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Case Report
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Metachromatic Leukodystrophy (MLD): A Rare Genetic Disorder in child

B. Sonawane V.[1], V. K.[2], Bainade K.[3], Deshpande V.[4*]

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[1] Vijay B. Sonawane, Associate professor, Department of Pediatrics, DY Patil school of medicine, Navi Mumbai, Maharashtra, India.

[2] Kotrashetti V., Professor, Department of Pediatrics, DY Patil school of medicine, Navi Mumbai, Maharashtra, India.

[3] Kapil Bainade, Associate professor, Department of Pediatrics, DY Patil school of medicine, Navi Mumbai, Maharashtra, India.

[4*] Vedashree Deshpande, Junior resident, Department of Pediatrics, DY Patil school of medicine, Navi Mumbai, Maharashtra, India.

Metachromatic leukodystrophy is a rare hereditary neurodegenerative disorder that causes fatty substances to build up in cells, particularly in the brain, spinal cord and peripheral nerves. This is caused by a deficiency of an enzyme that helps break down lipids called sulfatides. We present a case of a four-year-old boy born of non-consanguinous marriage with complaints of progressive loss of fully developed motor milestones as the inability to walk and sit (regression of achieved motor milestones). The patient was diagnosed with MLD based on whole xome sequencing and discharged on symptomatic care and physiotherapy to improve the patient's quality of life.

Keywords: Metachromatic leukodystrophy (MLD), Neurodegenerative, Hereditary disorder, Sulfatides, Whole-exome sequencing

Corresponding Author

Vedashree Deshpande, Junior resident, Department of Pediatrics, DY Patil school of medicine, Navi Mumbai, Maharashtra, India.
Email: vedashreedeshpande20@gmail.com

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Introduction

Leukodystrophies are a group of usually inherited disorders characterized by degeneration of the white matter in the brain. [1]. The leukodystrophies are caused by imperfect growth or development of the myelin sheath, the fatty insulating covering around nerve fibres. [2]. Metachromatic leukodystrophy is a rare hereditary (genetic) disorder that causes fatty substances (lipids) to build up in cells, particularly in the brain, spinal cord and peripheral nerves. This buildup is caused by a deficiency of an enzyme that helps break down lipids called sulfatides.

It includes three types of late infantile (< 4years of age), Juvenile (4- 16years of age), adult (> 16 years of age). Signs and symptoms may vary. The infantile form is the most common and progresses more rapidly than other forms. There is no cure for metachromatic leukodystrophy yet. Depending on the form and age of onset, early identification and treatment may help manage some signs and symptoms and delay the progression of the disorder.

Case report

We report a four-year-old male child born of the nonconsanguineous marriage, with presentation as of progressive loss of fully developed motor milestones in the form of inability to walk and sit since 8 months (regression of achieved motor milestones). The child has attained all developmental milestones as per age till 3 years of life and parents noticed gradual loss of achieved milestones thereafter.

The child was also not able to raise hands above the shoulder and hold or grasp things in hand. Head control, bowel and bladder control were lost. Speech abnormalities were present and the child was able to speak 2 words with meaning. There was a history of limb tightening, difficulty in chewing solid food and drooling of saliva. History of cyanotic spells present.

There was a history of the death of sons (4 out of 5) of paternal uncle 1 year after birth but no documents were available. The patient's antenatal history was uneventful with a birth weight of 3.6 kg and partially immunized till 1 year of life. On general examination we found the patient to be alert with a heart rate of 116 beats per minute, Blood pressure 98/48 mm Hg and oxygen saturation 97% and pallor were present.

The child was having protein-energy malnutrition (grade III) as per the Indian academy of paediatrics. On systemic examination, clasp knife spasticity was present in bilateral limbs (lower > upper). Power was 2/5 with areflexia in bilateral upper and lower limbs with no signs of meningeal involvement and cerebellar involvement. On investigating, haemoglobin was low (8.1 gm/dl), liver enzymes were normal, aldolase was normal (1 U/L), serum LDH was elevated 655 IU/L, serum CPK (total) was normal, Vit D was 26.8 ng/ml, serum lactate was 4.60 mg/dl.

