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Case Report

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An Infant with Sandhoff disease: A case report

Zahra sabzi[1], Negarin abkari[2] and Seraj aldin Arefnia[3*]

[1]Faculty of nursing, Nursing Research Center, Golestan University of Medical Scienses, Gorgan, Iran

[2]Faculty of Nursing, Istanbul University-Cerrahpasa, Istanbul, Turkey

[3]Department of Pediatrics, School of Medicine, Golestan University of Medical Sciences, Gorgan, Iran

Abstract

Introduction: Sand Hoff disease is a rare Lysosomal storage disorder which is inherited in an autosomal recessive pattern. Prevalence of Sandhoff disease is 1 in 384000 live births. The aim of this study was to introduce an infant with Sandhoff's disease.

Method: This study is a case study. Laboratory evaluation, physical examination and history of an infant with a rare disease were identified.

Result: We evaluated a boy aged 13 months with developmental arrest at the age of 6 months followed by Neuroregression and recurrent generalized seizures. According to the parents, from the age of 6 months, due to abnormal behavior in the infant, they had frequent visits but were not diagnosed. At 10 months, due to high AST, LDH, and normal AST, Pompe neuromuscular disease was first reported. But the baby did not have hepatomegaly. MRI was also normal. Therefore, the focus was on GM2, including T-Sack and Sand Hoff. Cherry-red spot was found in the ophthalmological examination report. Beta hexosaminidase A and B were requested for patients with suspected GM2. Enzyme studies revealed reduced levels of beta hexosaminidase A and B. The parents did not agree to the genetic test. Finally, according to the physical examination, history, and results of paraclinical procedures for the patient, "Sand Hoff" was confirmed.

Conclusion: For a child with developmental regression, even without splenomegaly and high AST, high LDH, and normal ALT, Hoff and T-sack syndrome should be suspected, and genetic testing should be considered.

Introduction

Sandhoff disease is an autosomal recessive genetic disorder. It is one of the most severe types of lysosomal storage disorders, accounting for 7% of cases [1]. It is diagnosed by evaluating hexosaminidase by sending a serum sample to the lab and detecting hexosaminidase A and B deficiency [2]. In this developmental disease, the infant is normal until 4-5 months of age [3].

Infantile SD presents with truncal hypotonia, muscle weakness, hyperacusis, developmental delay and regression, seizure and cherry-red spots in ophthalmologic exam around 6 months of age [4].

The severity of the disease and the age of onset depends on residual enzymatic activity. Hepatosplenomegaly, angry facial appearance, and bone involvement differentiate the Sandhoff from Tay-Sachs. Patients mostly die after 3 years due to intractable seizures and aspiration pneumonia [5].

There is no special treatment, but chaperone therapy with ketogenic diet and miglustat improve heart function and reduce seizures [4]. This case is introduced for the purpose of acquaintance with laboratory and clinical symptoms and due to the absence of hepatosplenomegaly and high AST and LDH and normal ALT.

Case Introduction

The patient is a 13-month-old infant who was brought to this office because of developmental delay by parents. During taking a history the parents acknowledged that they have a familial relationship (cousins). The mother did not have any problems or complications during pregnancy and labor. She did not have a history of miscarriage or stillbirth. The infant was the second child of the family and the product of the second pregnancy. It was the product of a term, normal delivery. The birth weight of the infant was 3400 grams and had no specific history of illness or problems at birth. According to the parents, they have noticed infant moans since the age of six months, with an increased reaction to the sounds and being startled with the slightest sound of closing a door. Consequently, they have had outpatient visits to physicians who have mentioned no special reason. At about 10 months of age, some tests were performed for the infant, the results of which are presented in Table 1.

Now, for the first time at 13 months of age, they referred to this office because of infant's problems in sitting and standing and complained about slight drooling and nasal congestion. Some tests were thus requested whose results are presented in Table 2.

