Sjögren-Larsson syndrome: A study of clinical symptoms in six children

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ABSTRACT

Sjögren-Larsson syndrome (SLS) is a rare autosomal recessive disorder characterized by triad of congenital ichthyosis, spastic paresis, and mental retardation. It is an inborn error of lipid metabolism caused by deficiency of the enzyme fatty aldehyde dehydrogenase. We report our observations of six children with SLS.

Key words: Congenital ichthyosis, mental retardation, spastic paresis

Access this article online

Website: www.idoj.in

DOI: 10.4103/2229-5178.131099

Quick Response Code:

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INTRODUCTION

Sjögren-Larsson syndrome (SLS) is an autosomal recessive neurocutaneous disorder characterized by clinical triad of congenital ichthyosis, diplegia or tetraplegia, and learning disability/mental retardation.[1] SLS is caused by mutation in the gene for fatty aldehyde dehydrogenase (FALDH) which catalyzes oxidation of long chain aliphatic alcohols to corresponding fatty acids. This leads to accumulation of aldehyde-modified lipids or fatty alcohol which probably disrupts the barrier function of skin and white matter of brain.[2] We describe a series of six children with SLS seen over a period of 1 year to highlight their varied clinical presentation.

CASE REPORT

The study comprised six children, ranging from 1 to 12 years with an equal gender ratio diagnosed as SLS seen during the period January 2012 to December 2012, referred from pediatric neurology department. The clinical summary of patients is described in Table 1. Four children were born of consanguineous marriage. Five children were born prematurely. History of collodion membrane was present in one child. All the children had ichthyosis since birth and were associated with delayed milestones and speech abnormalities [Table 1]. There was generalized ichthyosis in all patients with relative sparing of face [Figure 1]. Type of scales varied from fine [Figures 2 and 3] to lamellar type [Figures 4 and 5]. Pruritus was present only in two children. Five children had seizures and were on anticonvulsants. Spastic diplegia was present in four cases and two children had spastic quadriplegia [Figure 6]. One child (case 1) had cardiomegaly with congenital heart disease. One child had nystagmus. None of our children had any other ocular findings. Skin biopsy was done in all children; features showed hyperkeratosis, parakeratosis, and normal to thinned out granular layer with mild perivascular lymphocytic infiltrate in dermis consistent with ichthyosis [Figure 7]. Brain magnetic resonance imaging (MRI) in all children revealed delayed myelination with signal changes in periventricular region predominantly involving occipital region [Figure 8].

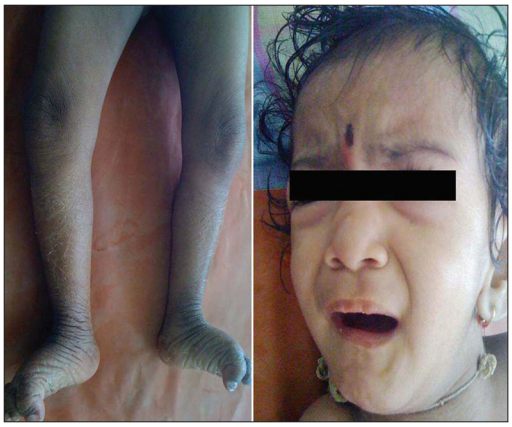

Figure 1: Case 1-Fine scaling over extremities with sparing of face in a 1.5-year-old female child

DISCUSSION

In 1957, Sjögren and Larsson described the

Table 1: Clinical summary of patients

Case	1	2	3	4	5	6
Age (years)	1.5	2.5	3	4	5	12
Sex	F	M	M	F	M	F
Consanguinity	–	–	+	+	+	+
Preterm/term	Term	Preterm	Preterm	Preterm	Preterm	Preterm
History of collodion membrane	–	–	–	+	–	–
Age of onset of skin lesions	Birth	Birth	Birth	Birth	Birth	1 week of age
Ichthyosis	Generalized, face spared	Generalized, flexures spared	Generalized	Generalized, face spared	Generalized	Generalized, face spared
Type of scales	Fine	X-linked type	Fine	Lamellar scales	Lamellar scales	Lamellar scales
Palmoplantar keratoderma	+	–	–	–	+	+
Age of onset of neurological symptoms (months)	6	8	12	12	12	18
Spastic paresis	Spastic quadriplegia	Spastic diplegia	Spastic quadriplegia	Spastic diplegia	Spastic diplegia	Spastic quadriplegia
Seizures	+	+	+	+	–	+
Type of seizures	GTCS	focal	Myoclonic/GTCS	GTCS		Focal
MR/delayed milestones	+	+	+	+	+	+
Eye abnormalities	–	Nystagmus	–	–	–	–
Speech disorders	Unable to speak any meaningful words	Unable to speak any meaningful words	Speaks few words with meaning	Speaks two word phrases with dysarthria	Speaks 2-3 words phrases with dysarthria	Speaks with single word sentences without dysarthria
Associated disorders	Cardiomegaly, CHD	–	–	–	–	–

