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ORIGINAL ARTICLE

# Sjogren Larsson Syndrome in three siblings of an Indian family

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***Abstract:***
*Sjogren Larsson Syndrome (SLS) is an uncommon autosomal recessive disorder characterized by intellectual disability, congenital icthyosis and spastic diplegia. Here we report three siblings with SLS from an Indian family with no history of consanguinity. One sibling had unusual features of spasticity and tremors in upper limbs.*

**Keywords:** Sjogren-Larsson syndrome, icthyosis, quadriplegia, tremors
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## Introduction

Sjogren Larsson Syndrome (SLS) is an autosomal recessive neurocutaneous disorder characterized by mental retardation, congenital icthyosis and spastic paraplegia and occasionally quadriplegia[1]. It is caused by mutations in aldehyde dehydrogenase 3A2 isoform 2 (ALDH3A2) which encodes fatty aldehyde dehydrogenase (FALDH)[2].Its deficiency leads to 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. SLS occurs in all races and its prevalence has been estimated as 0.4 per 100,000 or lower[3].There have been only few case reports from India [4,5]

## Case Reports:

We report a one and half year old male child presented with complaints of icthyotic skin changes, delayed developmental since birth, increased tone in all limbs and abnormal movements for one month. The child was a child of non consanguineous parent, and has no history suggestive of any perinatal insult. Laboratıry examination revealed as anemia, icthyotic skin changes mainly over all the four limbs and trunk and spasticity quadriplegia. Muscle tone was

increased more in the both upper limbs in comparison to lower limbs. Abnormal movements in the form of tremors were present in upper limbs. His development quotient was 25-30% and social quotient was 40-45%.Cardiovascular and respiratory system were normal. No facial dysmorphism or organomegaly was present (Figure 1).

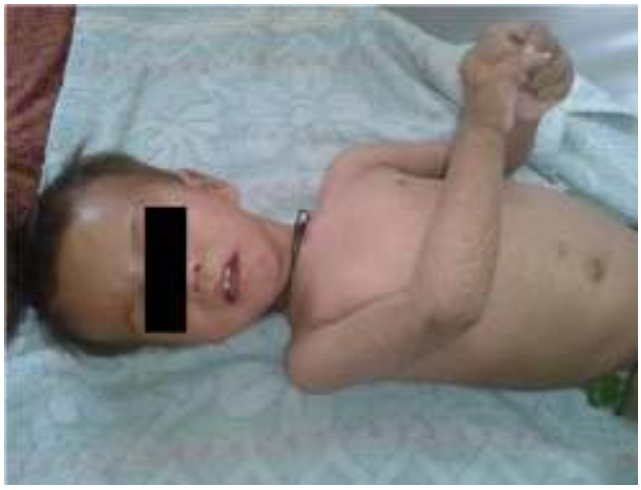


**Figure 1. Increased tone in upper limbs along with icthyotic skin changes in one and half year old male sibling.**

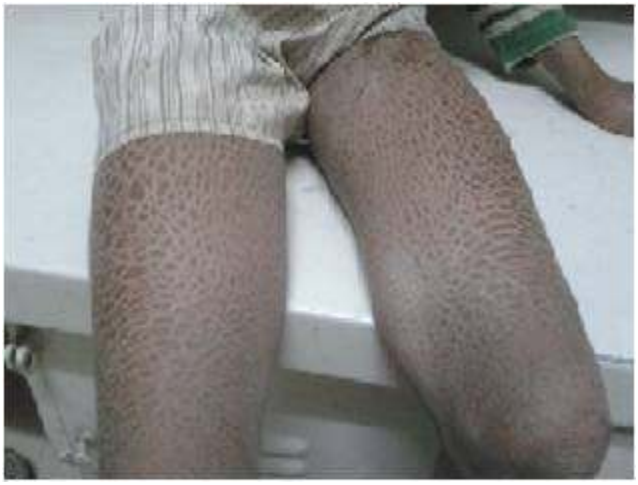
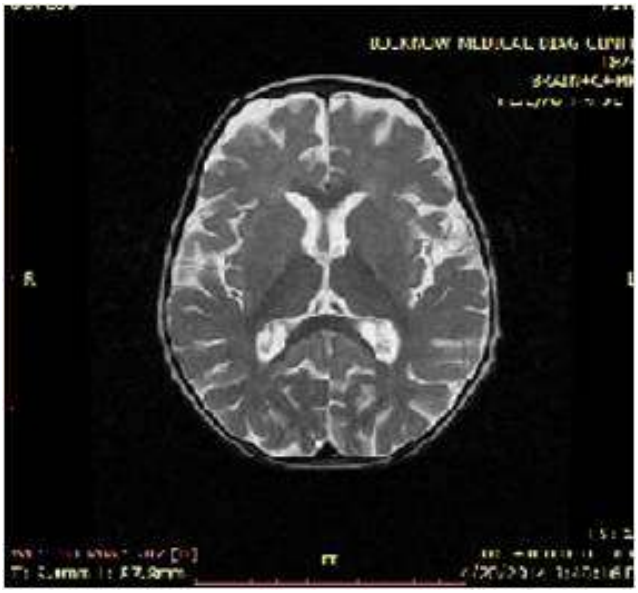


