Case Report

Metachromatic Leucodystrophy: A Case Report

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ABSTRACT

Metachromatic leukodystrophy (MLD) is a rare autosomal recessive inherited disease, which is caused by a deficiency in the enzyme activity of Arylsulfatase A (ARSA). Deficiency of this enzyme results in intralysosomal storage of sphingolipid cerebroside 3-sulfates (sulfatides), which are abundant in myelin and neurons. Demyelination and neurodegeneration, causing multiple and ultimately lethal neurological symptoms is the hallmark of MLD. Here we report a case of 29 months old female child presented with regression of neurological development in a decerebrate posture. Though it is a rare disease of frequency 1/100,000 live birth, typical history and brain imaging is being reported here.

Keywords: Arylsulfatase A; Metachromatic Leucodystrophy ; MRI

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INTRODUCTION

Among Lysosomal storage disease, Metachromatic Leukodystrophy (MLD), is commonly listed in the family of leukodystrophies .Mutations in the Arylsulfatase A (ARSA)gene which encodes on chr.22q13.31 is the main pathogenesis of this disease and it is inherited in an autosomal recessive manner.[1] Among white matter disorders it is one of the most common disease .[2] ARSA is required for the hydrolysis of sulfatides , deficiency of which leads increase of sulfatide in myelin of the nervous system.[3] The prevalence of MLD is about 1 per 100,000 live births.[4,5]

Previously healthy child when develops regression of neurological development, he or she be suspected for MLD.They are of 3 types: late infantile, juvenile, and adult MLD.[6]

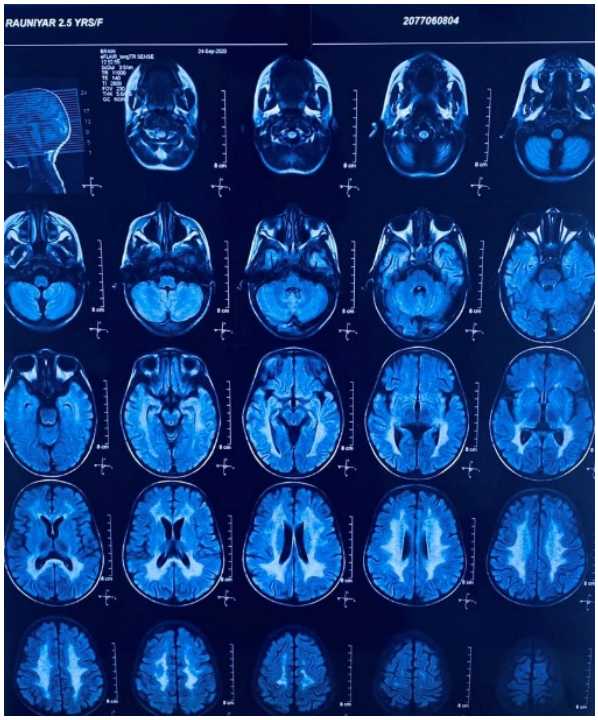
This disease is common in-between 18 and 24 months of age and gait disturbance is the first symptom following deterioration in speech, motor and intellectual functions.[7,8] As the disease progresses, decorticate postures, feeding and swallowing problems, seizures, and severe psychomotor retardation develops. Most of the patients eventually die within the first decade of life.[6] Palliative and supportive treatments are the only the options limited for its management to this date.[9,10]

CASE REPORTS

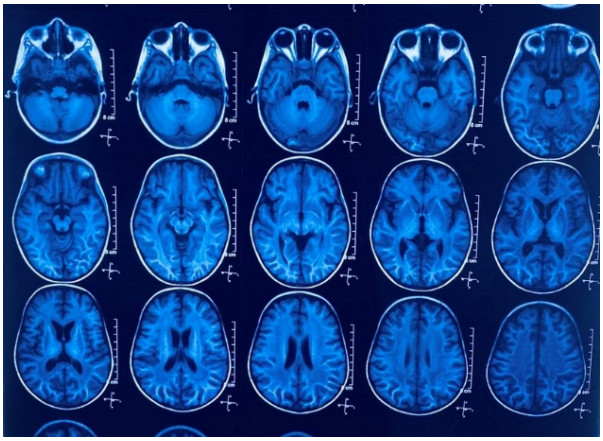
A 29-month old female child was presented with bilateral weakness of both upper and lower limbs for last 9 months associated with weakness and clumsiness of gait. School performance was also worsened for last 6 months. There was also incontinence of bladder and bowel habit for last 4 months. For last 2 months she also developed abnormal body movement along with stiffness of bi-lateral limbs with up rolling of eyes with deviation of head. There was no history of slurring of speech, loss of consciousness, headache or vomiting. She had not history of trauma, cyanosis, swelling of body or hypo pigmented lesions over body. Perinatal period of her was uneventful and prior to this illness developmental milestones were also age appropriate. The vision and hearing were normal. She is the second child in her family and the parents were non-consanguineous. Her elder sister was fit and fine.

