

Case Report

A case report of leukoencephalopathy with vanishing white matter disease

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ABSTRACT

Vanishing white matter disease (VWM) is one of the most prevalent inherited childhood leukoencephalopathies. Childhood ataxia and diffuse central nervous system hypomyelination are the common findings. The disease is characterized by chronic progressive and episodic deterioration with ataxia, spasticity and optic atrophy. VWM is caused by mutation in any of the five genes encoding the subunits of eukaryotic translation initiation factor eIF2B. The disease has an autosomal recessive mode of inheritance. The cause of the disease is unknown. Authors are reporting an 8 year old male child presented with complaint of difficulty while walking since one month and history viral fever was present one month back. MRI revealed bilateral symmetrical periventricular T2 hyperintensities with T1 hypointensities. Perivenular sparing was seen and molecular analysis shown eIF2B4 mutations confirmation of vanishing white matter disease. No specific treatment is available and advised to avoid stress and triggers.

Keywords: Cerebellar ataxia, eIF2B gene mutations, White matter disorders

INTRODUCTION

Vanishing white matter disease (VWM) is one of the most prevalent inherited childhood leukoencephalopathies. The disease is variably called Myelinopathia Centralis Diffuse. Childhood ataxia and diffuse central nervous system hypomyelination are the common findings. The disease is characterized by chronic progressive and episodic deterioration with ataxia, spasticity and optic atrophy.¹ VWM is caused by mutation in any of the five genes encoding the subunits of eukaryotic translation initiation factor eIF2B.^{2,3} The disease has an autosomal recessive mode of inheritance. The cause of the disease is unknown. Previously it was known that there is no biochemical marker for this disease, but recently analysis of body fluids has revealed only a few biochemical markers for VWM.⁴ The first marker found was a consistent elevation of cerebrospinal fluid glycine concentrations with an elevated ratio of cerebrospinal fluid to plasma glycine concentrations.⁵ A

decreased cerebrospinal fluid concentration of asialotransferrin is a recently identified biomarker for VWM.^{6,7}

CASE REPORT

An 8-year-old male child resident of Nalgonda was brought to pediatric OPD with complaints of difficulty while walking which had been gradually progressing since one month with no other complaints. He had past history of viral fever with thrombocytopenia one month back and no history of head trauma and contact with TB patients. Antenatal and birth history was uneventful. Other history was not significant. Developmental history adequate for age. Immunisation as per UIS and BCG scar is present. On general examination there was no malnutrition. On CNS examination, motor system, bulk and power was normal and tone is increased in both lower limbs. All the reflexes of lower limbs were exaggerated, plantar was extensor and ankle clonus was

also seen in both limbs. Ataxic gait was present and coordination was present. Sensory functions and cranial nerves were intact. Other systemic examination was normal. All the routine blood investigations were normal. MRI of brain showed bilateral symmetrical periventricular T2 hyperintensities with T1 hypointensities. Periventricular sparing was seen. Based on MRI report suspected as metachromatic leukodystrophy and vanishing white matter disease. Based on history, clinical examination and MRI reports most probable diagnosis could be vanishing white matter disease and sent for molecular analysis. It identified mutation in eIF2B4 gene.

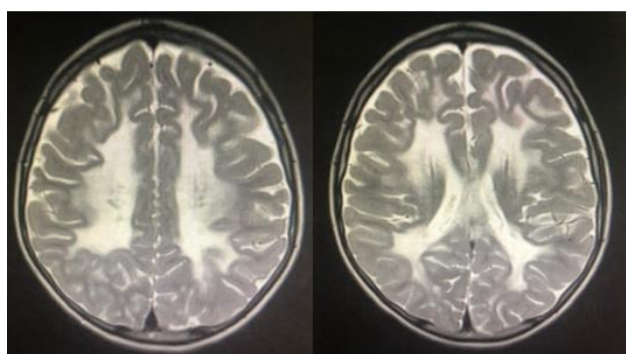


Figure 1: MRI of brain showed an abnormal signal of cerebral white matter.

No specific treatment had been found as per current evidence. Avoidance of stressful conditions that provoke progression and liberal use of antibiotics, antipyretics. Parents have been counselled regarding the nature and progression of the disease and need for regular follow up for assessment of progression of the condition.

DISCUSSION

The classical and most common variant of Vanishing white matter disease has its onset in childhood, at age 2-6 years.^{8,9} Though this disease may have an early infantile or antenatal onset.¹⁰⁻¹² that had happened in this patient. The first time this disease was documented in 1962 when Eickle studied a 36 year old woman.¹ In 1993-94, Dr. Hanefeld and Dr. Schiffmann and their colleagues identified the disease as childhood-onset progressive leukoencephalopathy.¹⁰ It is characterized by chronic progressive neurological deterioration with cerebellar ataxia, usually less prominent spasticity and relatively mild mental decline.^{8,9} Epilepsy is common. Characteristically, there are additional episodes of major and rapid deterioration following minor head trauma and especially febrile infections.^{9,11} Mutation in the eukaryotic translation initiation factor eIF2B was seen and 65% cases had eIF2B3 mutations and in this case mutation was found at eIF2B4 gene which is less common. In this case child had developed gait disturbances after viral illness and progressive and cerebellar ataxia was seen and mental functions were normal. MRI was suggestive of VMW and molecular

analysis confirmed diagnosis. The prognosis is more severe with early onset of disease. Infantile type is more severe. Avoiding stressful conditions which increase progression and liberal use of antibiotics, vaccination and antipyretics and abstinence of contact sports were advised.

CONCLUSION

Vanishing white matter disease is an intriguing disease, both from a clinical and molecular perspective. There is no specific treatment for VWM. Avoiding stressful condition should be done to which provoke progression. The most important consequence of research findings of the last 5 years probably is that prenatal diagnosis has become for families when index patient had identified.

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