Lipid Storage Diseases- A Clinico-haematological Study

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Abstract

Background: To study the clinico-haematological profile of lipid storage disorders in pediatric age group on bone marrow examination.

Methods: In this descriptive study, clinico-haematological profile of patients with lipid storage diseases in 1147 patients who underwent bone marrow examination, was studied.

Results: A total number of 20 cases of lipid storage disease were diagnosed. The mean age was 2 yrs. Thirteen(69%) were male, with a male to female ratio of 2.2:1. Ten (50%) cases presented with severe symptoms. Hepatosplenomegaly was present in majority(75%). Failure to thrive was the commonest clinical presentation. Pancytopenia was seen in 80%.

Conclusion: Niemann-Pick disease 65%) was the commonest, followed by Gaucher’s Disease (35%).

Key Words: Gaucher’s Disease; Lipid Storage disorders; Niemann-Pick Disease.

Introduction

The term storage diseases is used for certain metabolic disorders which cause accumulation of incompletely catabolised tissue products in the monocyte macrophage systems. The fundamental defect in all of these lipidoses is the accumulation of ceramide compounds in various cells and tissues. Gaucher’s and Niemann – Pick disease are autosomal recessive and Fabry’s disease is an X-linked storage disease. Gaucher’s disease is found in greater frequency in eastern and central European Ashkenazi Jews. These disorders are also called familial sphingolipidoses, since inherited deficiency of certain enzymes (glucocerebrosidase in Gaucher’s disease and sphingomyelinase in Niemann Pick disease) required for the catabolism of lipid compounds leads to the accumulation of these lipids and polysaccharides. The stockpiled substance is mainly accumulated in the macrophages. Accumulation of these lipid-laden macrophages in the blood, bone marrow, spleen, liver and other organs leads to manifestations like anaemia, leucopenia, thrombocytopenia and hepatosplenomegaly. 1-4.

Gaucher’s disease is characterized by a variety of phenotypes. The severity is extremely variable, with some patients presenting in childhood with virtually all the complications, while others remain asymptomatic and may present late. Gaucher disease is divided into three clinical subtypes, on the basis of neurologic involvement and its progression, e.g. type 1 - non-neuromyopathic form, type 2 - acute neuromyopathic form and type 3 - the chronic neuromyopathic form. Some patients, however defy classification.5-7

Niemann-Pick disease refers to a group of diseases passed down through families in which lipids collect in the reticuloendothelial cells of the spleen, liver, and brain .There are four most commonly recognized forms of the disease, i.e., types A, B, C, and D. Types A and B are also called Type I. Types C and D are also known as Type II.Both the types may involve different organs with or without central nervous system or respiratory involvement. Each type has different symptoms and may occur at different times throughout life, from infancy to adulthood.8

Patients and Methods

This study was performed from January 2005 to Sep 2010, in department of Pathology, Army Medical College and Military Hospital, Rawalpindi. During this period a total of 1147 patients underwent bone marrow aspiration for different indications in the Dept of Pathology MH/ AM College Rawalpindi. Bone marrow aspiration was done in the conventional way but with a 16 G spinal needle. The site of aspiration was posterior iliac spine in adults and tibial tuberosity in children up to two years. The slides were stained with Leishman stain Perl’s Prussian blue reaction was used to stain iron. Special stain, ACP, was used to distinguish between the Gaucher and the Niemann-Pick cell morphology.

Results

A total number of 20 cases of lipid storage disease were diagnosed. Out of these 13 were Niemann-Pick while 7 were Gaucher’s disease.
Table 1: Lipid storage diseases – Clinico-haematological profile

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
<td></td>
</tr>
<tr>
<td>-Niemann- Pick Disease</td>
<td>13(65)</td>
</tr>
<tr>
<td>- Gaucher’s Disease</td>
<td>7(35)</td>
</tr>
<tr>
<td>Failure to thrive</td>
<td>20(100)</td>
</tr>
<tr>
<td>Anaemia</td>
<td>20(100)</td>
</tr>
<tr>
<td>Pancytopenia</td>
<td>16(80)</td>
</tr>
<tr>
<td>Hepatosplenomegaly</td>
<td>20(100)</td>
</tr>
</tbody>
</table>

Table 2: Severity of Disease

<table>
<thead>
<tr>
<th>Severity of disease</th>
<th>No(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>5(25)</td>
</tr>
<tr>
<td>Moderate</td>
<td>5(25)</td>
</tr>
<tr>
<td>Severe</td>
<td>10(50)</td>
</tr>
</tbody>
</table>

Mild: Fever with cytopenias; Moderate: Above symptoms with organomegaly; Severe: Both of the above plus neurological deficit

Fig.1. Bone marrow aspirate showing a Niemann-Pick cell. Monocytes with foamy appearance of cytoplasm due to lipid vacuoles

Fig.2. Bone marrow aspirate showing Gaucher cells. Monocytes with pale blue cytoplasm and round to oval nuclei. Cytoplasm appear fibriller and wrinkled

Discussion

Storage disorders are uncommon amongst our population. Being a genetic disorder with high mortality rate, parents hesitate to bring forth these patients to hospital for treatment. Consequently the obvious outcome in our community is fatal. In present study 13 out of the 20 cases were of Niemann-Pick disease, while international studies reveal a higher incidence of Gauchers disease. Local data recorded variable results. A study from Islamabad correlated with present study.1,2

The true prevalence is difficult to assess because of the lack of awareness about these disorders and difficulty in the biochemical testing. Other reason could be that either the patients die before reporting to the hospital or the parents have already had children with the same disorder and they are aware of the fatal outcome so they hesitate to bring forth these patients as they are non affording and have social constraints.

The mean age was 2 yrs. 13 males(69%) and 7 females(31%) were affected. The male to female ratio was 2.2:1. Ten(50%) cases presented with severe symptoms while clinically hepatosplenomegaly was present in 15(75%) cases. Blood complete picture showed anaemia in all(Table 1). Nine patients of Niemann Pick disease had severe symptoms while only one patient with Gaucher’s disease had severe symptoms (Table 2). Almost all of these patients had failure to thrive and delayed milestones or deteriorating neurological signs. On bone marrow examination foamy accumulations were evident in Niemann –Pick, while fibriller cytoplasm was characteristic in Gaucher’s disease (Fig 1 &2)

The only diagnostic modality available in our country is bone marrow examination. In this study, all the diagnoses were made on basis of typical morphology of the storage cells in the bone marrow, which was augmented by PAS (Periodic Acid Schiff)and ACP (Acid Phosphatase) stains. At times, patients have to be subjected to bone marrow trephine and splenic puncture. At times we had to
subject the patients to trephine biopsy as well. Possibility of an enzyme biomarker, to make diagnosis, can not be ruled out. 10-12

Generally, the treatment is supportive. Enzyme replacement therapy (Alglucerase; Imiglucerase) is available for Gaucher’s disease, but is expensive. These patients are candidates for gene therapy. Bone marrow transplantation is the only curative option.

**Conclusion**
Detection of specific enzyme deficiency and genetic analysis can unearth more cases of lipid storage disorders

**References**
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