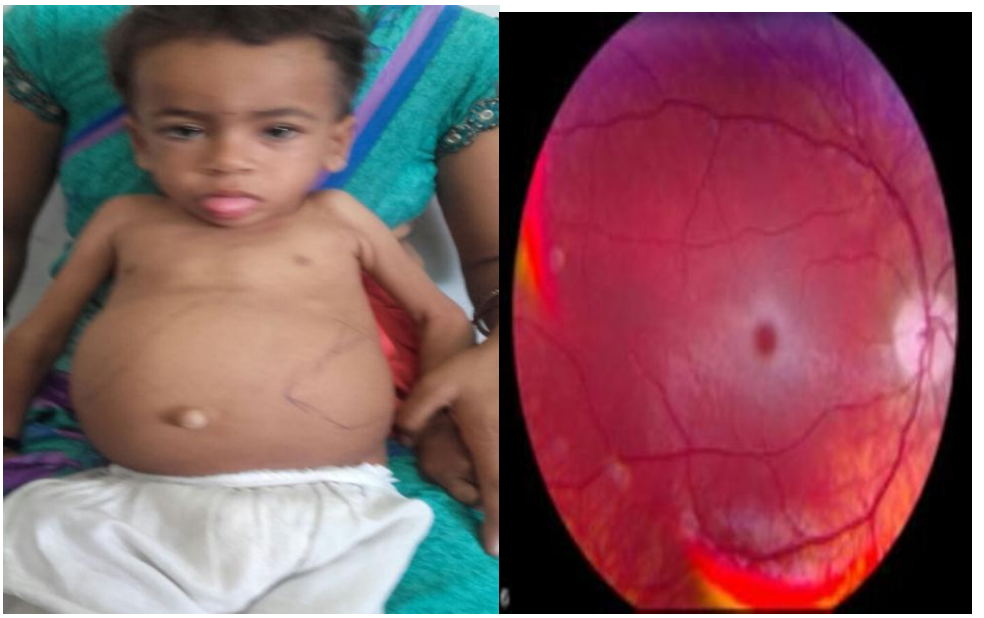
Introduction

Type A NPD is rare autosomal recessive disease characterized by absent or severely insufficienct enzyme activity .causing accumulation of sphingomyelin, a phopholipid in liver, spleen, lungs, adrenal cortex and central nervous system. This causes rapidly progressive neurodegenerative disorder, Hepatosplenomegaly, failure to thrive, cherry red macula, psychomotor retardation and death before 4 years.

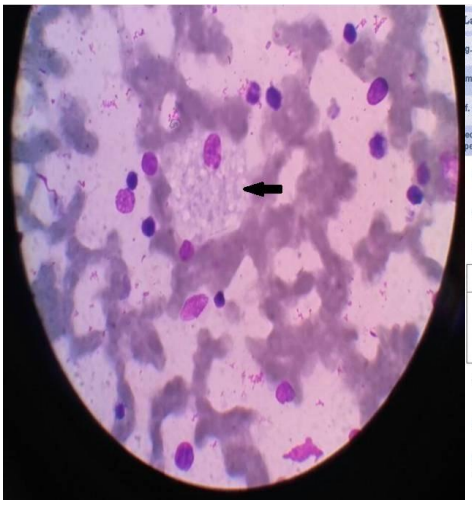
Case Report

A 2 years old girl child, born xecond to parents who was non consanguineously married presented with complaints of poor weight gain since birth, progressive abdominal distension since 6 months of age, delayed motor and language development. The child had been having frequent hospital visits for respiratory infections. She was diagnosed to have hypothyroidism at 6 months of age and was treated with thyroxine since then. Antenatal, natal and post natal periods were uneventful. There was a delayed motor development and language development with child only speaking a few meaningful word at 2 years. The child was able to walk with support previously, but has difficulty in standing and walking with support for the past month. There was no history of any metabolic disorder in family and she has a healthy elder sibling.

On examination, the child was emaciated and abdomen was distended with massive,firm hepatosplenomegaly. Tone was decreased in all limbs. The fundus examination revealed cherry red spot at the macula. Hence Gauchers disease and Niemann Pick disease were considered as differential diagnoses.



Blood investigations revealed anemia and mild elevation of liver enzymes. Renal functions and cholesterol were within normal limits. Ultrasonogram of abdomen confirmed hepatosplenomegaly with minimal free fluid. Blood for enzyme analysis of sphingomyelinase for diagnosis of Niemann Pick disease revealed a deficient activity of the enzyme in leukocytes and normal activity of beta galactosidase which ruled out Gaucher's disease. Histopathological examination of bone marrow aspirate showed large, lipid laden foamy histiocytes which confirmed the diagnosis of niemann Pick disease.