IgG CSF was elevated 11.7 mg/dl. EMG and NCS done suggested of peripheral neuropathy (generalized, motor, demyelinating, distal>proximal, lower limbs>upper limbs). Whole exon sequencing was done suggestive of PSAP (c.257T>A) variant on exon 4 and ACAD9 (c.1553G>A) variant on exon 15, showing metachromatic leukodystrophy due to saposin deficiency (249900) and mitochondrial complex I deficiency, nuclear type 20 (611126) respectively with autosomal recessive inheritance. Parents counselled about the fate of disease and treatment options available and discharged on steroids and physiotherapy.

Discussion

MLD is a lysosomal storage disorder from the family of leukodystrophies. It affects the metabolism of sphingolipids among the sphingolipidoses. Leukodystrophies affect the growth and production of myelin sheaths. MLD involves the deposition of cerebroside sulfate with an autosomal recessive pattern of inheritance [2]. The incidence of the disease is 1 in 40,000 cases, according to data from the United States. Mortality rates are high in metachromatic leukodystrophy due to the rapid progression of the disease condition. It is an autosomal recessive condition. MLD's characteristics include mental deterioration, developmental delay, speech abnormalities, hypotonia, mental capacity loss, blindness, stiffness, seizures, impaired swallowing, paralysis, impaired school performance, ataxia, tremors and dementia.

Our case is a type of late infantile MLD as the infant exhibited symptoms like inability to walk, loss of bowel bladder control, stiffness, regression of developmental milestones, speech abnormalities before 4 years of age. It is the most common variant of MLD. The diagnostic modalities for the disease include MRI scanning and enzyme assay.

MRI scanning reveals symmetric confluent areas with high signal strength in periventricular white matter with subcortical U fibre ranging. MRI is considered the primary imaging modality in patients with leukodystrophy and plays a role in recognizing, localizing, and characterizing anomalous white matter underlying it.[3]. There is no prescribed treatment for the disease. To minimize the symptoms of the subject and relieve discomfort, medications such as muscle relaxants, psychological medications, analgesics and epilepsy drugs, may be provided.[5]

To improve neurocognitive functions, bone marrow or cord blood transplantation is the solution available primarily in the case of asymptomatic late infantile and early juvenile forms. Future treatment options for the disease which include gene therapy, enzyme replacement therapy, substratum reduction therapy, and potentially enzyme enhancement therapy is currently being explored.[4].

Conclusion

MLD is a serious illness that gets worse over time. Individuals eventually lose all muscular and mental functions. The span of life varies depending on the age the condition started but the course of the disease usually runs from 3 to 20 years. The key to success is the right indications for both the doctor and the health professionals to reassure the patient throughout the entire course of treatment and to institute a strict and regular reminder regime to ensure a better prognosis.

Reference

01. Walterfang M, Mocellin R, Copolov D, Velakoulis D. Secondary hallucinations, In Sachdev PS, Keshavan MS, editors, Secondary Schizophrenia. Cambridge, UK- Cambridge University Press. 2010;21–43. *[Crossref][PubMed][Google Scholar]*

02. Vaibhav S Lokhande, Anil Gaur. A Case of Infantile Metachromatic Leukodystrophy. J Neurol Res. 4(5-6)2014;138-140. *doi: 10.14740/jnr294e [Crossref][PubMed][Google Scholar]*

03. Mallikarjun K, Deepak P Bhayya, Deepesh Singh, Tarulatha R Shyagali. Metachromatic Leukodystrophy- A Rare Case Report. Journal of Academy of Advanced Dental Research. 2(3)2011. *DOI: 10.1177/0883073814542948 [Crossref] [PubMed][Google Scholar]*

04. Gopen Kumar Kundu, Saheen Akhter, M Mizanur Rahman. Metachromatic Leukodystrophy- A Case Report. BSMMU J. 9(1)2016;62-65. *Doi: 10.47583/ijpsrr.2020.v65i02.018 [Crossref] [PubMed][Google Scholar]*