Case Report

Indian Journal of Genetics and Molecular Research
Volume 10 Number 2, July-December 2021
DOI: http://dx.doi.org/10.21088/ijgmr.2319.4782.10221.3

Sjögren–Larsson Syndrome (SLS) - A Case Report

Jyoti Yadav[1], Jitesh Kumar Gupta[2], Jyoti Prakash Maurya[3], Mona Srivastava[4]

How to cite this article:
Jyoti Yadav, Jitesh Kumar Gupta, Jyoti Prakash Maurya, Mona Srivastava/Sjögren–Larsson Syndrome (SLS) - A Case Report /Indian J Genet Mol Res. 2021;10(2):51–55.

Abstract

Introduction: Sjogren Larsson syndrome (SLS) is a rare autosomal recessive inborn error of lipid metabolism. The classical triad of ichthyosis, mental retardation and spasticity characterizes clinical features. There are only 200 cases reported worldwide.

Aim: To report 3 cases from the same family and the index patient having a classical presentation.

Case: Eldest female and two males, who display congenital ichthyosis, whose parents have no such symptoms. Both males complained of diffuse scales all over the body with mild erythema and severe itching, since birth, no history of blisters was present. Nails, teeth, hair and sweating were normal. They had itching all over the body with accentuation over flexural areas. The youngest has neurological as well as psychiatric problems as Bipolar disorder.

Discussion: Mental retardation is common, depressive episodes are a common sequlae, however clear bipolar illness is not reported. Some behavioral phenotypes of ADHD have been reported in the literature . Seizures are commonly reported, however our index patient did not have any history. Most studies on icthyosis give a similar picture as above cases.

Keywords: Sjögren–Larsson Syndrome (SLS); Ichthyosis; Autosomal recessive; Erythema; Contracture.

Introduction

Sjogren Larsson syndrome (SLS) is a rare autosomal recessive inborn error of lipid metabolism due to mutations in the ALDH3A2 gene that result in a deficiency of fatty aldehyde dehydrogenase (FALDH)(Fig 1).[1] The classical triad of ichthyosis, mental retardation and spasticity characterizes clinical features.[2] There are only 200 cases reported worldwide.[3] Preterm birth is common pre-sumably caused by abnormal lipid metabolism. It is hypothesized that preterm birth in SLS is di-rectly caused by increased fetal urinary excretion of (LTB4) leukotriene B4, a pro-inflammatory mediator into the amniotic fluid.[4,5] The diagnosis of SLS should be considered in a neonate or in-fant with congenital icthyosis and emerging neurological features.[6] One should look for ocular fea-tures and pruritus to make the diagnosis.[7] Cerebral MRI reveals arrested myelination or demye-lination in white matter and lipid peak on spectroscopy help in making the diagnosis.[8] In terms of behavioural features there is some limited evidence from case studies[3], and a more systematic study in 25 boys with XLI, that males with SLS may be at increased risk of developing Attention Deficit Hyperactivity Disorder (ADHD)(notably the inattentive subtype). Here we report of four children from India who are siblings, three males had mild to severe form of the disorder while an older sister had the mildest form of the disorder.

Author's Affiliation: [1,2,3]Junior Resident, [4]Professor & Head, Department of Psychiatry, Incharge De-addiction, Nodal officer CoE (NMHP) Institute of Medical Sciences, Banaras Hindu University, Varanasi 221005, India.

Corresponding Author: Mona Srivastava , Professor & Head, Department of Psychiatry, Incharge De-addiction, Nodal officer CoE (NMHP) Institute of Medical Sciences, Banaras Hindu University, Varanasi 221005, India.

E-mail: drmonasrivastava@gmail.com

Case Report

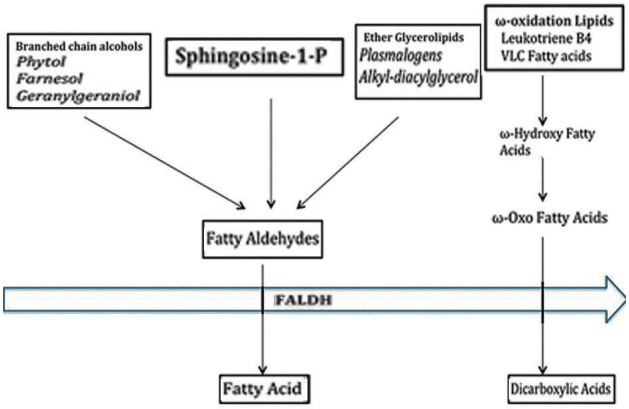

Fig. 1: Metabolic pathway and abnormality in SLS.