**Figure 2. Icthyotic skin changes in 13 years old female sibling.**

Laboratory examinations revealed an anemia with hemoglobin 4.2 g/dl (anisocytosis, poicylocytosis, and hypochromia) and total leukocyte count- 4000/$mm^3$, platelet count 480.000/ $mm^3$.Serum $B_{12}$ and folate levels were within the normal limits. Chest X Ray was normal. Fundus examination and electroencephalogram were found to be normal. Magnetic resonance imaging (MRI) showed hyperintense signal in peri and supraventricular white matter especially near bifrontal horn on T2 weighted and flair images, mild ventricular enlargement and restriction in diffusion weighted images in peri and supraventricular region. A Sharp lipid peak at TE 35 with mild decrease in NAA peak on 144 TE was found on magnetic resonance spectroscopy (MRS).



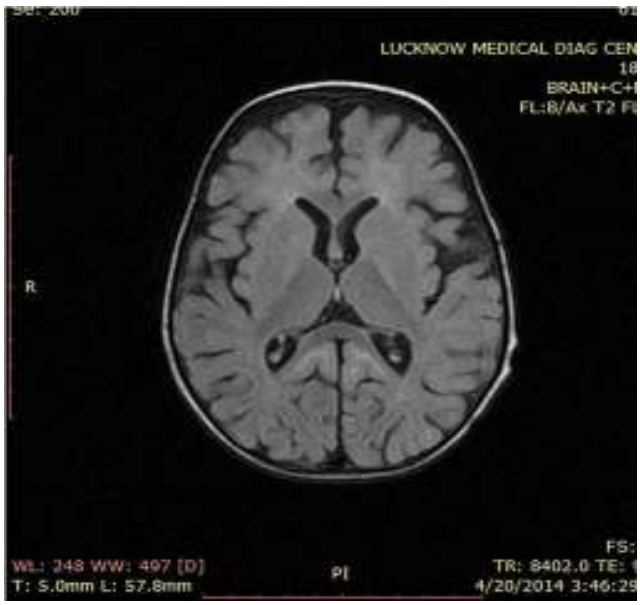


**Figure 3. T2W Axial and FLAIR image showing hyperintense signal in peri and supraventricular white matter especially near bifrontal horn**.

