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Sandhoff's Disease: A Case Report

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Case Report

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ABSTRACT

Sandhoff disease is a rare inherited disorder within the sphingolipidosis family, characterized by the accumulation of lipids in the nervous system due to a deficiency in hexosaminidase types A and B enzymes. This condition leads to progressive neurological disorders and eventual blindness, often resulting in fatality before the age of 4. We present the case of an infant who was admitted for psychomotor regression and generalized hypotonia, with the diagnosis of Sandhoff disease being supported by ophthalmological examination findings. Confirmation of the diagnosis was achieved through exome sequencing.

Keywords: Sandhoff disease; cherry-red spot; β-hexosaminidase A and B.

1. INTRODUCTION

Sandhoff disease is a rare autosomal recessive disorder characterized by lysosomal overload, belonging to the GM2 ganglioside family. It arises from a partial or total deficiency of β-hexosaminidase A and β-hexosaminidase B (HEX B), resulting in the accumulation of glycosphingolipids and oligosaccharides within intracellular environments, particularly in neuronal cells and viscera [1,2]. The disease presents in three clinical forms (infantile, juvenile, and adult), varying in age of onset and severity [3,4].

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The infantile variant of Sandhoff disease typically emerges between 6 and 18 months of age. It is marked by progressive neurological disorders, generalized hypotonia, auditory hypersensitivity, cherry-pink spots in both eyes, and bilateral damage to the thalamus [5,6]. Unfortunately, prognosis for these patients is poor, often resulting in death before the age of 4.

2. CASE PRESENTATION

An 18-month-old infant, delivered vaginally at term to first-degree consanguineous parents, was admitted to the hospital due to severe psychomotor regression and convulsive seizure disorder. Symptoms first appeared at 8 months of age, characterized by psychomotor regression, hypotonia, and audiogenic jerks. Clinical examination indicated macrocephaly with a head circumference of 51 cm, along with axial and peripheral hypotonia, and brisk osteotendinous reflexes (see Fig. 1).

Ophthalmological assessment revealed bilateral cherry-pink spots without Magnetic resonance imaging demonstrated T2 and Flair hyper-signals of the lenticular and caudate nuclei without diffusion restriction, alongside delayed demyelination of the white matter.

