

TAY – SACHS DISEASE: A CASE REPORT*

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SUMMARY: Arısoy AE, Özden S, Ciliv G, Özalp İ (Department of Pediatrics, İnönü University Faculty of Medicine, Malatya; Department of Ophthalmology, Firat University Faculty of Medicine, Elazığ; Departments of Biochemistry and Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey). Tay-Sachs disease: a case report. Turk J Pediatr 1995; 37: 51-56.

Tay-Sachs disease (G_{M2} gangliosidosis I) is an autosomal recessive lysosomal-storage disorder confined to the central nervous system, resulting from deficiency of hexosaminidase A.

The case presented is of a twelve-month-old girl brought to the hospital because of mental-motor deterioration and convulsions. She was the child of first cousins and had a history of the deaths of two siblings with the same manifestations. Generalized hypotonia, macrocephaly, hyperacusis and a retinal cherry red spot appearance were present. There was no organomegaly. The diagnosis of Tay-Sachs disease was made by means of absence of serum hexosaminidase A activity. *Key words:* Tay-Sachs disease, hexosaminidase A.

Tay-Sachs disease (G_{M2} gangliosidosis I) is an autosomal recessive lysosomal-storage disorder that results from a deficiency or defect of the α subunit of hexosaminidase A, which blocks the formation of intact hexosaminidase A¹. In the absence of enzyme activity, G_{M2} gangliosides cannot be hydrolyzed and therefore accumulate primarily in neuronal tissues. This results in progressive neurologic degeneration. The severity of the disease appears to correlate with the degree of enzyme deficiency². The disease is largely confined to children of Jewish ancestry with Eastern European origin (Ashkenazi) and only rarely has appeared in other Caucasians³. At four to six months of age, loss of interest in his or her surroundings, exaggerated startle response to noise (hyperacusis), and progressive psychomotor deterioration are the characteristic clinical findings in a previously well infant^{1,3}. With time, hypotonia, loss of previously acquired developmental skills, and then macrocephaly, seizures, hyperreflexia and

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spasticity develop. Nearly all cases have a macular cherry-red spot appearance^{1,3,4}. Patients with Tay-Sachs disease usually die before the age of four¹.

The present patient exhibited the classic findings and course of the disease, and is the first in our region in whom the diagnosis has been confirmed by an enzyme-based test.

Case Report

A twelve-month-old female infant was admitted to Firat University Hospital with symptoms of generalized and myoclonic convulsions that first presented one month prior to admission. She was the fourth child of healthy parents who were first cousins. The gestation, labor and delivery history was unremarkable. She had been irritable since birth. She had showed head control at two months and sat with support at five months of age. However, the parents reported that she had been unduly sensitive to sounds and startled by unexpected noises since four months of age. After five months of age, developmental regression and motor weakness had become evident. At the age of eight months she had become unable to hold her head and sit. She had convulsions for the last month. There was a family history of two siblings dying at the age of two and three years; they had apparently showed similar symptomatology and course, but no diagnosis had been established.

Physical examination revealed a head circumference of 47.5 cm (over 97th percentile), a height of 76 cm (between 75th-90th percentiles) and a weight of 11,500 g (between 90th-97th percentiles). The patient had no interest in her surroundings (Figs. 1, 2). She had a doll-like facial appearance and hyperacusis.



Fig. 1: The doll-like facial appearance in a twelve-month-old patient with Tay-Sachs disease.



Fig. 2: A twelve-month-old girl with Tay-Sachs disease exhibiting loss of interest in her surroundings.

There was no hepatosplenomegaly. Generalized motor weakness and hypotonia, hyperreflexia and bilateral clonus were present. Fundoscopic examination revealed the cherry-red spot appearance in both macular regions (Fig. 3). The other physical findings were normal.

