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AN INTERESTING CASE REPORT OF NIEMANN- PICK DISEASE.

Pathology

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ABSTRACT

Niemann Pick disease is a lysosomal storage disease and is autosomal recessive. Type A and B are both due to sphingomyelinase deficiency. There is lysosomal accumulation of sphingomyelin, cholesterol, glycolipid and acylglyceropyrophosphate(1). And patient clinically presents with hepatosplenomegaly with or without nervous system involvement and other signs and symptoms. Incidence in Ashkenazi Jews is 1 in 40,000 for type A, 1 in 2,50,000 for both Type A and type B and 1 in 1,50,000 for Type C (2). Our case was a 10 year old male patient who presented with fever and reduced appetite for 4 days. There was no history of vomiting , abdominal pain, yellow discoloration of sclera/ loose stools. On examination patient had cervical, axillary and inguinal lymph node enlargement, hepatosplenomegaly and cherry red spots in macula. Triglyceride levels were elevated. A clinical suspicion of storage disorder was made . FNA of cervical lymph node and bone marrow biopsy aspiration showed foamy histiocytes. Enzyme assay showed low serum acid sphingomyelinase level and genetic work up showed SMPD1 gene positivity. Niemann Pick disease type A/type B was confirmed. The clinical course of our patient was similar to type A/B cases. And patient is on enzyme replacement therapy and on follow up.

KEYWORDS

Niemann Pick Disease/lysosomal Storage Disease/NPD/ASM.

INTRODUCTION:

Albert Niemann published the first description of what now is known as Niemann-Pick disease, type A, in 1914. And Ludwig Pick described the pathology of the disease in a series of papers in 1930's. In 1961, the classification of Niemann –Pick disease into types A,B, and C was introduced , and type D was called the "Nova Scotian type". But genetic studies showed that type D is caused by the same gene as type C1 and type D designation is now redundant (3,4).

Currently, two distint entities are identified, first is acid sphingomyelinase deficient NPD (ASM-deficient NPD) due to mutation in SMPD1 gene and includes type A and type B; the second is NPD type C (NPC) including type D due to mutations in either NPC1 or NPC2 genes. In Type A and B there is lysosomal accumulation of sphingomyelin, cholesterol, glycolipid and acylglyceropyro phosphate. Type C and D show primary defect in non enzymatic lipid transport(5). Type A shows low serum sphingomyelinase level and phenotypically most severe. It's infantile, neuronopathic and can present with Hydrops fetalis, failure to thrive, hepatosplenomegaly and hypotonia, progressive neurological deterioration and death by 3 to 4 years of age occurs(1). Type B is phenotypically variable, more chronic and presents in older infants, non neuronopathic, hepatosplenomegaly may be seen, Progressive pulmonary disease may become a major complication (1). Type C may occur anytime from intrauterine life to adulthood. Hepatosplenomegaly may occur but regresses with time, neurologic disease is progressive with spasticity and seizures in this type(1).

Case Report:

A 10 year old male patient presented with fever and reduced appetite for 4 days. And the patient went to an Ayurvedic hospital and was on Ayurvedic medication. There was no history of vomiting, abdominal pain, yellow discoloration of sclera/ loose stools. Past history of abdominal distension for 6 months at 2 years and 2 months of age was noted and there was history of URTI for 1 week during that time for which they consulted a local hospital.

And there was no history of bleeding, petechia, purpura, recurrent fever, loose stools or progressive loss of weight. The patient was a 2nd child of non-consanguineous marriage. His Antenatal scan and developmental history were normal and child was immunized for age with normal IQ.

On clinical Examination:

The patient presented with cervical , axillary and inguinal lymph node enlargement and hepatosplenomegaly. Features of stunting and wasting were noted. Portal hypertension / ascites were also noted .

Fig1&2: Liver 15cm below RCM, firm in consistency, non nodular surface, non tender. Spleen reaching up to midline, soft in consistency.

Investigations:

Peripheral Smear: Hypochromic microcytic anemia.
SGOT/SGPT: 143/100 IU/L (elevated)
DCT: Negative
TG: 278 mg/dl (elevated)
HDL: 10 mg/dl (decreased)
USG abdomen & elastography: Chronic liver disease and portal hypertension.
HRCT chest: Diffuse smooth interlobular and intralobular septal thickening involving entire parenchyma with numerous miliary nodules.