On examination, the child looked lethargic with deprived facial expression; Head circumference(HC) was 49 cm (at the 75th centile of NCHS). There was no facial dysmorphism and no any neurocutaneous markers found. All cranial nerves were clinically normal. On motor system examination, baby was in abnormal decerebrate posture as shown in pic-1. Both the upper and lower limbs were hypotonic and power with 3/5. Deep tendon reflexes(DTR) were diminished in lower limbs and normal in upper limbs. Babinski sign was bilaterally present. Sensory involvement was intact and we could not assess cortical sensation and coordination. MRI of Brain showed diffuse symmetric T2 and FLAIR hyper intense areas involving bi lateral periventricular which were seen in the white matter, deep cerebral white matter, splenium, and posterior limbs of internal capsule region sparing the subcortical white showing no significant contrast enhancement with mild cerebral cortical atrophy which was a typical finding of MLD as shown in picture -2. CSF findings were normal. A diagnosis of MLD was suggested by typical clinical presentation and neuroimaging findings. So the patient was diagnosed to have MLD and was suggested for physiotherapy.

Photograph 1: Decerebrate posture



Photograph 2: Tigroid patterns around periventricular white matter



Photograph 3:Periventral white matter sparing the subcortical U fibers

DISCUSSION

Among lysosomal storage disease, metachromatic leucodystrophy mainly affects growth and development of myelin of the nervous systems.[1] It is an autosomal recessive pattern disease.[11]

MLD classically presents in 3 forms- Infantile, the commonest type (1in 100000), juvenile(1 in 150000) and the rarest adult form.[12]A survey done in Europe reveal 40-50% of patients have a infantile form while 30-40% have juvenile form and 18-20% have an adult form.[13]In Nepal such type of case was reported 10 years back in a 4 year old male baby in Kanti children Hospital.[14] Clinical features of MLD manifests in children of 12 and 18 months of age and was presented with gait disturbance as the first symptom. later there may be deterioration in speech, intelligence, coordination and gait disturbances. Patient may develop quadriplegia and blindness. Decerebrate posturing is the late manifestation of the disease. Death usually occurs in six months to four years after the onset of symptoms.[15] In juvenile MLD, alteration in personality and deterioration in school performances presents at the onset of the disease and these symptoms may be delayed upto 5–10 yrs. of age. Incoordination of gait, urinary incontinence, dysarthria and generalized tonic-clonic convulsions are the other common presentations whereas adult MLD occurs from the 2nd to 6th decade of life especially having abnormalities in memory and psychiatric instabilities.[16]

In T2 weighted MRI, the tigroid patterns and symmetric confluent areas of high signal intensity around periventral white matter sparing the subcortical U fibres are the specific feature of MLD.[16]

Confirmation of MLD is done by the measurement of Arylsulfatase A in leucocytes, or by ARSA gene detection and supported by estimating urinary sulfatides.[17,18] Antenatal diagnosis of ARSA gene sequence is possible in first trimester by assaying ARSA in chorionic villi or cultured fibroblasts for the possible prevention of the disease.[19]

Till date there is no definitive mode of treatment for MLD. Study is going on in the

field of bone marrow transplantation, stem cell transplantation, and genetic engineering but still the result is poor.[20,21]

Limitations: Unfortunately, Arylsulfatase A enzyme activity in leukocytes was not tested as it is not available in our center.

CONCLUSION

Infantile Metachromatic leucodystrophy being a rare lysosomal storage disease with autosomal recessive pattern presenting hasty and overwhelming clinical course, gait disturbance is the initial neurological feature followed by speech and bed ridden status within months to 2 years. The tigroid patterns and symmetric confluent areas of high signal intensity inside periventral white matter with sparing of the subcortical U fibres are the specific feature on brain MRI serve as a clue indicating the possibility of MLD. Clinical features, biochemical analysis of ARSA in leukocytes, MRI report confirms the diagnosis of MLD. Antenatal diagnosis with pathognomonic ARSA gene mutations provides proper genetic information and counselling to the family members.

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