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A Case Report of Juvenile Sandhoff Disease

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Abstract
Introduction: *Sandhoff disease is a rarely sosomal storage disorder with autosomal recessive inheritance. It is caused by the deficiency of both hexosaminidase A and B. It has been classified into three forms: infantile, juvenile and adult-onset type based on the age of onset and clinical features. There are very few cases of Juvenile Sandhoff disease reported from India.*
Case Report: *A 4-year 3-month-oldboy born out of third-degree consanguineous marriage second in birth order was brought by parents with complaints of regression of attained milestones since the past one year and seizures since three months. On examination, the child was wasted and stunted, head circumference at 3rd centile with no dysmorphic facies. There was exaggerated startle response, spastic quadriparesis, exaggerated deep tendon reflexes and truncal ataxia. His fundus examination revealed a bilateral cherry-red spot.GM2 gangliosidosis was suspected and ß-Hexosaminidase enzyme studies were sent. Total ß-Hexosaminidase A & B was decreased and child was diagnosed as Juvenile Sandhoff disease.*
Keywords: *Juvenile Sandhoff disease, GM2 gangliosidosis.*

Introduction

Sandhoff disease is a rare but severe lysosomal storage disorder with autosomal recessive inheritance. The prevalence of Sandhoff disease is 1 in 384,000 live births. It is caused by a deficiency of both hexosaminidase (HEX) A and B, resulting in the accumulation of glycosphingolipids and oligosaccharides in the brain. It has three clinical subtypes (infantile, juvenile, and adult forms) andrepresents around 7% of cases among all the lysosomal storage disorders.[1] There are very few cases of Juvenile Sandhoff disease reported from India.

Case Report

A 4-year three-month-old boy born out of third-degree consanguineous marriage second in birth order was brought by parents with complaints of regression of attained milestones since the past one year and seizures since three months. The child was able to run, scribble, speak bisyllables initially by the age of 2 years, which were gradually lost since the last 1 year with no visual and hearing problems. At the time of presentation, the child was able to walk a few steps with support, able to laugh aloud and able to hold objects with a single hand. There was no

significant perinatal history or family history. The elder sibling was normal.

Figure 1: Clinical picture of the child

On examination, the child was wasted and stunted, head circumference at 3rd centile with no dysmorphic facies. There was an exaggerated startle response and the tone was increased in all the four limbs (spasticity), with power of 3/5 (Medical Research Council Grade), exaggerated deep tendon reflexes and truncal ataxia. There was mild hepatomegaly, no splenomegaly with cardiovascular and respiratory systems examination being normal. His fundus examination revealed bilateral cherry-red spots (Fig-2)

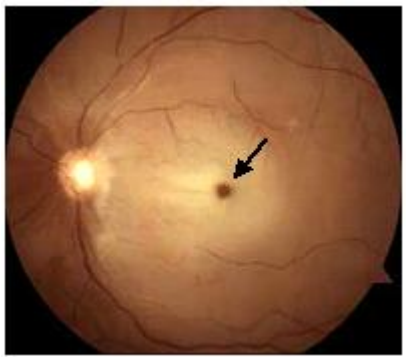

Figure-2: Optic disc showing temporal pallor with the arrow showing cherry-red spot

Routine blood investigations done were suggestive of microcytic hypochromic anemia, with normal liver, renal, and thyroid profiles. Ultrasound abdomen suggesting hepatomegaly with altered echotexture, EEG showed generalized epileptiform discharges, and the MRI brain showed diffuse cerebral atrophy (Fig-3).

