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Tay-Sachs Disease: A Rare Storage Disorder in Children

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ABSTRACT

Tay-Sachs disease is an autosomal recessive lysosomal storage disorder cause by deficiency of enzyme Beta Hexosaminidase A and leading to accumulation of GM2 gangliosides mainly in CNS, results in progressive loss of neurological functions.
We report a case of 14 month old male child presented to us with neuro-developmental regression, convulsions and bilateral cherry red spot on funduscopy. The diagnosis of Tay-Sachs disease was made by marked decrease level of enzyme Hexosaminidase A.

Key Words: Lysosomal storage disorder, GM2 gangliosides, neuro- regression, cherry red spot, Enzyme replacement therapy.

INTRODUCTION

Tay-Sachs disease results from deficiency of Beta-Hexosaminidase A activity and lysosomal accumulation of GM2 gangliosides, particularly in CNS. Autosomal Recessive disorder caused by mutation in alpha subunit of HEXA gene in chromosome 15q. It is more common in Ashkenazi Jewish population, in whom the carrier frequency is approximately 1 in 25. (1)

TSD is classified into infantile, juvenile and adult onset form based on age at onset and clinical features.

Infantile form of TSD has clinical manifestation in infancy such as loss of achieved motor skills, increased startle response and retinal cherry red spot. Affected individuals usually develop normally until 4-5 month, then gradual decreased in eye contact and exaggerated startle response to noise (hyperacusis) are noted. Macrocephaly, not associated with hydrocephalus may develop. In the 2nd year of life seizure developed which may refractory to antiepileptic drug. Death is evident by 4-5 years.

Juvenile and adult form initially present with ataxia & dysarthria, macular cherry red spot may be absent.

Diagnosis of infantile TSD is usually suspected in infants with neurologic features and cherry red spot. Definitive diagnosis is made by determination of Beta – Hexosaminidase A activity in peripheral leucocytes or plasma.

CASE REPORT

A 14 month old 2nd order male child born out of third degree consanguineous marriage with history of one sibling loss at 2 year of age admitted to our hospital for developmental regression, convulsion, and increased startle response.

On examination child was conscious with stable vitals. Generalized hypotonia, macrocephaly, exaggerated startle response and brisk deep tendon reflexes with bilateral retinal cherry red spot were present. There was no organomegaly.

On investigation Complete blood counts, liver functions and renal functions were within normal limit. MRI of Brain revealed benign enlargement of subarachnoid spaces. There was decrease total activity of hexosaminidase enzyme (79.99 nmol/hr/mg against normal biological reference of >1150.00) by which the diagnosis of Tay-Sachs disease was confirmed.

Child was managed symptomatically with antiepileptic medications and undergoing palliative measures like physical therapy, nutritional support, etc.

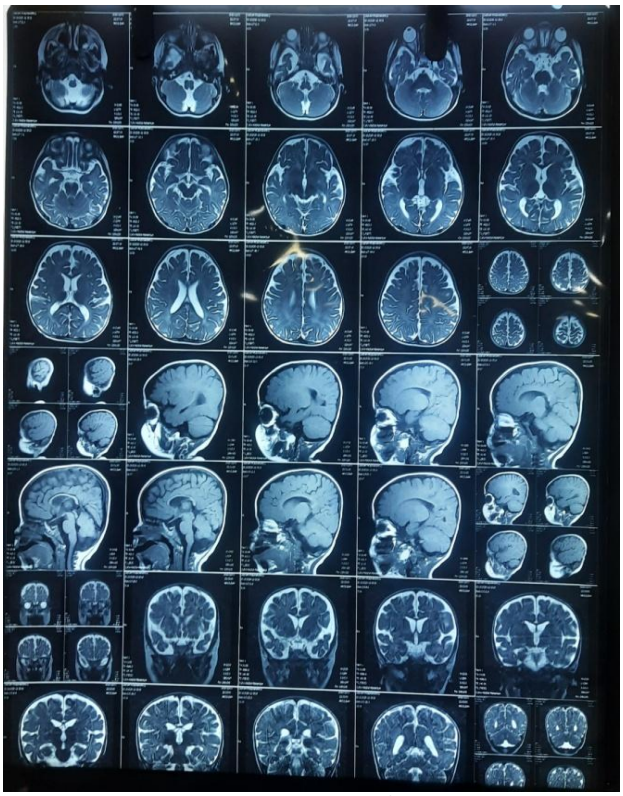

Fig1: MRI revealing benign enlargement of Sub-arachnoid spaces

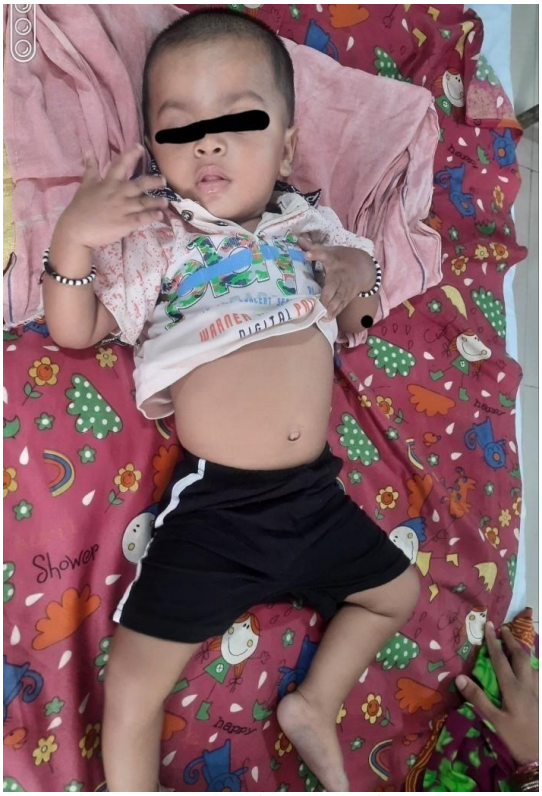

Fig2: Non syndromic floppy look of the child

DISCUSSION

TSD, described in 1881 by Warren Tay and in 1887 by Sachs , is currently most widely studied lysosomal storage disorder. The pathogenesis is attributed by accumulation of GM2 gangliosides secondary to deficiency of Beta – Hexosaminidase A enzyme caused by mutation in alpha sub unit of Hex A gene on chromosome 15 q.[(2)]

Symptoms onset occurs at 3-6 month of age; in our case the disease initially manifest as neuro-developmental regression at the age of 7 months. Later he developed seizure and exaggerated startle response. One of the ophthalmological sign described is cherry red spot in the macula results from accumulation of GM2 trihexosylceramide in retinal ganglion cells. [(3)] We got bilateral cherry red spot on funduscopy examination in our patient.

The diagnosis of TSD is mainly by assaying activity of Beta-Hexosaminidase A enzyme in peripheral leucocytes or plasma.

At present, there is no cure for GM2 Gangliosides. Typically treatment is supportive, focused on reducing symptoms, and improving the quality of life. Although experimental Research is ongoing to develop Enzyme replacement therapy (ERT) for TSD like other storage disorder.[(4)] Small molecule therapy called pharmacological chaperones (PC) has been shown to successfully enhance the enzymes level in Tay-Sachs disease.[(5)]

CONCLUSION

Tay-Sachs disease is a very rare storage disorder. It must be included in the differential diagnosis of pediatric neurological disorders causing neurodevelopmental regression with cherry red spot on fundoscopy.

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