

# A Case of Regression of Mile Stones with Cherry Red Spot

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**Abstract:** *Taysachs disease is a autosomal recessive disorder of sphingolipid metabolism caused by enzyme hexoseaminidase A deficiency that leads to an accumulation of GM2 in neurocytes which results in progressive loss of neuronal function. The accumulation of lipids in retinal ganglion cells that leads to a chalky white appearance of the fundus other findings include cherry red spot is hallmark of taysachsdisease . This disease is particularly prevalent in ashkenazijews in whom a carrier state of 1 in 30 has been reported.This is a case report of infantile taysachs disease in 1 year 10 months old female baby born of non consanguineous parentage who presented with seizures , exaggerated startle response, nystagmus , and regression of the acquired mile stones.*

**Keywords:** taysachs disease, sphingolipid,hexoseaminidase A , cherry red spot ,nystagmus , startle response.

## 1. Introduction

Taysachs disease is an autosomal recessive progressive neurodegenerative disorder which in the classic infantile form is usually fatal by the age of 3 years<sup>1</sup>. It is a sphingolipidosis characterized by the deficiency of lysosomal enzymes required for sphingolipid degradation of ganglioside, cerbroside and sphingomyelin<sup>2</sup>. Infantile taysachs is characterized by normal development until 2 years followed by progressive psychomotor retardation, megalencephaly,cherry red spot, blindness and death by the age of 3 to 5 years. The fundus appearance is also seen in other neuronal lipid storage diseases including Sandhoffs disease ,GM-2 gangliosidosis type 2, GM-2 gangliosidosis type 3,niemann picks disease ,sialidosis type 1 and type 2, farber disease , mucopolipidosis type 3, metachromatic leukodystrophy ,multiple sulfates deficiency, dapsone toxicity and wolmans disease<sup>4</sup>.

## 2. Case Report

A 22 month old female child brought to the hospital by her mother with the chief complaints of regression of mile stones since 7 months of age,seizures since 10 months of age difficulty in swallowing, regurgitation of feeds since 1 yr of age. The baby had normal development until 7 months of age when the mother noticed that child was listless lost the ability to move the limbs and roll over and since then the loss of motor skills became progressively evident. Child developed seizures at 10 months of age, since child is getting 3 to 4 episodes per month which are of generalized tonic clonic seizures .The baby was born at 38 wks of gestation to a healthy mother with no antenatal ,natal ,postnatal complications.

The patient is the only child of a healthy non consanguineous couple. There was no similar complaints in the families of both the parents.

On clinical examination baby was found to be having failure to thrive, macrocephaly , spastic quadriplegia , decreased eye contact, exaggerated startle response . Neuroimaging revealed leukodystrophic changes ophthalmic assessment

revealed severe visual impairment and fundoscopic examination showed bilateral retinal cherry red spot.

Clinical presentation associated with corroborative fundus finding guided the diagnostic work up towards lysosomal storage disorders in particular neurolipidoses. The diagnosis of taysachs disease was made by leucocyte lysosomal enzyme assay with analysis of leukocyte b hexoseaminidase A activity (5 nmol/min/mg) markedly below the normal range ( 10-50 nmol/min/mg) protein. A similar reduction was also evident in her plasma sample (0.3nmol/min/ml) normal range (.5 to 3.1nmol/min/ml)

Genetic counseling and options of prenatal diagnosis were provided to the parents in the subsequent pregnancies. The parents were also counseled regarding the appropriate health care for their daughter, probable outcome and advised regular follow up .

## 3. Discussion

The pathogenesis of taysachs disease is attributed to the accumulation of GM2 TRIHEXOSYL CERAMIDE secondary to the deficiency of beta-hexoseaminidase- A enzyme caused by the mutation in the alpha sub unit of the hexoseaminidase A gene on chromosome 15q<sup>1</sup>. GM2 trihexosyl ceramide accumulated predominantly in the retinal ganglion cells where by retina becomes turbid with milky white coloration<sup>2</sup>. Ganglioside is most plentiful in the gray matter with the most of the clinical and pathologic manifestations on the nervous system<sup>5</sup>. This is typically present early in the course of illness , is frequently a helpful clue in the diagnosis and can be detected even in the fetal stage<sup>3</sup>. As the ganglion cells atrophy and disappears the cherry red spot becomes less prominent and blindness with optic atrophy eventually ensues. Cherry red spot is a useful indicator in the taysachs disease and several other lysosomal storage disorders. A useful sign when associated with key clinical features and a good history , it often guides to the diagnosis. It serves as an ideal illustration of eyes as a window to the in born errors of metabolism. There are three distinct forms of taysachs disease

- 1) infantile taysachs
- 2) juvenile taysachs

3) late onset Tay-Sachs

Infantile Tay-Sachs is also characterized by loss of neurological function, hyperirritability and progressive weakness. The infant rapidly loses motor and intellectual skills after the end of the first year and crawls but never walks. The natural course leads to decerebrate vegetative state by two to four years of life and death. In the juvenile form it shows late onset and slower course but similar constellation of signs. The mildest form is the late onset disease also called as the adult subtype characterized by ataxia, dysarthria, muscle weakness.

The diagnosis of GM2 gangliosidosis is accomplished by the assaying for the activity of the individual's  $\beta$ -hexosaminidase isoenzymes in the serum of cultured cells from the affected individual. Gene therapy has the potential for wide spread correction of the underlying lysosomal defects by the means of secretion, capture, cellular pattern by enzymatic complementation. Gene delivery of  $\beta$ -hexosaminidase A by using adeno-associated viral vectors has realistic potential for treating the disease<sup>10</sup>.

Small molecule therapy called pharmacological chaperones that can stabilize the conformation of a mutant protein and also act as competitive inhibitors<sup>8</sup> has been shown to successfully enhance the enzyme levels in the Tay-Sachs disease<sup>9</sup>. Enzyme replacement therapies have been introduced for several lysosomal storage disorders. Intensive therapies are being carried out to develop other therapies but the treatment of the neurological symptoms of the disease is still not possible<sup>6,7</sup>.

#### 4. Conclusion

Infantile GM2 gangliosidosis remains one of the most devastating inherited neurological disorders despite advances in supportive care, loss of motor milestones and late recalcitrant seizures make the relentless disease course that pose a challenge to the caregivers and the specialists.

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**Cherry Red Spot**