M: Male, F: Female, +: Present, –: Absent, MR: Mental retardation, GTCS: Generalized tonic clonic seizures, CHD: Congenital heart disease

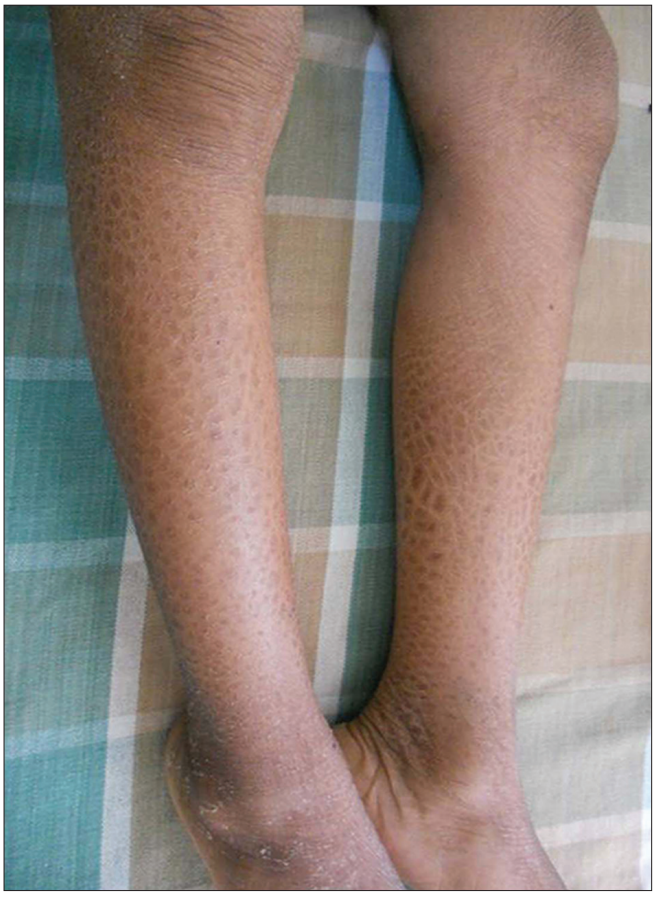

Figure 2: Case 2-X-linked type of ichthyosis over extremities

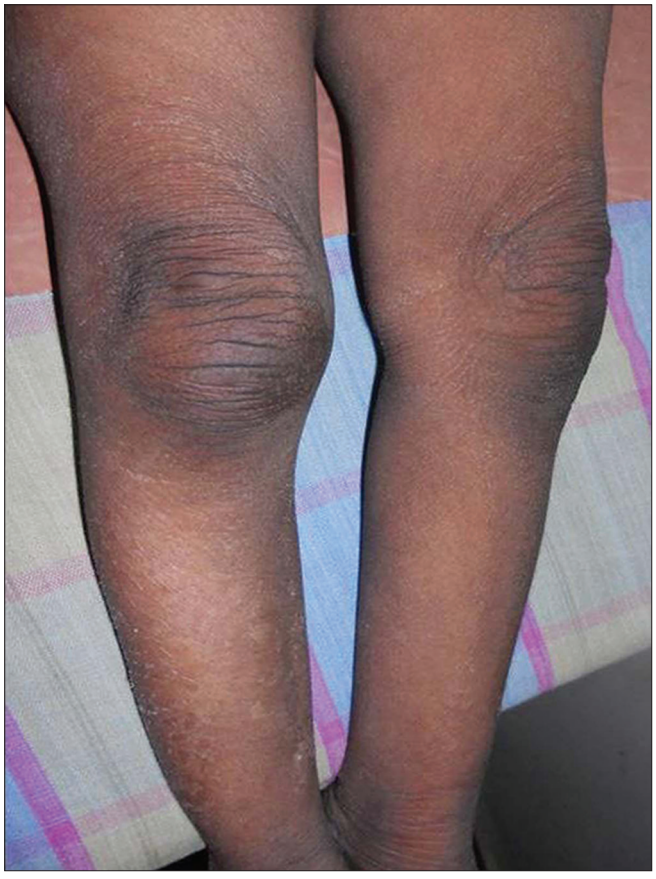

Figure 3: Case 3-Fine scaling over extremities similar to ichthyosis vulgaris

Figure 4: Case 4-Three-year-old male child with lamellar type of scales over the extremities

disorder affecting 28 patients from a highly consanguineous population in a remote area of Sweden with clinical triad of mental retardation, spastic diplegia, and congenital ichthyosis.[1] The incidence of SLS is 1 in 200,000 births in Sweden, but it occurs more rarely worldwide. SLS is caused due to recessive mutations in the fatty aldehyde dehydrogenase (FALDH) gene FALDH3A2 on the short arm of chromosome 17p11.[2] More than 72 mutations in FALDH3A2 are known in SLS patients.[3]

