

A Case of Infantile Metachromatic Leukodystrophy

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Abstract

Metachromatic leukodystrophy (MLD) is the neurometabolic disease caused by deficiency of enzyme arylsulfatase A resulting in deficiency of sulfatide degradation. The responsible gene is arylsulfatase A gene. We report a case of the infantile MLD that was confirmed by means of enzyme studies, nerve conduction velocity and typical MRI of brain findings.

Keywords: Infantile; Metachromatic leukodystrophy; Arylsulfatase A; *ARSA* gene; MRI brain

Introduction

Metachromatic leukodystrophy (MLD) is the typical white matter disease which belongs to the lysosomal sphingolipid storage group, and it is inherited in the autosomal recessive way [1]. MLD is caused by the deficiency of enzyme arylsulfatase A (*ARSA*) resulting in the deficiency of sulfatide degradation and the target gene is *ARSA* gene. The accumulation of sulfatide triggers leukodystrophy. The incidence of MLD is reported as about 1 per 100,000 live births in the European population, and is found at even lower rate in Asia [2, 3]. Clinically, it shows a wide range of spectrum with respect to the age of onset, the rate of progression and the initial following: 1) the late infantile form of disease that starts before the age of 2 or 3 years, 2) the juvenile form that starts between 2 or 3 and 16 years, and 3) the adult form that presents its first symptoms

after the age of 16 years [4-6].

Case Report

A 2 years and 6 months old male patient came with chief complaints of developmental delay and generalized tightness which started developing at the age of 1 year, and inability to seat and stand. He had no specific birth history and showed normal pattern of development including independent walking before the onset of symptoms. The developmental regression progressed continuously. His family history was found to be negative. Parents noticed weakness in bilateral lower limb and he was taken to general physician, where he was investigated. Routine investigations were found to be normal except serum calcium level was low. Hence he was treated with calcium

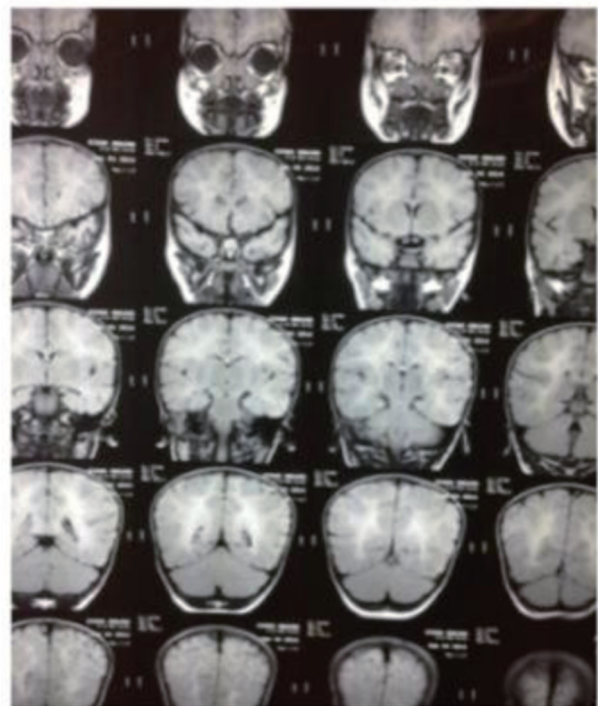


Figure 1. MRI of brain showing T2 hyperintense signals in bilateral fronto-parietal, parieto-occipital white matter.

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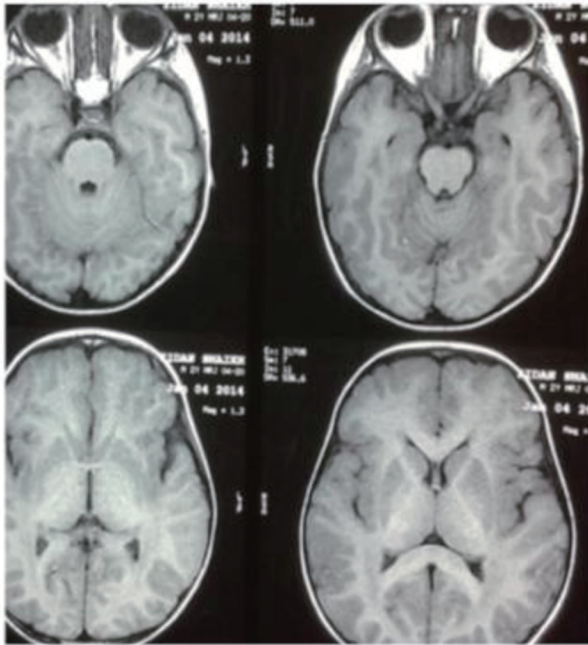


Figure 2. MRI of brain showing T2 hyperintense signals in posterior capsule.

