Intermediate severe Salla Disease in differential diagnosis of hypomyelinating leukodystrophy: the second and third case from Turkey

İlknur Erol[1], Yasemin Özkale[2], Özgür Kütük[3]

[1]Baskent University Faculty of Medicine, Adana Dr. Turgut Noyan Application and Research Center, Departmant of Pediatric Neurology,Adana, Turkey
[2]Baskent University Faculty of Medicine, Adana Dr. Turgut Noyan Application and Research Center, Departmant of Pediatrics, Adana, Turkey
[3]Baskent UniversityFaculty of Medicine, Adana Dr. Turgut Noyan Application and Research Center ,Departmant of Genetics, Adana Turkey

ICNC 2022
17th INTERNATIONAL CHILD NEUROLOGY CONGRESS
ANTALYA, TURKEY | OCTOBER 3-7, 2022

INTRODUCTION

Sialic acid storage disorder, known as Salla disease, is a rare autosomal recessive lysosomal disorder caused by mutations in the SLC17A5 gene encoding the lysosomal transport protein sialin. Clinical findings occur as a result of increased free sialic acid deposition in the brain and other visceral organs. The main symptoms are hypotonia, ataxia, developmental delay, seizures, inability to walk, organomegaly, coarse facial features, failure to thrive, and early death. According to the age and severity of the symptoms, the disease is classified into three types; as conventional SD (Salla disease), intermediate severe SD, and infantile SD. Conventional SD is the most common and mildest form of the disease while the infantile type is the most severe form. Intermediate severe SD is lie between conventional and infantile types of the disease. So far about 177 patients with SD and 23 patients with intermediate severe SD, one of which was from our country have been reported in the literature.

OBJECTIVES

In this case study, we present the clinical, genetic and radiological findings of a Turkish siblings with intermediate severe SD.

MATERIALS & METHODS

A 5-year-old female born from consanguineous parents presented with a complaint of delayed speech, gait disturbance and tremors. Systemic and neurological examinations were normal except for ataxic gait and titubation (Figure1, video 1). Although all laboratory and metabolic screening tests were normal, brain magnetic resonance imaging (MRI) showed hypomyelination leukodystrophy (Figure 2). İllumina TruSight Inherited Disease panel including 552 genes for mutations related to AR pediatric-onset diseases was performed for investigation of the causes of hypomyelination leukodystrophy. Homozygous SCL175A5NM 01234: exon3: c: A406G: p.K136E mutation was detected and the patient was diagnosed with intermediate severe SD. This mutation was also detected in her sister with similar symptoms (figure 3). Her parents also have the same mutation in a heterozygous form.

Figure 1.Our patient

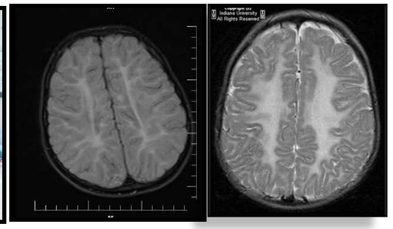

Figure 2. Hypomyelinating leukodystrophy

Figure 3. Sister of our patient

DISCUSSION

Intermediate severe SD is the intermediate form of SD. Patients are usually asymptomatic in the first year of life and progressive neurological problems begin between the ages of one and five years. The age of onset of symptoms and the severity of clinical findings are important in the differential diagnosis. In intermediate severe SD, symptoms begin at an earlier age and the life span is shorter than in the conventional type. On the other hand, the infantile type is the most severe form and patients usually die in early childhood. Intermediate severe SD can be distinguished from the infantile type by the absence of organomegaly, bone involvement, and the onset of the time of the disease. Hypotonia, growth retardation with or without coarse facial features, and varying degrees of hypomyelination in brain MRI are the characteristic findings of the disease. Leukodystrophy, hypomyelination, and corpus callosum hypoplasia are the other important neuroradiological findings in SD. Our patient was normal at birth and hypotonia was started at the age of one year. Delayed speech, gait disturbance and tremor occurred during the follow-up of the patient. She didn't have coarse facial features and organomegaly.

CONTACT
Prof. Dr. İlknur EROL
e-mail: ilknur_erol@yahoo.com
Phone: +905053837661

DISCUSSION

Hypomyelinating leukodystrophy was detected by brain MRI. Tru Sight inherited disease panel was performed for differential diagnosis of hypomyelinating leukodystrophy and SCL175A mutation was detected in our patient. Increased urinary excretion of free sialic acid and increased cerebrospinal fluid (CSF) concentration of free sialic acid can be detected in SD. We could not measure neither urinary excretion of free sialic acid nor CSF elevation of free sialic acid in our patients.

CONCULUSION

Our siblings are the second and third Turkish cases diagnosed with intermediate severe SD in the literature. Intermediate severe SD should be kept in mind in the differential diagnosis of hypomyelinating leukodystrophy especially in patients with progressive developmental delay and hypotonia.

REFERENCES

1. Barmherzig R, Bullivant G, Cordeiro D, ET AL.. A New Patient With Intermediate Severe Salla Disease With Hypomyelination: A Literature Review for Salla Disease. Pediatr Neurol. 2017 Sep;74:87-91.e2
2. Morse RP, Kleta R, Alroy J, Gahl WA. Novel form of intermediate salla disease: clinical and neuroimaging features. J Child Neurol. 2005 ;20(10):814-6