Mr. A the youngest male child of 6 siblings was the index patient who was, 25 years old unmarried male educated till class 2, belonging to LSES, Hindu by religion came with his elder brother and mother with total duration of illness since birth having an acute onset, continuously progressive illness with complaints of scaling and dryness of skin, peeling of the skin and erythroderma (more on flexure parts of extremities) and mental submormality since birth, increased tightness and contractures of both limbs since birth but worsening since 3 years of age. He had neurological as well as psychiatric problems as BPAD (bipolar affective disorder). He was bed ridden and unable to walk although able to sit (worsening since 2010) and there was widening of palpebral fissures and dryness of eyes

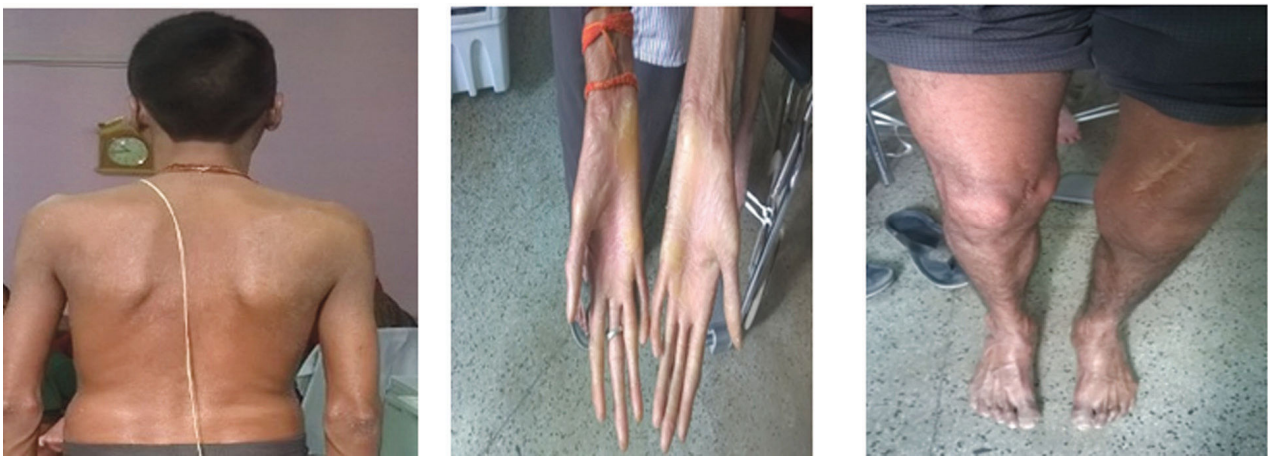

Fig. 2: Elder brother having mild symptoms.

Fig. 3: Skin and digits with scaly lesions and contractures.

(worsening since 2010). Episodes of feeling low and weeping spells lasting for a couple of months since 2011 and alternating episodes of feeling happy, energetic, making plans out of his real capacity and increase in demanding behavior with irritability since 2012.

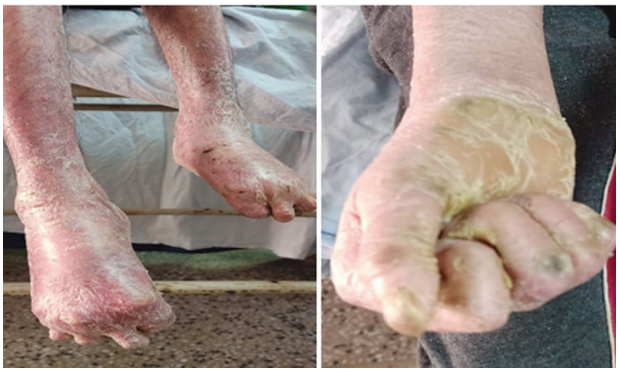

Fig. 4: Nail and terminal phalanges.

