



## White Matter Diseases YES, Multiple Sclerosis NO, Sjogren - Larsson Syndrome: Another Differential Diagnosis of Multiple Sclerosis

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### ABSTRACT

Sjogren-Larsson Syndrome (SLS) is an inherited autosomal recessive neurocutaneous disorder with congenital ichthyosis, spastic diplegia or quadriplegia and mental retardation.

We report a case of Sjogren-Larsson Syndrome with clinical profile (mental retardation, ichthyosis, spastic diplegia) and MRI findings such as seen in multiple sclerosis (MS). So this rare syndrome can be another differential diagnosis of MS.

**Key words:** Multiple Sclerosis; Sjogren-Larsson Syndrome

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### Introduction

Multiple sclerosis (MS) is the most common inflammatory demyelinating disease of the central nervous system in young and middle-age adults, but also affects older people (1,2). Typical features

include optic neuritis, motor weakness, numbness, diplopia, nystagmus, dysarthria, tremor, ataxia, impairment of deep sensation and bladder dysfunction and impairment of mental function with typical distribution of white matter lesions (WMLs) (1-3).

According to the McDonald criteria for MS, the diagnosis requires objective evidence of dissemination in time and space of lesions. This can be very helpful in differentiating them from vascular lesions and other WMLs (1,3). As a consequence, there is an important role for MRI in the diagnosis of MS, since MRI can show multiple lesions (dissemination in space), some of which can be clinically occult, and also can show new lesions on follow up scans (dissemination in time) (1-3). Typical sites for MS lesions are corpus callosum, U-fibers, temporal lobe, brainstem, cerebellum and spinal cord. All or some of these lesions can appear in other white matter diseases. In small vessel disease there may be involvement of the brainstem, but it is usually symmetrical and central, while in MS it is peripheral (1,2).

Sjogren-Larsson syndrome (SLS) is an inherited neurocutaneous disorder and autosomal recessive with congenital ichthyosis, spastic diplegia or quadriplegia and mental retardation. Less common features are retinal changes, short stature, kyphoscoliosis, preterm birth, seizure and delayed speech (1,2). SLS caused by mutations in the gene *ALDH3A2* for the

microsomal enzyme fatty aldehyde dehydrogenase (FALDH) on chromosome 17p11 (1).

### Case Presentation

Index patient was a 34 year-old female who was admitted to Ghaem hospital affiliated to Mashhad University of Medical Sciences in November 2013 because of weakness and inability to walk. She was the fourth child of healthy consanguineous parents. She had delivered at preterm (31 weeks of gestation) by normal vaginal delivery. Birth weight, length and head circumference measurements were unknown.

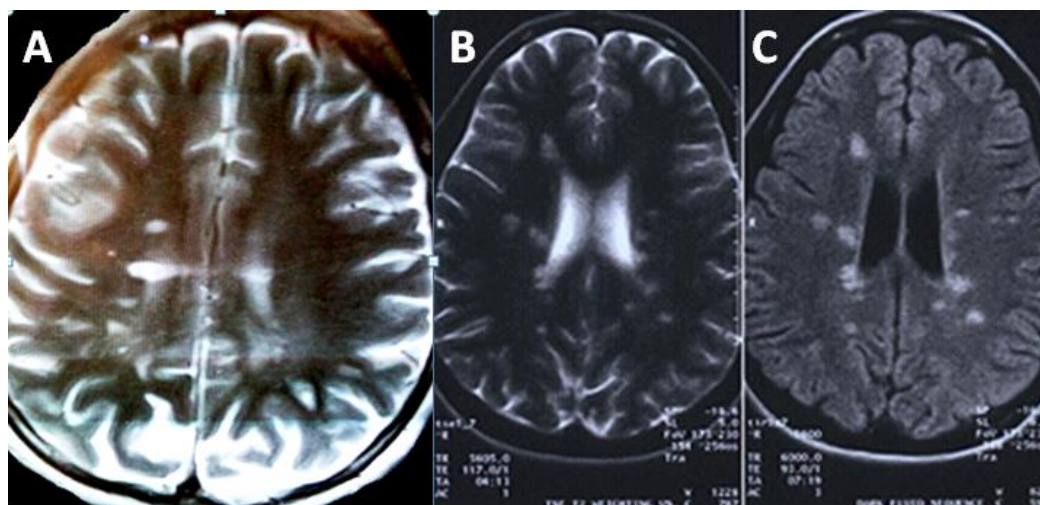
On detailed history, the child attained sitting without support at eighteenth month and walking with support at second year of age. She had global developmental delay. Stiffness in lower limbs started in 4 years before, with progressive increase up to the time of presentation. Physical examination showed generalized dryness of skin most prominent on lower limbs with severe pruritus, that is ichthyotic lesion (Figure 1A). The nail, palms and soles were affected (Figure 1B, 1C). In skeletal examination she had short stature.