The disorder presents at birth or in the neonatal period with varying degrees of erythema and ichthyosis, but a collodion membrane is rarely seen. Infants with SLS tend to be born prematurely. Although erythema may be present at birth, it is usually not evident after a year of age. Persistent pruritus is common. The morphology of the scaling may be fine, dandruff-like similar to ichthyosis vulgaris or X-linked recessive ichthyosis or lamellar similar to autosomal recessive congenital ichthyosis.[4] The ichthyosis is generalized, but sites more predominantly affected are lower abdomen, sides and nape of neck, and flexures. A distinctive sign is periumbilical hyperkeratosis with radiating furrows.[5] Palmoplantar keratoderma is seen in 50% of cases. The diagnosis of SLS is delayed until the onset of neurological

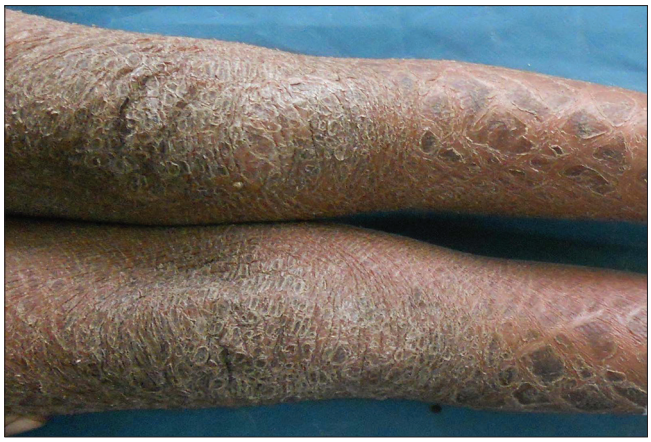

Figure 5: Case 5-Lamellar type of scaling over extremities

symptoms, because only cutaneous manifestations are present at birth.

The neurological symptoms appear in the first or second year of life. Speech and motor delays are the common initial signs. Spasticity appears before 3 years of age and is more severe in lower limbs. Seizures are present in one-third of patients. There is no progression of neurological findings or mental retardation after puberty.[6] Neuroimaging studies of the cerebral white matter and corticospinal tracts shows white matter disease, delayed myelination, periventricular gliosis, and a permanent myelin deficit.[7] One-third of patients present with perifoveal glistening dots in the ocular fundus which appear after several years of age.[8] None of the children in our cohort had retinal changes. Long-term follow-up is necessary to document retinal changes.

The histopathological features are nonspecific and include hyperkeratosis and acanthosis with a normal granular layer. The diagnosis of SLS can be confirmed by measurement of enzyme activity in cultured skin fibroblasts or leucocytes. Sequence analysis of FALDH3A2 gene causing mutations is highly sensitive and also detects possible carrier.[9]

There is no permanent cure for SLS and no specific therapy. Multidisciplinary approach includes team of dermatologist, neurologist, ophthalmologist, orthopaedician, and physiotherapist. Topical emollients, keratolytics, calcipotriol, and oral retinoids can be used to improve the cutaneous symptoms.[10] All our patients were managed symptomatically with topical emollients and keratolytics. Cutaneous symptoms improved after treatment.

In our case series, one child had congenital heart disease and cardiomegaly that has not been described in earlier reports. Due to the limited availability of diagnostic laboratories, enzyme analysis was not done in our study. High index of suspicion is necessary for the diagnosis of SLS. Any case of congenital