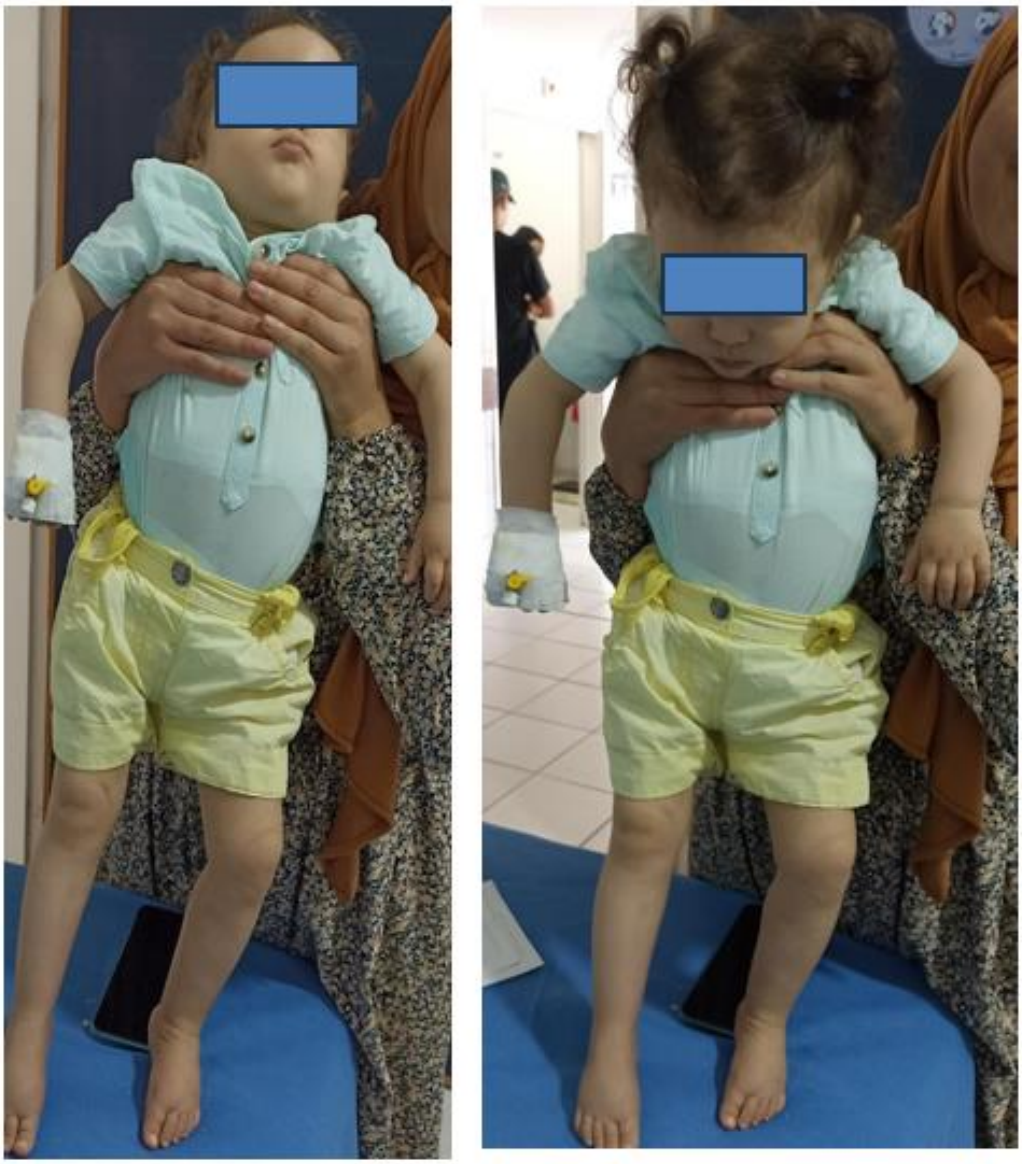

Fig. 1. Picture of 18 years old infant

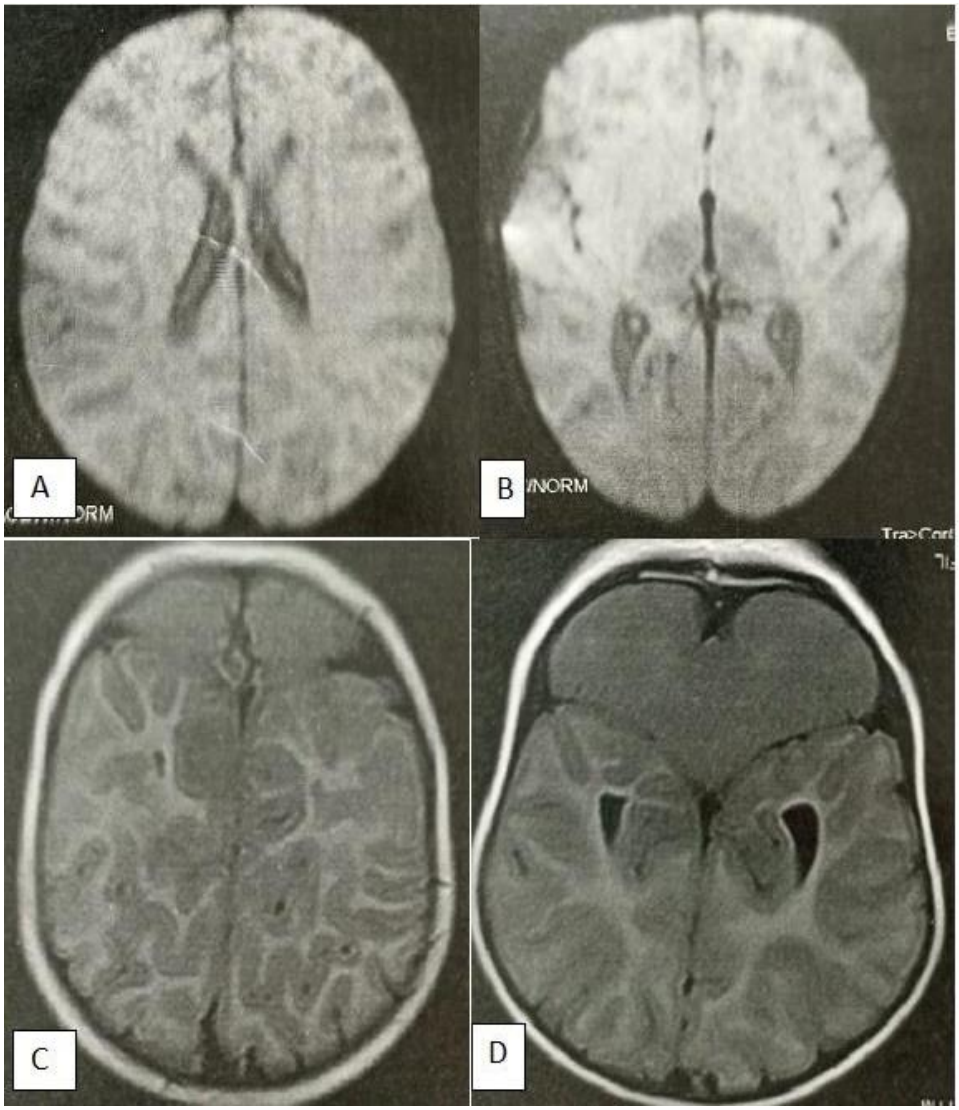

Fig. 2. Cerebral T2-weighted and Flair MRI images depicting hypersignal of the lenticular and caudate nuclei (A, B) and delayed myelination of the white matter (C, D)

3. DISCUSSION AND CONCLUSION

Sandhoff disease is a rare recessively inherited metabolic disorder caused by mutations in the HEXB gene located on chromosome 5q13. It was first identified by Konrad Sandhoff in 1968 [7]. This condition constitutes 7% of cases of GM2 gangliosidosis, with an estimated incidence of 1 in 384,000 births [8].

The age at which Sandhoff's disease manifests itself has been correlated with the residual quantity of GM2 ganglioside degradation activity in the patient's cells. There are three distinct forms of the disease: the classic infantile form, the juvenile form, and the late adult form. The classic infantile form, which is the most common and severe, typically emerges between 3 and 9 months after normal development. It is characterized by muscle hypotonia, tonic-clonic or myoclonic seizures, blindness, psychomotor retardation, and paralysis. A nonspecific feature of this form is the presence of a cherry-red spot in the macular areas. The juvenile and adult forms of the disease are exceedingly rare and can manifest at different stages of life, with symptoms generally being milder than those observed in the infantile form. As of now, there is no known treatment for Sandhoff's disease, and patients with the infantile form typically succumb before the age of 3.

The distinctive cherry-red spot observed in the macula is attributed to the accumulation of

