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Case Report

An interesting case of neurocutaneous syndrome

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ABSTRACT

Neuroichthyosis is a group of rare genetically determined disease with cutaneous and neurological manifestations due to abnormalities in any of the following: lipid metabolism, glycoprotein synthesis, or intracellular vesicle trafficking. There are about 16 disorders with known genetic aetiology like Sjogren Larssons syndrome (SLS), Refsum disease, Gauchers disease type 2, ELOVL4 deficiency etc. Among the various neuroicthyosis syndromes, Sjogren Larsson syndrome is the most common entity characterised by ichthyosis, spastic diplegia or tetraplegia, cognitive dysfunction, seizures, and a maculopathy with glistening white dots. We hereby report a case of neuroichthyosis disease who presented to us with developmental delay, spastic paraplegia, seizure and ichthyosis, whose genetic testing showed homozygous mutation in ALDH3A2, suggestive of Sjogren Larsson syndrome.

Keywords: Neuroichthyosis, Seizures, Genetic disease, Cognitive dysfunction, Sjogren Larsson syndrome

INTRODUCTION

Neuroichthyosis is a group of rare genetically inherited disease with cutaneous and neurological manifestations.

There are about 16 disease with known genetic locus like Sjogren Larsson syndrome (SLS), Refsum disease, multiple sulfatase deficiency, keratitis-ichthyosis-deafness syndrome etc.

SLS is the most common entity among the neuroichthyosis syndromes. SLS is an autosomal recessive disease, characterised by ichthyosis, spastic diplegia or tetraplegia, cognitive delay, seizures, and a maculopathy with glistening white dots.[1] Mutations of the ALDH3A2 gene which encodes for the fatty aldehyde dehydrogenase (FALDH), a microsomal enzyme that oxidizes long-chain aldehydes to fatty acids is responsible in about 95 percent of cases.

It was first described by Sjögren and Larsson in 1957. It is a very rare disease in Indian and Asian population.[2]

CASE REPORT

A seven year old girl came to our out-patient department, with history of motor and language developmental delay and fever provoked seizures since 3 years of age. She had dry thick skin since 1 year of age. She was born to parents with history of second degree consanguineous marriage. There was similar neurological and cutaneous complaint in patients elder sister as well as four other family members. On examination she had generalised ichthyosis with relative sparing of face. She had spastic quadriparesis with bilateral ankle contractures. Fundus examination showed pigmentary changes at macula. Routine counts and blood chemistry were within normal limits. EEG, MRI brain were normal. Cardiac evaluation was normal. Clinical diagnosis of neuroichthyosis syndrome was made, with SLS as first in the differential diagnosis. Whole exome sequencing was done which showed homozygous mutation in ALDH3A2 in exon 9, suggestive of SLS. Her whole exome sequencing also showed MVK heterozygous positivity in exon 11 which is known to occur in hyper IgD syndrome.

Figure 1: Generalised ichthyosis of trunk and limbs with sparing of face.

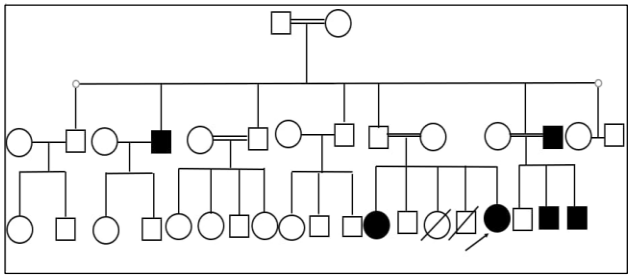

Figure 2: Pedigree chart analysis showing similar illness in elder sibling and 4 other family members.

Gene# (Transcript)	Location	Variant	Zygosity	Disease (OMIM)	Inheritance
MVK **(+)** (ENST00000228510.8)	Exon 11	c.1129G>A **(p.Val377Ile)**	Heterozygous**	Hyper-IgD syndrome (OMIM#260920)	Autosomal recessive**
ALDH3A2 **(+)** (ENST00000176643.1)	Exon 9	c.1277T>C **(p.Leu426Ser)**	Homozygous	Sjogren-Larsson syndrome (OMIM#270200)	Autosomal recessive

Figure 3: Genetic test report.

DISCUSSION

Sjögren-Larsson syndrome (SLS) is a rare autosomal-recessive neurocutaneous disorder which has been rarely reported in Asian and Indian population. Triad of ichthyosis, mental retardation, and spastic diplegia or quadriplegia is present.[2] It is caused due to mutation in the gene for fatty aldehyde dehydrogenase (FALDH) which catalyzes oxidation of long chain aliphatic alcohols to corresponding fatty acids. Due to defective oxidation, there is accumulation of aldehyde-modified lipids or fatty alcohol .These products probably disrupts the barrier function of skin and white matter of brain. It was first described Sjogren and Larsson in Sweden.[3]

It has cutaneous, neurological and ocular manifestations. The hallmark cutaneous manifestation is presence of generalised ichthyosis with relative sparing of face. Neck, axillary fold, lower abdomen usually have prominent icthyotic lesions seen. Icthyosis is mild at birth, however in first year of life skin has yellowish brown discolouration with hyperkeratosis. Pruritus and thin scalp hair is usually present. Neurological abnormality frequently seen is delayed development milestones and delayed walking with variable spasticity of limbs. Patient may have diplegia/quadriplegia and 50 percent of cases will be non-ambulatory. About 40 percent of cases will have seizure. Cognitive deficits and dysarthria is also present. Retinal crystalline inclusions called as glistening white dots present around fovea is pathognomic of this syndrome. Retinal pigmentary degeneration changes may be seen.[4-6]

MRI brain may be normal in the first few years of life. White matter disease involving the centrum semiovale, corpus callosum, periventricular regions, and parietal and frontal lobes. May be seen in older children and adult. The diagnosis of SLS is by either measurement of fatty aldehyde dehydrogenase in cultured skin fibroblasts or demonstration of mutations in ALDH3A2, which are detected in >95% of patients.[1]

Treatment is mainly supportive care like antiepileptic drugs for seizure and physiotherapy, botulinum toxin injection for spasticity. Topical keratolytics, emollients, and calcipotriol are used for ichthyosis.[2]

CONCLUSION

SLS is a rare neuroichthyosis syndrome characterized by ichthyosis, spastic weakness of limbs, cognitive decline and retinal abnormality. Diagnosis is by genetic testing of ALDH3A2 gene for presence of mutation. With our extensive literature review, we couldn't find any association between hyper IgD syndrome and SLS. Clinical and genetic association between these two syndromes need to be studied in future.

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