

Sjogren-Larsson syndrome: A case report of a rare disease

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ABSTRACT

We report a case of Sjogren-Larsson syndrome with clinical profile (spastic diplegia, ichthyosis, mental retardation) and imaging findings on magnetic resonance imaging.

Key words: Diplegia, ichthyosis, MRI, Sjogren-Larsson syndrome

INTRODUCTION

Sjogren-Larsson syndrome (SLS) is a recessively inherited disease with congenital ichthyosis, spastic diplegia or tetraplegia, and mental retardation, caused by a deficiency of fatty aldehyde dehydrogenase.^[1] SLS is an inborn error of lipid metabolism caused by a deficiency of the microsomal enzyme fatty aldehyde dehydrogenase (FALDH), a component of fatty alcohol: NAD-oxidoreductase enzyme complex. FALDH deficiency may lead to an accumulation of long-chain fatty alcohols with structural consequences for cell membrane integrity which disrupt the barrier function of skin and the white matter of the brain.^[2] In 1994, the FALDH gene was mapped to chromosome 17p11.2. Mutation analysis has identified many different mutations in the FALDH gene in SLS patients.^[3]

CASE REPORT

A 4-year-old male child born from a consanguineous marriage presented to the pediatrics department with complaints of delayed development and a skin ailment since infancy. His birth was at full-term from an uneventful pregnancy. On detailed history the child attained head holding at 6 months, sitting without support at 1 year age and walking with support at 2 years. Stiffness in lower limbs started in later part of the first year of life with progressive increase up to the time of presentation. Neurological examination revealed mental retardation, increased tone in both lower limbs, brisk deep tendon reflexes, and bilateral

extensor plantar response suggestive of spastic diplegia. Upper limbs did not show any tone or deep tendon reflex abnormalities. There was also evidence of conduction aphasia in the child. Skeletal, dental, eye/ fundus examination and eye or limb movements were normal. Child had a normal head circumference for his age.

Skin examination showed scaly ichthyotic lesions with severe pruritus presently affecting all body parts and which started in late infancy on the face [Figures 1 and 2].

Chest radiograph and all routine hematological investigations were normal. Electroencephalogram (EEG) was normal. Patient was sent for the MRI of brain. MRI was done on 0.2 tesla Signa (GE systems, USA) MRI with T2W, T1W, FLAIR sequences in all three planes [Figures 3 and 4]. The MRI showed diffuse and symmetrical high signal intensity on T2W sequence in bilateral deep periventricular white matter in the frontal and parietal lobes and in the corona radiata. These areas were hypointense on T1W sequence. Subcortical U fibers were normal. Ventricles and gray matter of brain, corpus callosum, thalami, brainstem, and cerebellar hemispheres were normal. All these clinical and radiological findings were diagnostic of Sjogren-Larsson syndrome.

DISCUSSION

In 1957, Sjogren and Larsson described a rare syndrome consisting of congenital ichthyosis associated with spastic diplegia or tetraplegia

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Figure 1: Ichthyotic lesions over trunk and hands



Figure 2: Ichthyotic lesions over lower extremities and hands

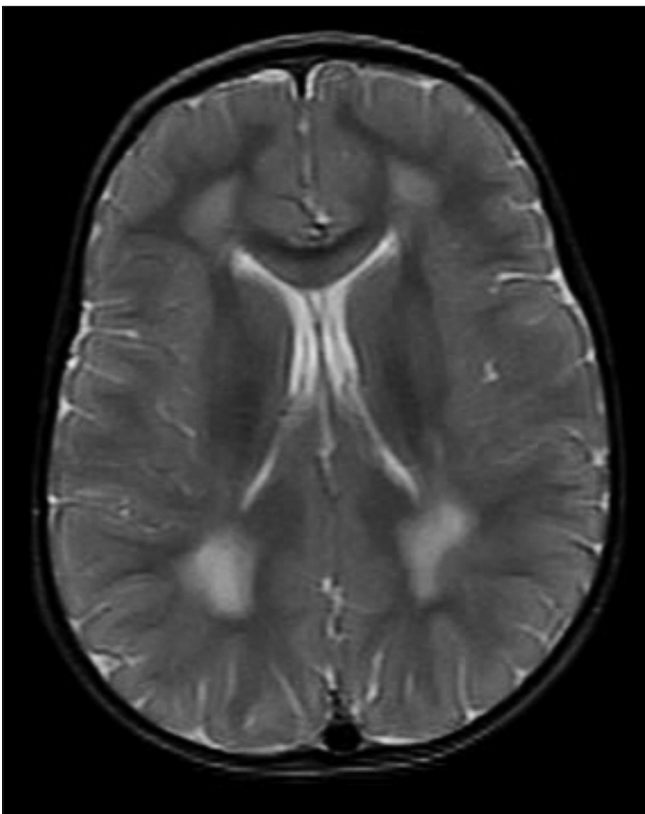


Figure 3: T2W axial MRI image showing bilateral symmetrical hyperintense lesions in periventricular white matter

