

Niemann - Pick Disease Type B: A Case Report

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Abstract:

Niemann-Pick disease is a rare lysosomal storage disease responsible for numerous cytological abnormalities involving liver, spleen, lymph nodes, nervous system, lungs and bone marrow. This disease occurs due to accumulation of sphingomyelin in various tissues. Our patient is a 4 years boy presented with hepatosplenomegaly and growth failure. Cherry red spot was found on ophthalmologic examination. Niemann Pick cell was found on bone marrow examination. As because enzyme estimation is not available in Bangladesh, we diagnosed the case as Niemann Pick disease considering the clinical and laboratory findings.

Key words: Children, hepatosplenomegaly, Niemann-Pick disease.

Introduction:

Niemann–Pick disease (NPD) is a group of inherited, severe metabolic disorders in which there is accumulation of sphingomyelins in lysosomes. NPD was first described by Albert Niemann in 1914. But Ludwick Pick conclusively showed the tissues affected due to deposition of sphingomyelin in 1927, hence the name Niemann-Pick Disease.¹ NPD affects all segments of the population with cases reported in North America, South America, Africa, Europe, Australia and Asia. However, a higher incidence of NPD has been found in some populations like Ashkenazi Jews, Spanish- American population of southern New Mexico and Colorado and French Canadian population of Nova Scotia, Maghreb region (Tunisia, Morocco, and Algeria). The incidence of NPD is estimated to be about 1:40,000 among Ashkenazi Jews. The incidence of both NPD types A and B in all other populations is estimated to be 1 per 250000 populations.² Prevalence of the disease in Bangladesh is not known. Accumulation of sphingomyelin in NPD type A and B is caused by mutations in the sphingomyelin phosphodiesterase 1 gene (SMPD1) encoding for acid sphingomyelinase.² Niemann-Pick disease type C is caused by impaired cholesterol

transport though it shows a similar clinical appearance and sphingomyelins accumulation.⁴ All form of NPD present with neurological deficit except type B, which is non-neuropathic form. Type B form NPD presents with hepatosplenomegaly. We are reporting this case because NPD though common in Ashkenazi Jews is rare amongst people of South East Asia. This case emphasizes the need to keep NPD in differential diagnosis of children presenting with hepatosplenomegaly, short stature and pulmonary symptoms.

Case report:

A 4 years old boy first issue of consanguineous marriage got admitted with progressive abdominal distension and not growing well since 1 year of his age. He had no history of jaundice, hematemesis, melena, convulsion, developmental delay and any other neurological manifestation. On query he gave history of recurrent respiratory distress during this illness. On general examination he is anicteric, vitally stable and developmentally age appropriate. He had no stigmata of CLD; lymph nodes were not palpable, BCG mark present. Anthropometrically he is severely underweight and severely stunted. On abdominal examination, liver was palpable with liver span 12 cm and spleen palpable 6 cm from left costal margin along its long axis. Ascites was absent (Figure 1). There were no other abnormalities in other systems. Complete blood count was normal other than mild anaemia. Liver function tests were normal. Serum LDH, lactate, blood glucose, uric acid were normal. Lipid profiles shows hypertriglyceridemia. Haemoglobin electrophoresis was normal. Ultra sonogram of whole

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Fig.-1: Abdominal distention, short stature.

abdomen shows marked hepatosplenomegaly (liver 11.7 cm and spleen 11.4cm). There was no varix in upper GI endoscopy. Chest X-ray shows diffuse pulmonary infiltration bilaterally (Figure 2). There are cherry red spot in both eyes on ophthalmologic



Fig.-2: Chest X-ray showing bilateral diffuse pulmonary infiltration.

examination (Figure 3). Bone marrow morphology revealed lipid laden macrophage resembling Niemann-Pick cells (Figure 4). The child was diagnosed as NPD type –B on the basis of clinical manifestations, presence of cherry red spot on both eyes and Niemann-Pick cells in bone marrow. Sphingomyelinase enzyme activity could not be seen due to lack of facilities. We discharged the patient with genetic counseling of parents.

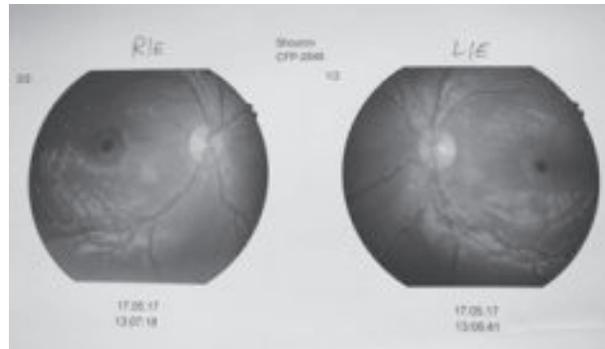


Fig.-3: Ophthalmoscopy shows macular Cherry red spot on both eyes.