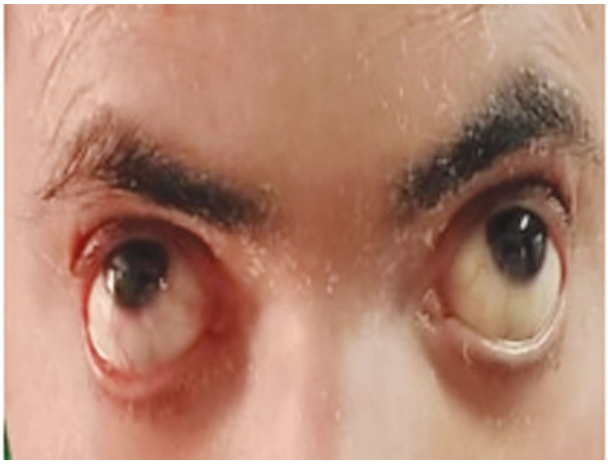

Fig. 5: Ophthalmological changes.

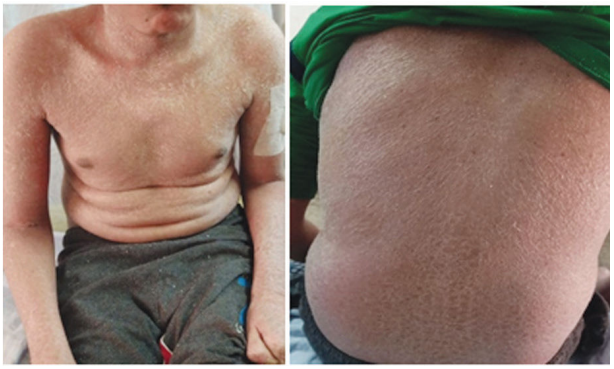

Fig. 6: Scoliosis of spine.

At the age of 2 years, he consulted in Dermatology and a diagnosis of Congenital Ichthyosis was made and asked to apply coconut oil over the skin. Since 3 years of age, he was bedridden and his limbs were folded and tight and appeared thin and wasted. At 15 years of age, consulted in Neurology OPD for difficulty in sitting and walking with increased tone in all muscle groups. He was investigated and advised medications as well as physiotherapy. A diagnosis of spastic quadriplegia was made . He as referred to Psychiatry OPD in 2011 with the complaints of dry scaly skin with itching mainly over flexural aspects with patches of peeling of skin over palmer and planter regions with episode of sadness of mood, withdrawn behavior, suicidal ideations, hopelessness, decreased appetite and weight loss. He was started on antidepressants from Psychiatry OPD but he discontinued treatment after 2-3 months on his own.

1 year later, he had an episode of increased talks, demands, decreased need for sleep, irritability, aggressive and abusive behavior for which he was started on antipsychotics and mood stabilizers and symptoms remitted. Since then, he has been having 2-3 manic episodes every year as the compliance to the medications is poor due to financial constraints faced by the family. He was pre term normal delivery (32-33wks of gestation) at hospital. He cried immediately after birth and his mother noticed dryness of skin after 2 days of birth and dryness & scaling of skin after a couple of days involving his limbs, neck and trunk. His face was only slightly involved. He had delayed walking around 3 years of age, speech was delayed and inability to pronounce certain words with all other milestones attained on time. Born of a non consanguineous marriage. Three generation family history did not reveal any positive finding. Patient was 4th in the order of 6 siblings. Eldest sister expired at the age of 16yrs, had minor scaly lesions on back and palm. 2nd sibling(brother) expired at 2 yrs of age due to diphtheria, he was also having some similar lesions. The elder male 3rd sibling(34 yr married male, teacher) has mild ichthyosis fine large scales covering the body, more pronounced on extremities with mild redness.

Lichenified plaques over antecubital and popliteal fossae were also noted. Mild keratoderma was identified but no blisters were seen. Teeth, nails and hair were all normal. He had mild redness of the eyes without ectropion. Hair examination under microscope was normal. Scalp showed thin layer of scales. Excoriations over arms and legs were also noticed (Fig 2) . Younger 2 sisters 20yrs and 18 yrs respectively are healthy. Physical examination revealed, Skin having diffuse scales all over the body with mild erythematic patches, pruritic patches with accentuation over flexural areas. Nails: absent with atrophy of the terminal digits (Fig. 3 & 4). Teeth: irregularly placed and

crooked with overlapping. Hair: dry, thin and brittle. Eyes: B/L scaly lesions over eyelids; alternate divergent squint with left eye dominance; sclera show inferiorly.

