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Case Report

"Convulsion" – in a Niemann Pick Disease (NPD): A Case Report

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Abstract

Niemann Pick disease is a metabolic disorder, a fatal disorder of infancy characterized by delayed developmental mile stone, failure to thrive, hepatosplenomegaly and rapidly progressive neurodegenerative changes.

A 16 month female child was admitted in IBMCHR with the complaints of convulsion with ARI. She had recurrent history of ARI & convulsion. She had failure to thrive, hepatosplenomegaly delayed developmental mile stone. He was diagnosed as a case of NPD with Seizure disorder. He was treated with anticonvulsant drugs & some injectable medication as a conjurvative treatment. She was discharged with further advice & ultimately the child died.

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Introduction

Niemann – Pick Disease is a metabolic disorder, of lipid storage (autosomal recessive disorder), a fatal disorder of infancy characterized by delayed developmental mile stone, failure to thrive, hepatospleno- megaly and rapidly progressive neurodegenerative changes. The defect is due to reducing enzyme (Sphingomyelinase) & accumulation of lipid (cholesterol), appearance of large foamy cells in histocytes specially in liver, spleen & bone-marrow[1].

Albert Niemann published the first description of what is now known as Niemann-Pick disease, type A, in 1914. Ludwig Pick described the pathology of the disease in a series of papers in the 1930s[2]

Storage of lipid (cholesterol) is not well understood but there seems to be a close relationship between the metabolism of sphingomyelin & that of cholesterol[3].

There are four types of Niemann – Pick Disease, like A, B, C & D. NPD types A (Acute neuropathic form) & B (Chronic non neuropathic form) are due to deficiency of sphingomyelinase activity and NPD types C (Sub Acute neuropathic form) & D (Nova Scotian variant) sphingomyelinase activity is normal but there is partially reduction of sphingomyelinase in some cells[3].

There are other types of lipid storage disease. eg. – Gaucher disease (glucocerebrosidase), Krabbe disease (galactocerebrosidage), Metachromatic leukodystrophy (arylsulfatase A), Fabry's disease (alpha-d-galactosidase). All of these except Fabry's disease (x-linked) have autosomal recessive inheritance[3,4].

This disease begins at 6 months of age (usually 3-4 months of age) with feeding difficulties & failure to thrive, Neurologic function is gradually

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deteriorated and delayed developmental mile stone, ultimately mental development is grossly retarded[5].

Although the disease (NPD) is common among Jewish individual but is rare in south Asians particularly in Bangladeshi[6]. A previous Child (1st child) of this family died of same disease.

This child was early detected in India & treated there. This time the child was admitted in IBMCHR with the above mention complaints. As because the incidence is rare in this country and convulsion is unusual presentation, so we decided to report this case for being it in notice to our colleague. It is sorry to say that both the children ultimately died.

Case study

Samia a 18 months old female child with a consanguineous parents of middle class family coming from kumarpara, Boalia, Rajshahi was admitted in this hospital (IBMCHR) on 8.11.08 with the complaints of high fever, Cough, Breathlessness & convulsion.

She was born with uneventful birth history and apparently normal growth & development up to 4 months of age. There after the child developed gradual distension of abdomen, delayed developmental mile stone & gradual reduction of developmental milestone like disappearance of social smile, inability to neck control & inability to sit etc.

She was suffering from recurrent ARI, UTI, Ent. Fever, Heart failure & also recurrent convulsion with or without fever. Later on the patient also developed Seizure disorder.

Her Parents also gave history of Similar type of problems of 1st child (Rahat) & he died as a diagnosed case of NPD.

On examination- the child was anxious, ill looking & moderate pale, pulse 96/min. respiratory rate 46/min. OFC was 45cm (50th centile in NCHS), Weight – 8.5kg was below 3rd centile in NCHS standard.