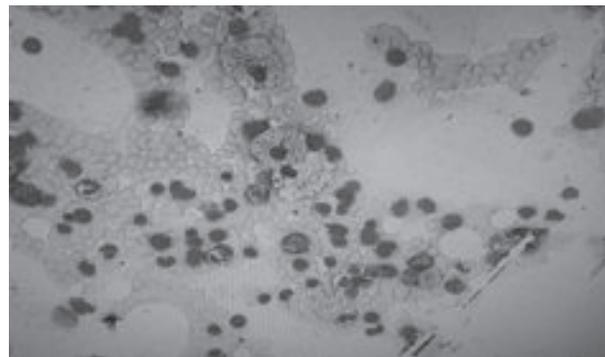


Fig.-4: Medulogram shows Niemann-Pick cells.

Discussion:

Type-B NPD is heterogeneous, pan-ethnic and non-neuropathic form, characterized by growth retardation, hepatosplenomegaly, hyperlipidemia, pulmonary disease and variable survival into adulthood. Cherry red spot or haloes are seen in the maculae of some B type patients.⁵ The presenting case also had the similar manifestations. Cherry red spot develop due to deposition of sphingomyeline in retinal ganglionic cell. It is also found in other metabolic diseases like type-A, type-C NPD, Farber disease, Gm1, Gm2 gangliosidosis, Galactosialidosis, Metachromatic leukodystrophy and Krabbe disease. The above mentioned diseases have got neurodegenerative course,

but type-B NPD patients do not have any neurological manifestations.⁶ Hepatosplenomegaly is due to accumulation of sphingomyeline in reticulo-endothelial system. In severe forms, liver involvement leads to life-threatening cirrhosis, portal hypertension, ascites, and pancytopenia due to hypersplenism that may require splenectomy. However, this should be avoided as splenectomy may leads to the progression of pulmonary involvement.⁶ Sutay et al. also reported a case of a 7 year old female child with significant abdominal distension with moderate hepato-splenomegaly and neurological manifestations in the form of developmental delay and seizure.⁷ At diagnosis, type B NPD patients usually have evidence of mild pulmonary involvement, usually detected as diffuse reticular or finely nodular infiltration on chest radiograph. Pulmonary symptoms usually present in adults. In some type B NPD, decreased pulmonary flow caused by alveolar infiltration is evident in late childhood. Progression happens by 15-20 years of age and may cause life-threatening bronchopneumonia and corpulmonale.⁶ The present case also has infiltration on chest X- ray without any symptom. Motamedi et al. also reported a 10 year female child with hepatosplenomegaly and diffuses military mottling detected on chest X-ray without any respiratory symptom. She was diagnosed as Niemann-Pick disease type B by bone marrow findings and liver biopsy.⁸ The present case also had no respiratory symptom but chest X-ray showed diffuse infiltration in both lung fields. Type A NPD, with Ashkenazi Jewish predilection, is a fatal disorder of infancy characterized by failure to thrive, hepatosplenomegaly, cherry red maculae, and rapidly progressive neurodegenerative course, presents as psychomotor and neuro-developmental regression, loss of motor function, intellectual impairment, spasticity, rigidity that may lead to death by 2 – 4 years of age.⁹ Though the clinical manifestations in type-A patients are uniform, there is marked variability in the phenotype among type B patients, ranging from severe disease in childhood to milder course. Like other reports, our patient also had hepatosplenomegaly, short stature and pulmonary symptoms but no neurological manifestation which is uncommon in NPD type B. Macular cherry red spots are found in both eyes on fundoscopy though it is rare in type B. Bone marrow morphology showed Niemann-Pick cells but enzyme activity could not be seen due to lack of facilities. Prenatal diagnosis of NPD type A and B is possible by doing sphingomyelinase assay.¹⁰ The only effective method for prevention of disease appears to be the identification of heterozygotic individuals and the prevention of marriage of such individuals with each other.

Limitation:

Acid sphingomyelinase activity was not performed due to lack of facilities.

Conclusion:

Though uncommon in South East Asian countries including Bangladesh, NPD should be kept in differential diagnosis of children presenting with short stature, hepatosplenomegaly and pulmonary complaints.

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