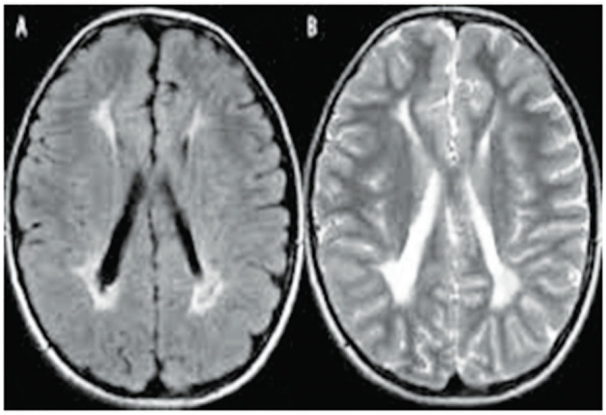

Fig. 7: MRI brain showing periventricular gliosis.

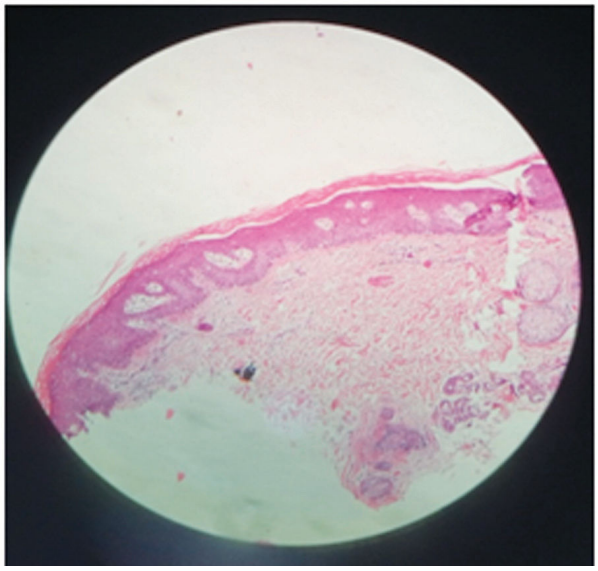

Fig. 8: Skin biopsy.

Ectropion of lid more in right eye than in left; conjunctiva dry and lusterless; cornea clear; pupis normal in size and reacting normally; lens clear; fundus disc- normal (Fig 5). Psychiatric examination showed a kempt cooperative young adult who was lying down. Sat with assistance, eyes wide, blinking infrequent, talking excessively, distracted easily, irritable, expansivity present. He kept demanding for eating different food items. No delusions or hallucina-tions could be elicited. Oriented; impaired intellectual ability, impaired judgment. Insight present for physical problems but absent for psychiatric problems. Systemic examination revealed, motor- power-3/5 in all 4 limbs, Hypertonia in all limbs, Contractures- in both extremities, Deep reflexes brisk, plantars were bilateral flexor response, Ankle clonus was present and scoliosis of spine present (Fig 6). Nails- onychomycosis and absent with atrophy of the terminal digits with erythema and, distal yellowish discoloration (Fig 4). The investigations revealed that all routine were normal, EEG was normal; MRI(Brain)- periventricular gliosis (Fig 7); MRI (spine)- lumbar levoscoliosis with Grade 1 anterolisthesis over L5 over S1 with L5-S1 pseudodisc bulge without nerve root compression (film not available, report was seen); Skin biopsy- hyperkeratosis, mild acanthosis and mild perivascular dermal lymphocytic infiltrate overall features (Fig 8). IQ was measured and found to be mild retardation (70). The parents had no such symptoms. All children were born at full term after an uneventful pregnancy except the index patient.