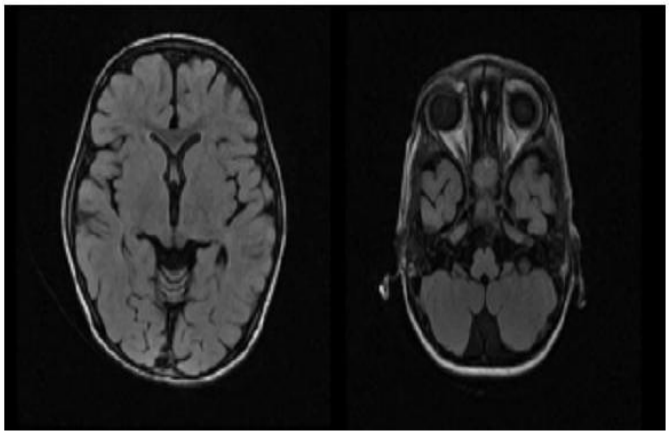

Figure -3: MRI Brain showing diffuse cerebral atrophy

As the child was having a neurodegenerative disorder with a cherry-red spot, GM2 gangliosidosis was suspected and ß-Hexosaminidase enzyme studies were sent. ß-Hexosaminidase A was 71 nmol/hour/mg (Normal 62-310 nmol/hour/mg) which was normal ruling out Tay-Sachs disease and Total ß-Hexosaminidase A & B was 183 nmol/hour/mg (Normal 905-2878 nmol/hour/mg) which was low suggesting Sandhoff disease. Hence the child was diagnosed to have juvenile Sandhoff disease.

Discussion

Lysosomal storage disorders (LSDs) are a specific group of inborn errors of metabolism, including more than fifty different diseases caused by a structural defect or deficiency of lysosomal enzymes[2].

GM2 gangliosidosis is one group of LSDs which occurs due to deficiency of ß-Hexosaminidase and is classified into three types: Sandhoff (0 variant), Tay-Sachs (B variant) and GM2 activator deficiency (GM2A-AB variant).

β-Hexosaminidase occurs as 2 isozymes: β-hexosaminidase A, which is composed of 1 α and

1 β subunit, and β-hexosaminidase B, which has 2 β subunits. β-Hexosaminidase A deficiency results from mutations in the α subunit and causes Tay-Sachs disease, whereas mutations in the β-subunit gene result in the deficiency of both β-hexosaminidases A and B and cause Sandhoff disease.[3] The gene causing Sandhoff disease is located on chromosome 5, specifically 5q13.[4]. It is called the HEX B gene. Konrad Sandhoff, a German Chemist, first described this disease, and hence it is named after him.

It is classified into three forms as infantile, juvenile and adult-onset type based on the age of onset and clinical features. Infantile form presents with loss of head/trunk control and smiling, by about 6months, macrocephaly, cherry-red macular spot, highstartle response to noise, muscle hypotoniaby 1 year, epilepsy, quadriparesis with somespasticity, dementia, blindness and hepatosplenomegaly. Clumsiness, lower motor neuron disease, denervation muscle atrophy and cerebella ataxia are the usual presenting features in the adult-onset form.[5]

The classical description of 'Juvenile Sandhoff 'disease given by MacLeod et al.[6] develops in mid-childhood, initially with clumsiness due to ataxia. Signs of spasticity, athetosis, loss of language and seizures gradually develops. This course describes only a minority of the cases and patients with juvenile Sandhoff disease can present from infancy to early adolescence with much more varied clinical signs and symptoms[7]. The majority show some features between the ages of 3 and 5 years of age and the initial symptoms are variable. Cherry red spot and visceromegaly are present very rarely. The most common presentation is with gait disorder or ataxia or both. Speech problems are difficult to classify at this young age.[7]

A.G Unnikrishnan et al.[8]. reported a 14-year-old girl who presented with ataxia, seizures, peripheral neuropathy, bilateral cherry-red spots without organomegaly and diagnosed as juvenile Sandhoff disease. However, in our patient, there was truncal ataxia with spastic quadriparesis, bilateral cherry-red spots and mild hepatomegaly.

There is no specific treatment or cure for Sandhoff disease. Management is symptomatic and supportive. Supportive treatment includes proper nutrition and hydration. Anticonvulsants may be used to control seizures.[9] There are current research efforts underway, including experimental gene therapy, substrate reduction therapy, bone marrow transplants, and stem cell therapy[10]. Diagnosis is essential for preventive genetic counseling.

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