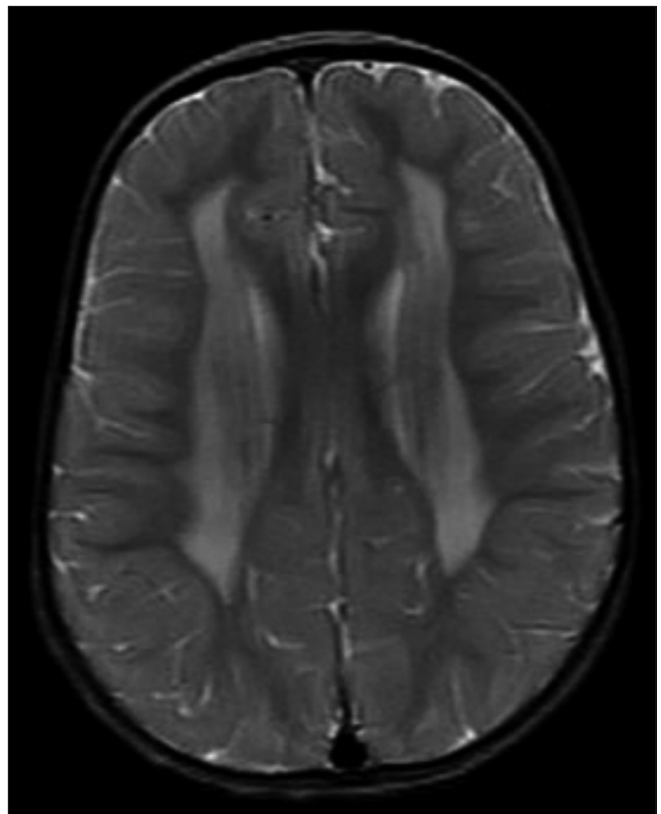


Figure 4: T2W axial MRI image showing bilateral symmetrical hyperintense lesions in corona radiata

(spastic pyramidal symptoms), aphasia, and low-grade dementia.^[4]

SLS is an inherited neurocutaneous disorder caused by mutations in the ALDH3A2 gene that encodes fatty aldehyde dehydrogenase (FALDH). More than 70 mutations in ALDH3A2 have been discovered in SLS patients including amino acid substitutions, deletions, insertions, and splicing errors.^[5] FALDH

catalyses the oxidation of long chain aldehyde to fatty acids. Due to deficiency of this enzyme, there is an accumulation of aldehyde-modified lipids or fatty alcohol in the skin and in the myelin.^[3]

There is usually spastic diplegia, occasionally tetraplegia, with mental retardation, epilepsy, speech defects, dental, dermatological, skeletal, and retinal changes.^[6] Skin changes

are in form of ichthyosis which is a generalized hyperkeratosis of the trunk, joints, and the dorsal aspects of the hands and the feet. Most patients have erythema at birth with worsening of cutaneous symptoms during the first year of life. Pruritus is a prominent feature that is not found in other types of ichthyotic skin disorders.^[3]

Photophobia, macular dystrophy and decreased visual acuity are the most prominent ophthalmologic abnormalities and may be caused by accumulation of long-chain fatty alcohols or fatty aldehydes.^[3] These features are seen in one third of cases but not seen in our case.

Neurological component usually starts between 4 and 30 months and remains static after puberty. The main neurological features are spastic diplegia or quadriplegia, mental retardation, conduction aphasia.^[6] In our case all three neurological findings were present. Neuropathologically, the hallmark of SLS is demyelination of the cerebral white matter and corticospinal and vestibulospinal tracts which causes spasticity.^[7] These abnormalities are due to accumulation of lipids and fatty alcohol in the myelin as a consequence of an enzymatic defect.^[3] Demonstration of elevated concentrations of free fatty alcohol in cultured fibroblast or in plasma can provide biochemical confirmation.^[3]

Few reports have described CT and MRI findings in SLS. MRI shows diffuse symmetrical white matter hyperintensities on T2W sequence especially in periventricular frontal, parietal lobes, corpus callosum, and corona radiata. Typically, subcortical white matter U fibers are spared.^[2,8,9] In our case, T2W hyperintensities were seen in bilateral periventricular frontal and parietal white matter, corona radiata with sparing of subcortical U fibers.

Recently, few reports have described proton MRI spectroscopy findings in Sjogren-Larsson syndrome which shows abnormal lipid peak at 1.3 ppm at both TE-30 and 135 ms in the area of T2 white matter abnormalities.^[2,3] We could not carry out spectroscopy because of equipment limitation.

In conclusion, the diagnosis of SLS should be considered in a neonate or infant with congenital ichthyosis and emerging neurological features. One should look for ocular features and pruritus to make the diagnosis. Cerebral MRI reveals arrested myelination or demyelination in white matter and lipid peak on spectroscopy help in making the diagnosis. Though in such cases biochemical (urinary concentration of leucotriene B₄ and 20-OH-LT B₄) and genetic studies (for ALDH3A2 gene) are desired we could not perform these due to paucity of resources.

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