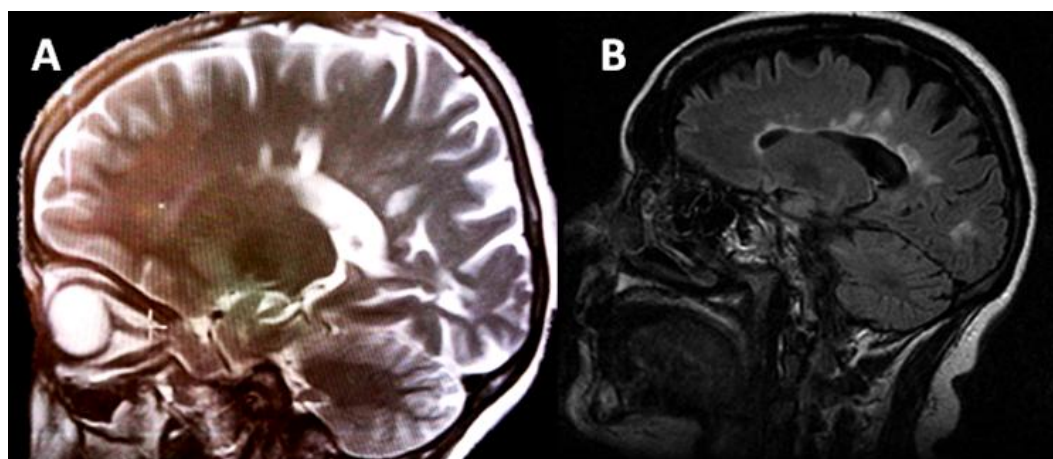
**Figure 1:** Ichthyotic lesions over lower extremities (A), Ichthyotic lesions associated with involved nails (B), Nails deformity (C)

In neurological examination she revealed mental retardation, spasticity in both lower limbs; brisk deep tendon reflexes and symmetric bilateral extensor plantar response. Hoffman sign in upper limbs were detected. She had photophobia and decreased visual acuity but her fundoscopy was normal. Chest radiography and all routine hematological investigations were normal.

Electroencephalogram (EEG) showed mild slowing over both hemispheres. CSF analysis was normal. MRI of the brain showed diffuse and nonsymmetrical plaques with high signal intensity on T2 weighted sequence in bilateral deep periventricular white matter and corpus callosum. Some of these lesions were also plumb to the ventricles (Figure 2, 3).



**Figure 2:** T2 weighted axial MRI image showing bilateral hyperintense lesions in periventricular white matter in Sjogren-Larsson syndrome (A), T2 weighted (B) and Fluid Attenuated Inversion Recovery (FLAIR) axial MRI image (C) showing bilateral hyperintense lesions in periventricular white matter in MS (B).



**Figure3:** T2 weighted sagittal MRI image showing oval demyelinations over corpus callosum in Sjogren-Larsson Syndrome (A), T2 weighted sagittal MRI image showing corpus callosum involvement in MS (B)

## Discussion

The disorder was first described in 1957 by Sjogren-larsson, who reported a series of 28 patients with a clinical triad of ichthyosis, spastic diplegia or quadriplegia and mental retardation (4-8). SLS is a recessively inherited neurocutaneous disorder that is caused by mutation in ALDH3A2 gene that encodes fatty aldehyde dehydrogenase (FALDH) and more than 70 mutations have been described (7). The deficiency of FLADH also affects the metabolism of leukotriene B<sub>4</sub>(LTB<sub>4</sub>), a proinflammatory mediator, leading to accumulation of LTB<sub>4</sub> and omega-hydroxy-LTB<sub>4</sub> which are probably responsible for the severe pruritus that is characteristic of the disease (4-9).

The cutaneous symptoms are in form of ichthyosis which is a generalized hyperkeratosis of the trunk, joints, and the dorsal aspect of the hands and the feet. Pruritus is a prominent feature that is not found in other types of ichthyotic skin disorders (4-11).

The occurrence of glistening clots on fundoscopic examination strongly suggests SLS, other ophthalmologic abnormalities are photophobia, macular dystrophy and decreased visual acuity, these features are seen in one third of cases (4-11).

The neurologic symptoms develop later in the first or second year of life. Spasticity impedes motor development and prevents many patients from walking. Mental retardation ranges from mild to moderate severity. Most cases with SLS have learning disability and speech disorders (12,13).

The hallmark of SLS is demyelination of the cerebral white matter and of the corticospinal and vestibulospinal tracts. MRI reveals abnormal high signal intensity on T2

weighted and Fluid Attenuated Inversion Recovery (FLAIR) sequences especially in periventricular frontal, parietal lobes, corpus callosum and corona radiata. Typically, subcortical white matter U fibres are spared (10,14).

Mutation analysis of the ALDH3A2 gene is a highly sensitive method of confirming the diagnosis of SLS (4,12). We could not carry out mutation analysis because of equipment limitation.

## Conclusion

The diagnosis of SLS should be considered in a neonate or infant with congenital ichthyosis and neurological features. One should look for ocular features and pruritus to make the diagnosis. Brain MRI reveals arrested myelination or demyelination in white matter and lipid peak on MRS help in making the diagnosis. White matter lesions that mimic those of multiple sclerosis may be detected in patients harbouring different diseases. Virtually all the characteristic features of multiple sclerosis are sometimes met in other settings affecting predominantly the white matter.

Though in such cases biochemical and genetic studies are desired because we could not perform these due to paucity of resources.

## Conflict of Interest

No Conflict of Interest.

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