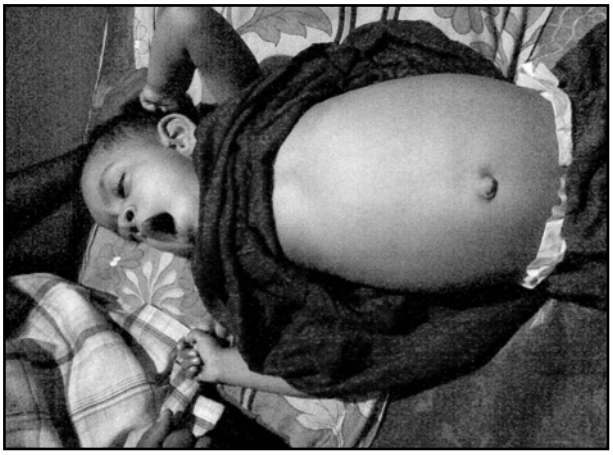

Fig 1: Patient of Niemann Pick Disease.

Heart was enlarged (cardiomegaly) and rhonchi & crepitation present in lungs. Liver was enlarged 12cm below the Rt. costal margin which was firm. Smooth & nontender. Spleen was enlarged 14cm from the Lt costal margin which was firm, smooth & non-tender. There was hypotonia in all limbs & all the deep reflexes were diminished. Sensory system could not be examined properly but pain sensation was preserved occasionally.

Following Investigation were done :

CBC (Complete blood count)-

TC – 4100/cmm

DC – Neutrophil – 61%

- Lymphocyte – 31%
- Eosinophil – 2%
- Monocyte – 6%
- Hb% - 9.2gm/dl
- ESR – 30mm is 1st hour.
- Platelate count – 2,00000/cmm
- Reticulocyte count – 1.2%

S – Creatinine – 1.4 mg/dl

S. Albumin – 3.5 mg/dl

S. Electrolytes – Na^+ - 131 mmol/L

K^+ - 4.8 mmol/L

Prothrombin time – 13.4 sec.

X-ray chest showed cardiomegaly

USG of W/A $\rightarrow$ hepato-spleenomegaly present.

Hb- electrophoresis – HbA - 97.2%

HbA_2 - 2.8%

EEG – Seizure disorder:
Fundal examination revealed cherry red spot in the macula in both eyes. Bone marrow showed infiltration of numberous foamy cells in the macrophage.

Discussion

NPD has been reported in Bangladesh in a child ® published at Rajshahi Medical College, TAJ, June 2002, Volume 15 Number 1. He was the brother of this child (samia), It is a very rare disease in our country & more common in person of Ashkenazi Jewish descent[7,8,9.]

The clinical manifestations & course of most common type A (NPD) is uniform & is characterized by a normal appearance at birth. Hepatosplenomegaly, lymphodenopathy and psychomotor retardation are evident by 6 months of age. These are the usual presentation and our patient has the similarity of this presentation. Convulsion is unusual presentation and usually there is no reported history of convulsion in NPD but in our case patient has repeated history of convulsion.

Followed by neurodevelopmental regression & most of the patients was type-A NPD die in the first 1-2 year of life. Both Patients ultimately died at the age of 22 month & 23 month respectively.

Niemann- Pick disease types A and B result from the deficient activity of sphingomyelinase, a lysosomal enzyme encoded by a gene located on chromosome bands 11p15.1-p15.4[7,8,10]. The complete sphingomyelinase genomic region has been isolated and sequenced. A total of 12 mutations that cause Niemann-Pick disease types A and B have been identified, namely , 9 single-base substitutions and 3 small deletions.

- Geneticist: Evaluation and ongoing care by a trained metabolic geneticist should occur.
- Counsel families regarding genetic risk and the availability of prenatal testing.
- For excellent patient education resources, visit eMedicine's Cholesterol Center and Statins Center. Also, see eMedicine's patient education articles High Cholesterol, Cholesterol FAQs, and Atorvastatin (Lipitor).

There is no specific treatment for NPD. Liver transplantation, amniotic cell transplantation or bone marrow transplantation in some cases but the results were unsatisfactory, future prospects for treatment of NPD include enzyme replacement & gene therapy.

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