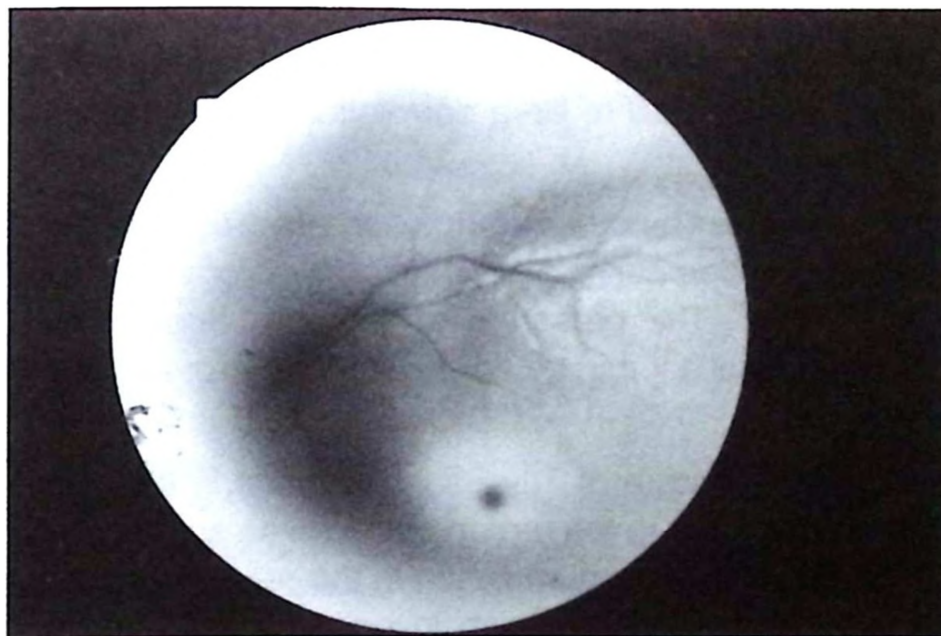


Fig. 3: The characteristic cherry-red spot appearance in a twelve-month-old patient with Tay-Sachs disease.

Laboratory studies revealed normal hematologic and biochemical findings. Urinalysis and roentgenograms of the skull, chest and spine were normal. The bone marrow examination showed no abnormality. Hexosaminidase A enzyme activity in serum was totally absent.

Discussion

Neuronal storage diseases are characterized by accumulation of lipid substances in cerebral neurons. The stored material in Tay-Sachs disease is G_{M2} ganglioside, a sphingolipid which is a main product of the degradative pathway of several gangliosides. The deficiency of hexosaminidase A results in abnormal accumulation of G_{M2} ganglioside within neuronal cytoplasm, causing cell dysfunction and eventually death¹. Its accumulation starts at an early embryonic age and has been observed in the brain of 18- to 20-week-old Tay-Sachs fetuses⁵.

The cherry-red spots of Tay-Sachs disease were first described in 1881 by Tay in a one-year-old child with mental and physical retardation¹. In 1896, Sachs determined the relationship between the cherry-red spot and progressive involvement of the nervous system, characterized by loss of vision, impairment of hearing, convulsions, psychomotor deterioration and early death, and termed this disorder by the name of "familial amaurotic idiocy"¹.

In the present case, hyperacusis first noted at four months of age, neuromotor deterioration and hypotonia first noted at five months of age, and seizures represented the classical findings and course of the disease. In Tay-Sachs disease, progressive macrocephaly usually develops after the age of 16 months and is due to cerebral gliosis^{1,3}. For our patient, the presence of macrocephaly at 12 months of age and the early deaths of two siblings with similar symptoms and course can be considered to be a correlation with the absence of enzyme activity².

In classic cases, mental and motor deterioration progress rapidly after one year of age, and progressive deafness, blindness, convulsions and spasticity appear after 18 months of age¹. The presence of seizures, hyperreflexia and clonus in our twelve-month-old patient can be considered the representations of a severe metabolic defect.

The most characteristic feature of Tay-Sachs disease is the cherry-red spot of the macula, a bright red area in the region of the fovea surrounded by a grayish-white rim which is due to lipid accumulation in the retinal ganglion cells^{1,4}. Later the spot becomes darker and brownish in color as the macula degenerates, and opaque whitish streaks, probably lipid deposits, along vessels may be observed^{1,4}. The cherry-red spot is not pathognomonic for Tay-Sachs disease. It can be seen in retinal ischemia and contusion of the globe, generalized gangliosidosis, Sandhoff disease, metachromatic leukodystrophy, Niemann-Pick disease, Farber disease and sialidosis (types 1 and 2)⁴. However, the typical course and the absence of organomegaly were strongly suggestive clinical clues of Tay-Sachs disease in our patient.

The diagnostic test for Tay-Sachs disease is the measurement of hexosaminidase A in serum plasma, leukocytes and cultured fibroblasts in affected infants⁶⁻⁸. A carrier state affects approximately one in 31 individuals of Ashkenazi Jewish ancestry, but only one in 167 individuals in the non-Jewish population¹.

Heterozygous carriers can be identified by measurement of the enzyme⁷. A newer DNA-based test has proven useful when used as an adjunct to screen carriers for this disorder². Prenatal diagnosis can be accomplished by enzyme assay in amniotic fluid, amniocytes, or chorionic villus samples^{9,10}. If one of the siblings had been diagnosed, the parents could have had genetic counseling and a prenatal diagnosis during this pregnancy. No specific therapy for the treatment of Tay-Sachs disease is available. Therapy consists mainly of supportive care for seizures and intercurrent infections.

Hyperacusis since four months of age followed by progressive psychomotor retardation presenting at five months and physical signs consisting of macular cherry-red spot, macrocephaly and absence of organomegaly were the main clinical findings suggesting Tay-Sachs disease in our patient. The definite diagnosis was made by detecting the deficiency of hexosaminidase A in serum.

Anticonvulsive therapy was initiated and genetic counseling offered to the child's parents. We want to emphasize the importance of genetic counseling in such a case in which prenatal diagnosis is currently possible.

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