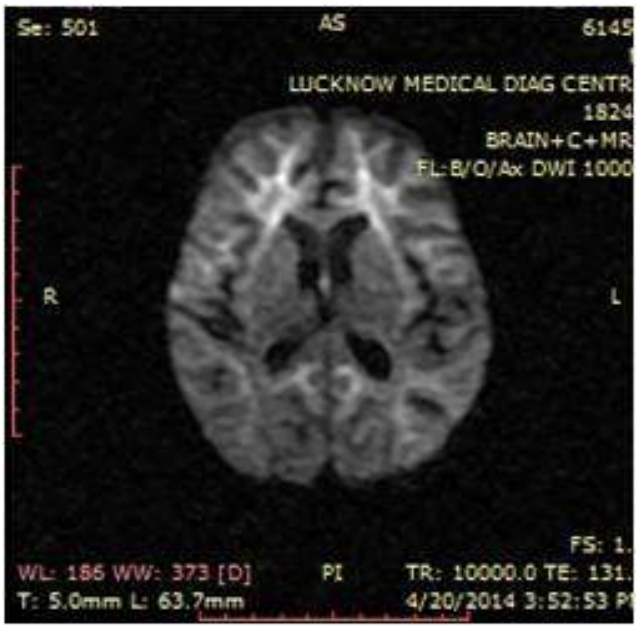



**Figure 4. Restriction in Diffusion weighted imaging in periventricular and supraventricular region.**

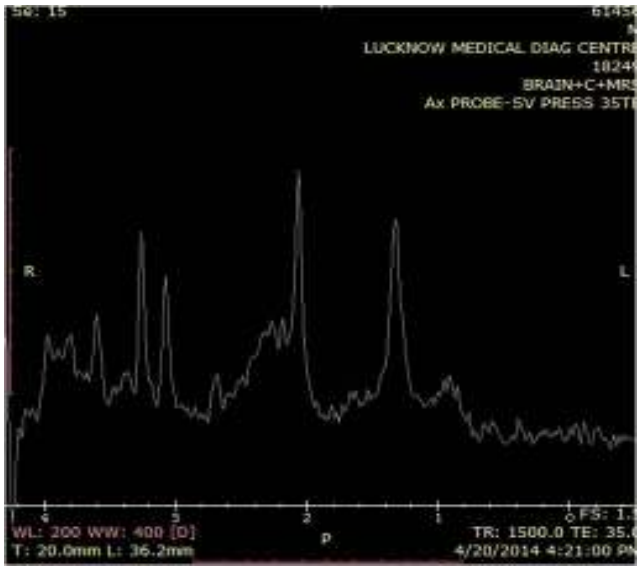



**Figure 5. MRS showing sharp lipid peak at TE35 with mild decrease in NAA Peak on 144 TE.**

Based on clinical picture, MRI and MRS findings diagnosis of Sjogren Larsson Syndrome was made. The child was transfused packed red blood cells and iron, folate and multivitamins supplementation was given. Propanolol and baclofen were started for tremors and spasticity respectively. Fat restricted diet was advised and attendants were trained for physiotherapy. With treatment general condition improved and tremors subsided.

Two female siblings of child aged 6 and 13 years also had features of SLS. Both had intellectual disability, icthyosis involving limbs, trunk and neck and spastic paraparesis (Figure 2). They had skin changes and global developmental delay since birth. Both female siblings could not be investigated because of financial problems. Parents did not have any other normal child in the family.

**Discussion**

Sjögren-Larsson Syndrome (SLS), is an uncommon neurocutaneous disorder that exhibits autosomal recessive inheritance. It is characterized by intellectual disability, congenital ichthyosis and spastic diplegia or quadriplegia [1]. Though a high prevalence of SLS has been observed in north east of Sweden, it is rare in other parts of world and only few cases have been reported from India till now. [4,5]

SLS is 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 [2]. FALDH catalyses the oxidation of long chain aldehyde to fatty acids and its deficiency leads to accumulation of aldehyde-modified lipids or fatty alcohol in the skin and in the myelin [6]. There is also evidence of defective leukotriene B4 (LTB4) degradation caused by FALDH deficiency in patients with SLS.[7,8]

There is usually spastic diplegia, occasionally tetraplegia, with intellectual disability, epilepsy, and speech defects, dental, dermatological, skeletal, and retinal changes [4]. In quadriplegic patients also lower limbs are predominantly involved. In reported youngest sibling tone was increased more in upper limbs as compared to lower limbs. Other two female siblings had predominantly lower legs involvement. We also observed tremors in upper limbs in youngest sibling which have not been reported previously in SLS patients. Skin changes in SLS are in form of icthyosis 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 [6]. Neurologic symptoms and signs appear during the first year or two of life. Approximately one-half of the patients are non-ambulatory and most others require braces or crutches to walk [3]. A distinctive ophthalmologic finding is the presence of retinal crystalline inclusions, so-called glistening white dots, surrounding the fovea [9,10]. Although all SLS patients do not have the retinal inclusions, their presence is a pathognomonic feature for this neurocutaneous disease. Photophobia and myopia are also often present. Our patients presented with classical features including icthyosis and spastic quadriplegia but no ophthalmological findings.

MRI shows periventricular lesions, high intensity on T2-weighted and low intensity on T1-weighted images at trigones of the lateral ventricles. Corpus callosum were involved. No atrophy or circumscribed lesions were seen on MRI. 1H-MRS of these lesions revealed high lipid and low N-acetyl aspartate peaks. MR imaging and proton MR spectroscopy of gray matter were normal [11,12,13]. The skin biopsy in SLS patients shows hyperkeratosis, focal parakeratosis, acanthosis, papillomatosis, and sparse dermal lymphocytic inflammatory infiltrate [5]. Genetic study and enzyme analysis could not be done due to financial constraints.

Treatment is mainly supportive. Oral acitretin therapy and dietary intervention a low-fat diet supplemented with medium-chain fatty acids is currently being evaluated in controlled trials for efficacy in improving neurologic and dermatologic symptoms. Improvement has been reported anecdotally[14,15] Topical medications, such as calcipotriene ointment, urea cream, and mineral oils, as well as frequent bathing or showering, have limited efficacy for patients with SLS. Favorable results have been reported with the use of zileuton, which inhibits LTB4 synthesis [16]. Physical therapy is important to counteract spasticity and preserve mobility for as long as possible [15,17].

So, skin examination should be done in all children presenting with developmental delay and/ or epilepsy and presence of icthyosis should prompt the diagnosis of Sjogren Larsson Syndrome.

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