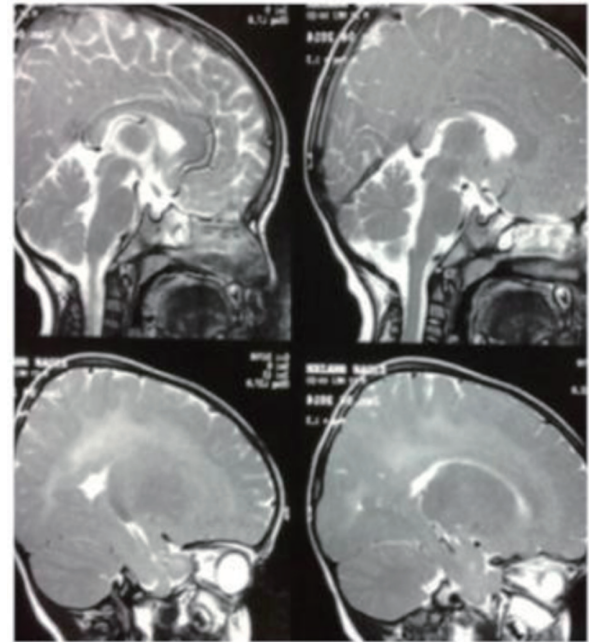


Figure 3. MRI of brain showing T2 hyperintense signals in corona radiata.

and vitamin-D supplements. Parents noticed no improvement. On clinical examination bilateral knee reflex exaggerated and Babinski’s sign was positive. So MRI of brain was done which was suggestive of T2 hyperintense signals in bilateral fronto-parietal, parieto-occipital white matter, corona radiata and posterior capsule. This was likely suggestive of dysmyelination/demyelination sequelae to MLD (Fig. 1-3).

Nerve conduction velocity study was done for lower limbs weakness which was indicative of bilateral sensory motor neuropathy.

Arylsulfatase A enzyme activity in leukocytes was tested and found to be decreased to 5.3% of normal control value. Thus, the patient was confirmed to have metachromatic leukodystrophy (method: artificial chromogenic and fluorogenic substrates (Fig. 4)).

Discussion

MLD is a lysosomal storage disease from the family of leukodystrophies and among the sphingolipidoses it affects the metabolism of sphingolipids. Leukodystrophies affect the growth and/or development of myelin, the fatty covering which acts as an insulator around nerve fibers throughout the central and peripheral nervous systems. MLD involves cerebroside sulfate accumulation. MLD has an autosomal recessive inheritance pattern [7].

There is currently no treatment or cure for MLD and future treatment options are currently being investigated. These include gene therapy, enzyme replacement therapy, substrate reduction therapy and potentially enzyme enhancement ther-

Clinical History: Not Enclosed.

Leukocyte Enzyme Activity:

Test (Units)	Disorder	Results	Reference Range (Mean ± SD)	Status
Arylsulfatase A (nmol/17h/mg)	MLD	5.3	67 – 396 (187.5 ± 63.9)	Low
β-Galactosidase (nmol/h/mg)	GM1	220	70 – 324 (148.17 ± 35.7)	Normal

* Reference enzyme.

Method: Artificial chromogenic & fluorogenic substrates.

Result: A reduced activity of arylsulfatase A is obtained in leukocytes.

Interpretation: Reduced activity of arylsulfatase A in leukocytes is consistent with the diagnosis of metachromatic Leukodystrophy (MLD) disease.

Recommendations:

- It is suggested to confirm the enzyme deficiency from cultured skin fibroblasts.
- ARSA gene mutation analysis is recommended for identification of causative mutation/s.

Figure 4. Arylsulfatase A enzyme activity in leukocytes by “artificial chromogenic and fluorogenic substrates” method.

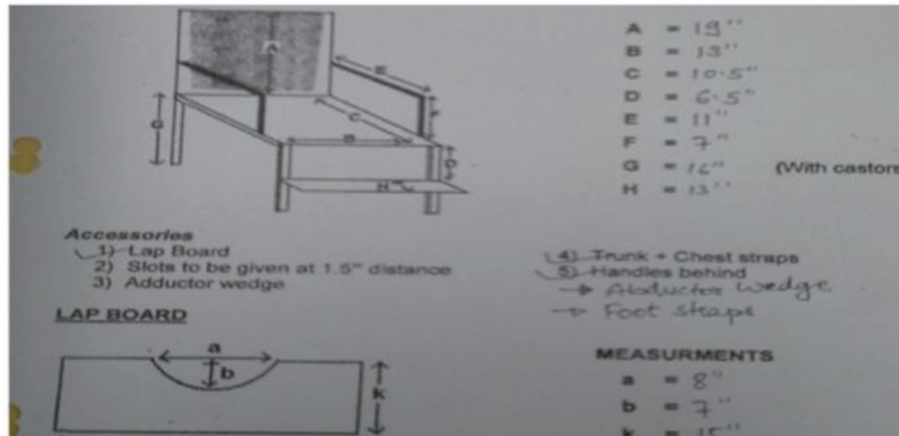


Figure 5. Seating device for patient designed by our institute.

apy.

Our patient is not able to sit, therefore seating device was provided from our institute (Fig. 5). For bilateral lower limb spasticity “knee ankle foot orthosis” was provided. Prognosis was explained and also medical and social counselling was done to parents. We were not able to do *ARSA* gene testing due to lack of affordability.

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