Lab Report — Department of Enzymology

g. ID	: 36233	Test ID	: 28517	Date of Report	: 17/01/18
me	: Ishani Singh	DOB/Age	: 17/10/15	Gender	: Female
f. Doctor	: Dr. Pramila	Ref. Institute	: Institute of Child Health		
ecimen pe	: Sodium Heparin Blood	Specimen Collected	: ***	Specimen Received	: 09/01/18

Enzyme analysis of sphingomyelinase for diagnosis of Niemann Pick A/B disease

Clinical History: Hepatosplenomegaly and cherry red spot.

Leukocyte Enzyme Activity:

Test	Disorder	Results	Biological Reference Interval (Mean ± SD)	Status
Sphingomyelinase (nmol/17h/mg)	Niemann pick A/B	Not detected	5.8 – 55 (12.8 ± 4.28)	Deficient
*β-Galactosidase (nmol/h/mg)	GM1-gangliosidosis	82	70 – 324 (148.17 ± 35.7)	Normal

* Reference enzyme. **Method:** Artificial Fluorogenic substrates.

Result: A deficient activity of sphingomyelinase is obtained in leukocytes.

Interpretation: Deficient activity of sphingomyelinase in leukocytes may be **consistent with the diagnosis of Niemann Pick A/B disease**.

Discussion

History

Dr.Albert Niemann, a German paediatric doctor reported the first NPD patient in the year 1914 in an infant from Ashkenazi who had with massive hepatosplenomegaly and a clinically rapidly progressive neurodegenerative disorder .

Genetics

The affected chromosome is 11p15.4 and The affected single gene is (*SMPD1)* Both Types A and B of NPD are follow recessive traits of inheritance, the level of clinical involvement and presentation depends upon the inherited gene mutations involving the *SMPD1* gene. The various types of mutations include point mutations, splicing, missense and nonsense and small deletions.

Pathology

Phosphocholine and ceramide (N-fatty acylsphingosine) is produce the following reaction. The hydrolytic cleavage of sphingomyelin in lysosomes is catalyzied by acid sphingomyelinase (ASM). Accumulation of sphingomyelin is caused because of reduced activity of ASM ,which is a major component of cell membranes and the principal phospholipid of the myelin sheath.

Clinical Features

TYPE A -Clinically ,failure to thrive,profound hypotonia, delayed milestones, on abdomen examination – hepatosplenomegaly present within one year Fundus examination shows cherry red spot in 50% of cases Most of the child have very poor prognosis .die within 3 year of life.

Type B mostly CNS involvement, on abdomen examination reveals hepatosplenomegaly with signs of liver failure. High Serum triglycerides and high LDL-cholesterol low HDL-cholesterol.fundus examination reveals reddish-brown halo surrounding the macula & cherry red spot can be identified.

Diagnostic Evaluation

The diagnostic procedure which confirm the disease is quantifying the acid sphingomyelinase activity in cultured fibroblast of skin or leukocytes which is circulating .another confirmatory diagnosis is *SMPD1* gene sequencing.Recent studies on Dried blood spot enzymatic assays found to detect patients of type a and type b NPD.

Conclusion

Main stay treatment of lysosomal storage disease is enzyme replacement therapy Size of the liver and spleen is reduced in patients who underwent Hematopoietic stem cell transplant

Genetic Counselling

As the disease is an autosomal recessive trait, there is 25% risk of recurrence of the disease in subsequent pregnancies. Genetic counseling gives details about the type of the diseases, inheritance and indication of the disease and also aids birth prevention . Optimal time to findout the risk and to determine carrier level is before preganancy. Prenatal diagnosis in pregnant women with 25% risk of ASMD is done by direct enzyme assay on uncultured CVB. In families with known mutations molecular analysis of fetal cells is diagnostic.

References

1. Nelson text book of Pediatrics, 20th edition
2. https://nnpdf.org/files/2015/10/A-Guide-to-ASMD-Niemann-Pick-Disease-Types-A-and-B.pdf
3. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5347465/
4. McGovern MM, Aron A, Brodie SE, Desnick RJ. Natural history of type A Niemann-Pick disease; possible endpoints for therapeutic trials. Neurology. 2006;66:228–232.
5. Brady RO, Kanfer JN, Mock MB, Fredrickson DS. The metabolism of sphingomyelin. II. Evidence of an enzymatic deficiency in Niemann-Pick disease. Proc. Natl. Acad. Sci. U.S.A. 1966;55:366–369.