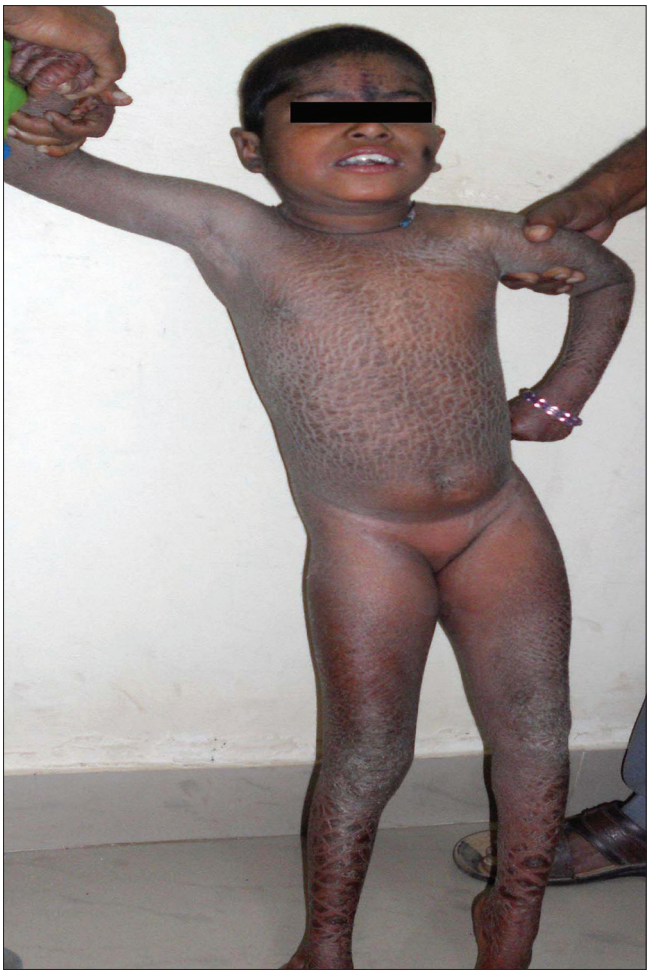

Figure 6: Case 6-Generalized ichthyosis (lamellar type scales) with spastic quadriplegia

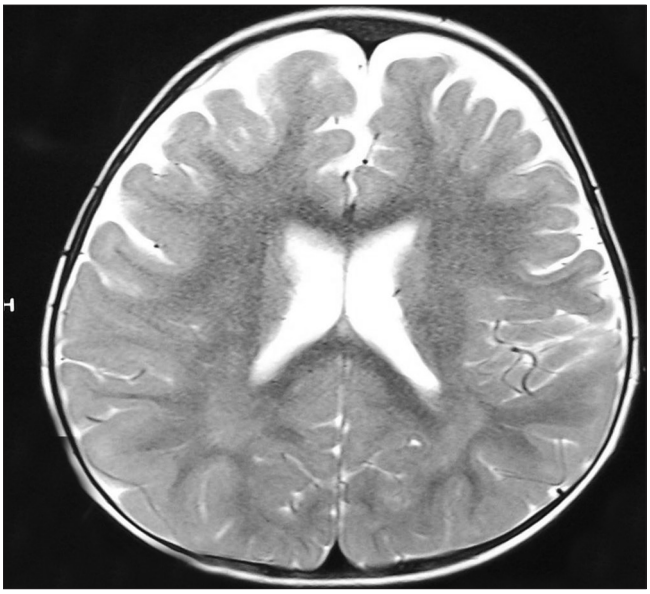

Figure 8: T2-weighted magnetic resonance imaging (MRI) showing signal changes in bilateral peritrigonal regions

ichthyosis with spastic paresis and mental retardation should be evaluated for SLS.

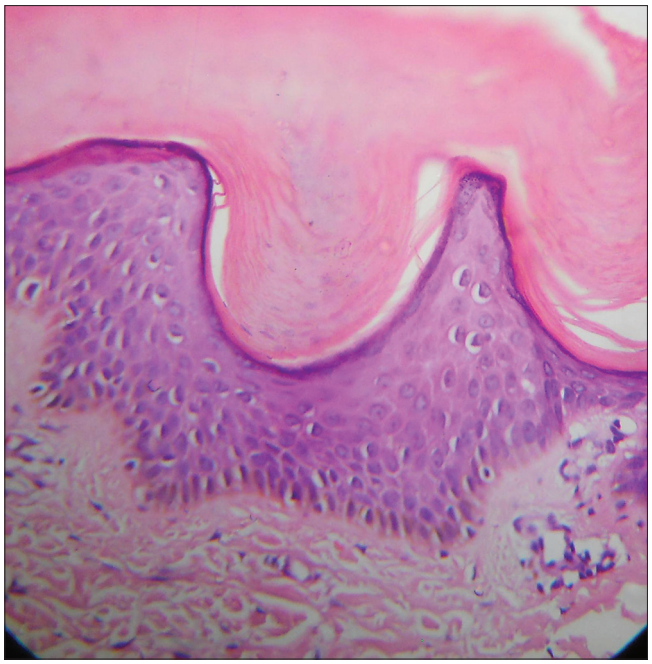

Figure 7: Epidermis shows hyperkeratosis, parakeratosis, thinned out granular layer with mild perivascular lymphocytic infiltrate in dermis (H and E, ×40)

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Cite this article as: Srinivas SM, Raju KV, Hiremagalore R. Sjögren-Larsson syndrome: A study of clinical symptoms in six children. Indian Dermatol Online J 2014;5:185-8.

Source of Support: Nil, **Conflict of Interest:** None declared