Case Report

Niemann-pick disease type A-a case report

Ashwini Tangde*, Shubhajyoti Pore, Anjali Kulkarni, Anil Joshi, Rajan Bindu

Department of Pathology, Government Medical College, Aurangabad, Maharashtra, India

Received: 27 October 2017

Accepted: 30 November 2017

***Correspondence:**

Dr. Ashwini Tangde,

E-mail: ash.51090@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Niemann-Pick Disease is an autosomal recessive disorder of infancy, characterized by failure to thrive, hepatosplenomegaly and neurodegenerative changes. It is caused by inherited deficiency of an enzyme, acid sphingomyelinase. It leads to deposition of sphingomyelin and cholesterol within the lysosome of reticuloendothelial cells of various organs. Niemann-Pick Disease is classified into four types such as A, B, C and D. We present a case of niemann-pick disease type A. This case report encompasses an 18-month-old male child brought with complaints of progressive abdominal distension, developmental delay, intermittent fever and excessive cry. On examination patient had developmental delay and significant abdominal distension with moderate hepatosplenomegaly. Bone marrow examination showed characteristic lipid laden foamy histiocytes termed as niemann pick cells and sea blue histiocytes. Later on, liver biopsy and splenic aspiration cytology was performed, which also showed same type of foamy cells. Type A is very rare and a severe infantile form with neurologic degeneration resulting in death usually by 3 years of age. No treatment available for type A so far. It's a rare disease in India. Genetic counseling.

Keywords: Acid sphingomyelinase, Developmental delay, Genetic counseling, Hepatosplenomegaly, Niemann-Pick Disease

INTRODUCTION

Niemann-Pick Disease is an autosomal recessive lysosomal storage disorder of infancy. It is characterized by failure to thrive, hepatosplenomegaly and neurodegenerative changes. It is caused by inherited deficiency of an enzyme, acid sphingomyelinase which leads to deposition of sphingomyelin and cholesterol within the lysosome of reticuloendothelial cells of various organs like liver, spleen, bone marrow, lymph node, brain, nerves and kidney.^{1,4} It is classified into two major entities

- Acid sphingomyelinase deficient Niemann-Pick Disease which result from mutations in SMPD1 gene and it includes type A and type B,
- Niemann-Pick Disease type C and type D result from mutations in NPC1 and NPC2 gene.²

The incidence of type A and B in general population is estimated to be 1 in 250,000 while that of type C is 1 in 150,000. NPD type A is more common in Ashkenazi Jewish population with estimated incidence of 1 in 40,000 and the carrier frequency among this population is 1 in 90. Both sex is affected equally.¹ A review of English medical literature shows that 1,200 cases of NPA and NPB worldwide have been reported with the majority being Type B or an intermediate form.³

CASE REPORT

An 18months male child, 2nd birth by order, born of 2nd degree consanguineous marriage with normal delivery. He was brought with complaints of gradually increasing abdominal distension since age of 2months with developmental delay and excessive cry. It was associated

with low grade Intermittent fever. There was history of pneumonia at the age of 6 months. Developmental history showed delayed milestones in the form of neck holding at the age of 7month and social smile at the age of 8month. There after child developed gradual regression of developmental milestones like disappearance of social smile, inability to seat, inability to hold neck.

On general examination, the child was irritable had mild pallor and was afebrile. All vital parameters were stable. He had frontal bossing, depressed nasal bridge, undescended testis and persistent mongolian spot all over body, with features of undernutrition.

On per abdominal examination, Liver was enlarged 10cm below costal margin. It was hard, nontender with sharp borders. Spleen was enlarged by 10cm and it was non tender (Figure 1). All the deep reflexes were diminished and there was hypotonia in all four limbs. Other systemic examinations was normal.

Figure 1: Clinical photograph of patient showing mongolian spot on abdomen and hepatosplenomegaly.

Complete blood count and peripheral blood smear examination done which was suggestive of moderately hypochromic anemia [6.7gm%], Total leukocyte count was within normal limit [5600/cmm] and platelet count was normal [2.2lac/cmm], occasional monocytes showed vacuolations. The levels of SGOT and SGPT were elevated. Xray chest showed nothing abnormal. USG of the abdomen showed hepatosplenomegaly with normal echotexture without ascitis. MRI brain showed thalamic involvement. Fundal examination showed cherry red spot in the macula in both eyes.

Bone marrow examination showed characteristic lipid laden foamy histiocytes termed as niemann pick cells and few sea blue histiocytes with normoblastic erythroid hyperplasia. Niemann-Pick cells are large cells 20-90micrometer in size with foamy pale cytoplasm (Figure 2). These cells on special staining showed PAS negativity. We couldn't perform Sudan black due to unavailability. Histopathological examination of liver

biopsy showed foamy cells (Figure 4). On Periodic-Acid-Schiff staining, it was negative.

Figure 2: Bone marrow aspiration (40x): showing foamy histiocytes with soap-bubble appearance.

Figure 3: Bone marrow aspiration (100x): showing foamy histiocyte.

Figure 4: Liver biopsy (H and E stain-40x)-Showing Foamy cells.

Splenic aspiration was done with aseptic and antiseptic precaution. The wet smear was dried and stained with leishman stain. The smear was cellular and showed large oval to polygonal macrophage like cells with central to eccentrically placed small nuclei and abundant amount of foamy cytoplasm. These cells were negative for Periodic-Acid-Schiff stain.