Due to high ALT and LDH and normal AST, the neuromuscular disease of Pompe was initially diagnosed. In physical examination, despite a clear developmental delay and sitting disorder, the infant did not have hepatosplenomegaly and could control the head. The infant is currently weighed 8 kg, with a head circumference of 46 cm and a height of 71 cm. Examinations showed normal heart, lungs, genitalia, and fontanelle. There was hypotonicity, and at the same time, spasticity of the lower extremities. It had hyperreflexia but the Babinski reflex was normal. It did not communicate and was restless

Correspondence to: Seraj Aldin Arefnia, Department of Pediatrics, School of Medicine, Golestan University of Medical Sciences, Gorgan, Iran, E-mail: serajarefnia@gmail.com

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Table 1. Results of the patient's initial tests

PTH	25OHD	LDH	CPK	ALp	ALT	AST
29	46	1491	40.5	396	28	150

Table 2. Results of the patient's repeated tests

mg	ca	Serum homocysteine	Lactate	Ammonia	LDH	ALT	AST
1.9	8.6	8.6	9	91	1306	23	176

Table 3. Hexosaminidase test results

Dimension		Clinical chemistry
nmol/ml/min	0.14	HexosaminidaseA 9.4%activity
nmol/ml/min	0.00	Hexosaminidase B 0.0%activity
nmol/ml/min	0.66	Hexosaminidase A and B 2.7%activity

and crying during the examination. The infant did not have angry facial appearance. The most important reason that focused the diagnosis on GM2, including Sandhoff and Tay-Sachs, was the cherry-red spot in ophthalmology consultation report of eye examination. With suspected GM2, hexosaminidase A and B tests were requested whose results are presented in Table 3.

Physical examinations, histories, and results of the paraclinical procedures confirmed the "Sandhoff" disease. The family was briefed on the course and progress of the disease and the necessary attention. It was also emphasized for having genetic tests and follow-ups for the next pregnancy.

Discussion

Sandhoff disease is an autosomal recessive genetic rare metabolic inherited disorder due to mutations in HEXB genes on chromosome 5q13 and was first described by Konrad Sandhoff in 1968. There are three types of infantile, juvenile and adult hate onset [3]. An enzymatic defect in the disease is related to defects in beta-hexosaminidase enzyme. Mutation of the sub-unit beta gene leads to lack of both beta-hexosaminidase A and B isoenzymes, which result in the Sandhoff disease [6]. Sandhoff and Tay-Sachs symptoms are similar except that Sandhoff patients suffer hepatomegaly, heart engagement and mild bone disorders [6]. Their infantile type has similar clinical signs. Weak motor skills and hypotonia are the most common first symptoms around 4-6 months old. They are mostly associated with consistent typical startle response to sound that manifests with arm extension (hyperacusis). Hypotonia develops and acquired skills are lost [6]. By the age of 3 years old, the child becomes demented and decerebrated. The cause of death is often pneumonia aspiration. The classic infantile type is the most common and most severe form, and the cherry-red spot is a prominent but not exclusive feature [3]. This patient referred with clinical symptoms of the disorder in sitting and standing, without hepatosplenomegaly, and with cherry-red spot. The is interesting point in this case was high AST and LDH with normal AST, which was confirmed in several repeated tests. At first and before eye examination, the diagnosis was pro neuromuscular diseases including the Pompe disease. In a study conducted on diagnosed patients, the AST and ALT levels were reported high and normal, respectively [3]. Accordingly, laboratory results showed high AST and normal ALT in the present case. Therefore, high AST can be a useful and important biomarker for diagnosis. It may even be a biomarker for follow-up, prognosis, and monitoring of response to treatment, should a treatment be found in the future [7]. LDH was also high in this patient. In a study on Tay-Sachs patients, they had specific and similar characteristics such as Deficiency of fructose-1-phosphate, etc. and significant increase in AST and LDH, which may help confirm the diagnosis in the future [8]. The head circumference was normal in the present patient. It did not have angry facial appearance, and hepatosplenomegaly was not detected in abdominal examination. In a study conducted on 18 patients with GM2 by Karimzadeh, 7 patients had macrocephaly, 3 had microcephaly and 8 patients had normal head circumference. Also, only 2 of the 18 patients had hepatosplenomegaly [9].

The clinical image distinguishing Sandhoff from Tay-Sachs is hepatosplenomegaly [6]. No such case was however found in this patient.

Bley et al. [10] reported that exaggerated startle response was manifested at an average age of 7.2 months, limb spasticity at 13.4 months, and pneumonia aspiration onset at 22 months; of whom 75% underwent gastrostomy. This patient, however, had a severe startle response since the age of 6 months and was not hospitalized for pneumonia aspiration or other reasons, yet. Patients with Sandhoff disease are given genetic counseling and other supportive management [2]. A genetic test was thus requested for this patient, but the family has so far been reluctant to take it.

Conclusion

Therefore, it can be acknowledged that for a child with developmental regression even without splenomegaly and high AST and LDH and normal ALT, Sandhoff and Tay-Sachs syndromes should be suspected, enzymatic evaluation performed, and genetic testing considered.

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