Fine needle aspiration cytology:

Pap stained moderately cellular smears show loose clusters of foamy histiocytes, lymphocytes and histiocytes in a background of blood and granular material (see.Fig 3,4 &5)

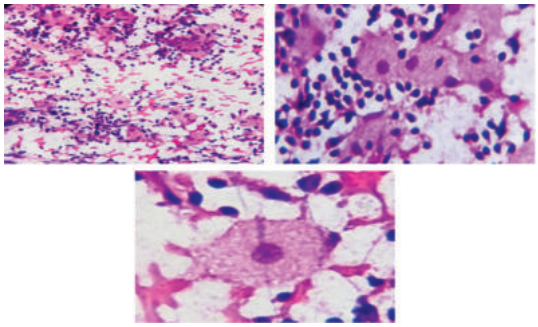
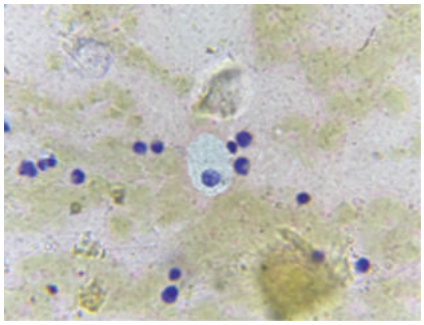


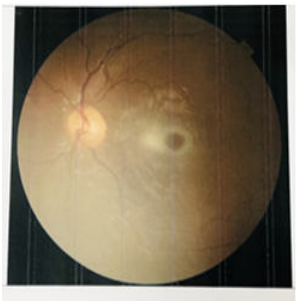
Fig 3,4&5



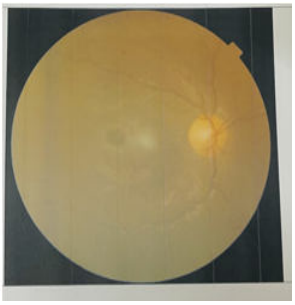
(Fig 6)

Bone marrow aspirate :
Giemsa stained marrow aspirate smear showed foamy histiocytes and sea blue histiocytes were also noted (see . Fig 6.).

Eye examination: Cherry red spots were noted in macula (Fig 7&8).



(Fig 7)



(Fig 8)

Enzymatic study :
Peripheral blood leukocyte ASM level was 3 nmol/mg protein/18 hr .

Genetic study:

Gene#*(transcript)	Location	Variant	Zygosity	Disease (OMIM)	Inheritance
SMPD1(+) (ENST00000342245.9)	Exon 4	c.1276G>A (p.Gly426Ser)	Homozygous	Niemann – Pick disease type A/ Niemann – Pick disease type B	Autosomal recessive

Final Diagnosis :
- **Niemann Pick disease type A/type B**.

Differential:
Gaucher Disease – The gaucher cells show crumpled tissue paper appearance.

Follow Up:
Patient is on enzyme replacement therapy and doing well.

DISCUSSION :
Our case was a 10-year-old male patient who presented with fever and reduced appetite for 4 days. There was no history of vomiting, abdominal pain, yellow discoloration of sclera/ loose stools. Past history of abdominal distension for 6 months at 2 years and 2 months of age was noted and there was history of URTI for 1 week during that time for which they consulted a local hospital. And there was no history of bleeding, petechia, purpura, recurrent fever,loose stools or progressive loss of weight. On examination patient presented with cervical, axillary, inguinal lymph node enlargement and hepatosplenomegaly .Serum triglycerides levels were elevated and FNA cervical node and bone marrow aspirate smears showed foamy histiocytes. Therefore, a suspicion of storage disorder was made and on further enzymatic and genetic study a diagnosis of Niemann Pick disease type A/type B was confirmed. So, it is important to think about such storage disorders whenever evaluating a child presenting with hepatosplenomegaly with elevated triglycerides besides other signs and symptoms and foamy histiocytes in affected organs. And further work up of enzymatic and genetic studies for confirmation. As early treatment can prolong the life of the patient with enzyme replacement therapies now available for NPD.

CONCLUSION:
The clinical course of our patient was similar to those seen in classic phenotypes and patient is on enzyme replacement therapy and on follow up. The criteria for type A and B sphingomyelinase deficiency and SMPD1 gene analysis were diagnostically met. It's diagnosis is important due to its multisystemic involvement. Due to it's rarity and myriad presentations of the disease, the diagnosis can sometimes be missed or delayed. And it is usually diagnosed late in the final stages when symptoms are severe. Through our case report we wanted to make awareness about the signs to recognize for an early and correct diagnosis. And also to think of NPD when organs affected show foamy histiocytes on biopsy or aspirate smears. Besides correlating the other laboratory parameters with enzymatic and genetic assays for confirmation. This will help with prompt diagnosis and intervention with enzyme replacement therapies before life-threatening complications ensues and patient is able to live longer.

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