Further confirmatory investigations were not done because of unavailability. On the basis of clinical findings and microscopic findings of bone marrow aspiration, liver biopsy and splenic cytology, we reach to diagnosis of Niemann pick disease-Type A.

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 lipidosis.² Niemann-Pick Disease is an autosomal recessive disorder. The name Niemann-Pick is derived from two German pediatricians - Albert Niemann, who first described it in 1914, and Ludwick Pick who showed tissue deposition of spingomyelinase in 1927. In 1980, Crocker classified NPD into 4 types-²

- Acute neuropathic infantile,
- Chronic non-neuropathic/visceral,
- Sub-acute neuropathic/juvenile,
- Nova scotial.

Neyman pick disease type A

Acute neuropathic infantile form presents at the age of 3-6months with failure to thrive and rapidly progressive neurodegenerative disease and death by the age of 3years. A macular cherry red spot presents in nearly 50% of patients. Baby is normal at birth, but then develops failure to thrive, hepatosplenomegaly and psychomotor retardation by the age of 6months. As age advances deterioration of intellectual capabilities and in final stage spasticity and rigidity occurs. Enzyme activity is very low (1-10% of normal).^{1,5,6}

Neyman pick disease type B

It is chronic non-neuropathic form observed in children and adult. Central nervous system usually unaffected. Splenomegaly and pulmonary involvement are initial manifestation in most of the patients. Enzyme activity is very low (about10% of normal). The life expectancy of NPD type B patients is highly variable depending on the severity of their symptoms.^{1,5,6}

Neyman pick disease type C

This is most common sub-acute neuropathic form results from defective cholesterol transport with secondarily decreased acid spingomyelinase activity. Onset is at 2-3years of age but can occur in adult. Clinical manifestations include jaundice, ataxia, quadriparesis, seizures and moderate hepatosplenomegaly.

Hepatosplenomegaly is less severe than type A and type B. neurologic deterioration continues in 2nd dacade.^{1,5,6}

Neyman pick disease type D

It involves a defect which interferes with movement of cholesterol in between brain cells. It is now considered as variant of type C.

Apart from clinical findings, Peripheral smear and bone marrow examination for Niemann pick cells, histopathological examination of liver biopsy and splenic aspiration cytology can help to establish the diagnosis. Diagnosis is confirmed by measurement of sphingomyelinase enzyme in leukocytes and cultured skin fibroblasts and by genetic testing for genetic mutation. Lack of widespread availability of the enzyme assay and genetic study has as yet limited its application in clinical practice, and led to many cases of niemann pick disease being diagnosed by bone marrow and liver biopsy. Staining with sudan black B, oil red O, sudan III and fillipin is useful in demonstration of lipid in cells. High performance liquid chromatography (HPLC) using plasma instead of leucocytes is a very reliable and highly sensitive technique to determine ASM activity for accurate diagnosis of NPD patients or carriers.²

No specific treatment is known for type A, but symptoms are treated. In Type-B the cholesterol level is kept in limit. For type-c treatment with 2-hydroxypropyl- β -cyclodextrin has showed some good results. Prognosis is very bad in type A (85% die before 18months). Type B children live comparatively longer but require supplemental oxygen due to lung impairment.^{3,7} Genetic counselling and genetic testing is recommended for families who maybe carriers of Niemann Pick.²

CONCLUSION

Type A is fatal disease, death occurs by the age of 3years. Although no definitive treatment available till now, only supportive treatment is offered, early diagnosis and management of complications can improve life expectancy.⁸ Bone marrow aspiration examination, Liver biopsy, Splenic aspiration cytology are helpful investigations to establish the diagnosis of Niemann pick disease.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

REFERENCES

1. Mane V, Joshi RT, Mane VP. Niemann pick disease-a case report. *J Evol Medic Dental Sci.* 2012;1(6):955-58.
2. Sutay NR, Choudhary D, Samariya P, Jha S, Gangul S. Niemann-pick disease type B-a case report. *JMSCR.* 2017;5(4):19732-6.

3. Shubhankar M, Sunil KA, Bikash RP, Shantanu KM. Niemann pick disease type A in an Infant: a case report. *Sch Acad J Biosci.* 2014;2(10):728-30.
4. Bari MI, Haque MI, Siddiqui AB, Hossain MA, Alam T. Niemann Pick Disease: A Case Report. *TAJ: J Teachers Association.* 2011;15(1):32-4.
5. National Institute of Neurological Disorders and Stroke. (NINDS). Niemann Pick Disease Information Page. Available at <https://www.ninds.nih.gov/Disorders/All-Disorders/Niemann-Pick-Disease-Information-Page>.
6. Gregory M. Pastores, Edwin H. Kolodny-lysosomal storage disease. In: Kenneth F. Swaiman, Stephen Ashwal, Donna M. Ferriero editors-Pediatric Neurology: Principle and Practice. 2006;1(4):673-677.
7. Liu B, Turley SD, Burns DK, Miller AM, Repa JJ, Dietschy JM. Reversal of defectively lysosomal transport in NPC disease ameliorates liver dysfunction and neurodegeneration in the npc1^{-/-} mouse. *Proc Natl Acad Sci.* 2009;106(7):2377-82.
8. Sriram S, Ahmed J, Saminathan S, Annie S, Raj S. Case study on type A Niemann pick disease. 2016;11(4):36-8.

Cite this article as: Tangde A, Pore S, Kulkarni A, Joshi A, Bindu R. Niemann-pick disease type A-a case report. *Int J Res Med Sci* 2018;6:366-9.