Discussion

Most studies on icthyosis gives a similar picture as above cases. A study using an online survey(3), advertised worldwide, collected detailed self- or parent-reported information on behavior in adult (n = 58) and younger (≤18yrs, n = 24) males with XLI for comparison to data from their non-affected brothers, and age/gender-matched previously-published normative data. The survey comprised demographic and background information (including any prior clinical diagnoses) and validated questionnaires assaying phenotypes of particular interest (Adult ADHD Self-Report Scale).[9] Result showed that the individuals with SLS generally exhibited normal sensory function. Boys were at increased risk of developmental disorder, whilst adults with the condition were at increased risk of both developmental and mood disorders. Both adult and younger groups scored significantly more highly than male general population norms on measures of inattention, impulsivity, autism-related traits, psychological distress and disruptive behavioral traits.[3,6]

Similar problems was seen in the younger adult in our case too. Mental retardation is common, depressive episodes are a common sequlae, however clear bipolar illness is not reported. Some behavioral phenotypes of ADHD have been reported in the literature.[6,9] Seizures are commonly reported, however our index patient did not have any history. Though in such cases biochemical (urinary concentration of leucotriene B4 and 20-OH-LT B4) and genetic studies (for ALDH3A2 gene)[6,8] are desired we could not perform these due to paucity of resources. "Glistening white dots" in the retina is a pathognomic clinical feature[7] (could not be visualized in this case). Cerebral MR

spectroscopy reveals a characteristic abnormal lipid peak at 1.3ppm and a small peak at 0.9ppm correlating with Fatty aldehyde dehydrogenase.[8] The primary role of FALDH is oxidation of medium and long-chain aliphatic aldehydes derived from fatty alcohol, phytanic acid, ether glycerolipids and sphingolipids. Improvements have been observed following treatment with citicoline, due to the role this nootropic plays in the biosynthesis of structural phospholipids involved in the formation and repair of the neuronal membrane.[1,2,8] Since this is an autosomal recessive disorder hence this could be also the reason why the female reported in our case had less severe symptoms than the males. Newer modes of treatment include: diet changes specifically, regimen consisting of reduction of dietary fat to 30% of the total intake of calories. The diet can also was also be supplemented with n-3 and n-6 fatty acids to obtain a linoleic/linolenic acid ratio of 6. The cheapest option is using coconut oil.[4] Other potential dietary management includes restriction of phytanic acid and its alcohol precursor phytol. Apart from diet certain agents called as Aldehyde Scavengers are also used; the aldehyde scavengers include hydroxylamine derivatives and amino-containing small mol-ecules.[4] A phase 2 trials has been initiated with this agent and the results are awaited.[4]

Limitations

There are a lot of limitations to this report, as many documents were missing when the individuals were brought to us and adequate information was difficult to collect about their childhood and adolescence. Also limited studies were found which talked about human cases and explanation of the causes in humans.

References

1. De Laurenzi V, Rogers GR, Hamrock DJ, Marekov LN, Steinert PM, Compton JG, Markova N, Rizzo WB. Sjögren–Larsson syndrome is caused by mutations in the fatty aldehyde dehydrogenase gene. Nature genetics. 1996 Jan;12(1):52-7.
2. Rizzo, W.B. (2007). Sjö gren-Larsson syndrome: Molecular genetics and biochemical pathogenesis of fatty aldehyde dehydrogenase deficiency. Mol. Genet. Metab. 90, 1–9.
3. Chatterjee S, Humby T, Davies W.Behavioural and Psychiatric Phenotypes in Men and Boys with X-Linked Ichthyosis: Evidence from a Worldwide Online Survey. PLoS One. 2016; 11(10): e0164417.
4. Clinical, biochemical and molecular genetic characteristics of 19 patients with the Sjögren–Larsson syndrome. 2019 Brain 124(7).
5. Jagell S, Liden S. Ichthyosis in the Sjögren Larsson syndrome. Clinical genetics. 1982 Apr;21(4):243-52.54.
6. Srinivas SM, Raju KV, Hiremagalore R. Sjögren-Larsson syndrome: A study of clinical symptoms in six children. Indian dermatology online journal. 2014 Apr;5(2):185.
7. Sheth HG. Ocular features of Sjogren–Larsson syndrome. Clinical & experimental ophthalmology. 2007 Jan;35(1):98-9.
8. Rizzo, W.B., Carney, G., and Lin, Z. (1999). The molecular basis of Sjo gren-Larsson syndrome: Mutation analysis of the fatty aldehyde dehydrogenase gene. Am. J. Hum. Genet. 65, 1547–1560.
9. Shah V, Rambhia K, Mukhi J, Singh RP. Sjogren–larsson syndrome: A rare case report. Indian dermatology online journal. 2018 Sep;9(5):338.