sphingolipids within the ganglion cells, rendering them opaque. Interestingly, the macula remains transparent as it lacks ganglion cells. However, as the disease progresses, optic atrophy may develop.

It's important to note that the cherry-pink spot is not specific to Sandhoff disease; it arises from the accumulation of calcium in the retinal ganglion cells and may advance to optic atrophy.

In cases where the central nervous system is affected, T2-weighted brain MRI images typically reveal low signal intensity in the thalamus but high signal intensity in the basal ganglia and cerebral white matter. These imaging findings are attributed to calcium accumulation associated with intracellular storage of GM2 ganglioside.

However, bilateral T2 thalamic hypointense signaling, a hallmark of lysosomal diseases, which can manifest in Tay-Sachs disease, GM1 gangliosidosis, late-stage Canavan disease, and Krabbe disease [9], was not observed in our patient.

The diagnosis of Sandhoff disease was confirmed through the identification of an enzyme deficiency in β-hexosaminidase A and β-hexosaminidase B, along with the detection of a mutation in the HEXB gene.

Treatment for the infantile form of Sandhoff disease primarily focuses on symptom management, typically addressing seizure control and implementing intervention programs to mitigate motor and cognitive impairment. Unfortunately, due to the severe involvement of the central nervous system, lethality typically occurs before the age of 4 [7,10].

CONSENT

As per international standards, parental written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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