Abstract
Vanishing white matter (VWM) disease is a chronic progressive childhood onset leukodystrophy that result in central nervous system demyelination, often precipitated by some stressful events. There is wide phenotypic variation buy typical MRI findings are diagnostic in most of the patients. Here we report two cases of vanishing white matter disease with typical MRI findings.

Introduction
Vanishing white matter (VWM) disease is a childhood onset progressive leukoencephalopathy transmitted by autosomal recessive inheritance. Synonyms are ‘childhood ataxia and central nervous system hypomyelination (CACH)‘, ‘myelinopathycentralis diffusa‘. It is one of the prevalent leukoencephalopathy characterized by normal or near normal early developmental period followed by an episodic and chronically progressive neurological deterioration. Though It can occur in any age from neonate to adulthood, classical and most common variant occur in childhood between age 2-6 year. Clinically characterized by progressive cerebellar ataxia, spasticity and optic atrophy after an episode of physiologic stress like fever, freight or trauma(Ref). VWM is caused by mutation in the genes encoding the translation initiation factor eIF2B. MRI of the brain is essential for diagnosis. Management is only supportive and symptomatic, as there is no specific treatment available. We are presenting two cases of vanishing white matter disease based on typical clinical presentation and MRI findings.

Case Report-1
A 5 years old female child, 3rd issue of non-consanguineous parents presented with progressive deterioration of motor skill and visual impairment for 2 and ½ years. Prior to this illness she had history of febrile status epilepticus followed by unconsciousness. Then she developed walking difficulty and cannot maintain balance properly. She also had history of difficulty in seeing far and near objects. Another episode of afebrile status epilepticus occurred 1 and ½ months back. There is no history of speech difficulty or memory loss .There was no history of trauma. This child was delivered by normal vaginal delivery and cried immediately after birth. She was developmentally age appropriate upto 2 and ½ years of age. She was immunized as per EPI schedule .Other family members was healthy. She was conscious, cooperative, oriented. Her vitals were stable. Anthropometrically she was well thriving. Nervous system examination shows tone increased in lower limb, deep tendon reflexes exaggerated, and planters were bilaterally extensor and

![Fig.-1: T2 image showing bilateral symmetrical involvement of white matter with near CSF intensity, sparing of subcortical white matter and FLAIR image showing hypointense signal in involved white matter (case 1).](image-url)
gait ataxic. All cranial nerves were intact. Ophthalmological examination showed nystagmus, optic atrophy in both eyes. Her blood picture was normal. Brain MRI shows periventricular white matter hyperintensity with near CSF intensity in T2 image. EEG shows multifocal discharge. This patient was treated with antiepileptic drugs and other supportive management. Parents were counseled about the prognosis and outcome of the disease. This patient was discharged with advice to avoid head trauma, and any stressful condition. Now she is on regular follow up.

**Case Report-2**

An 11 months old male child, presented with loss of acquired skill following fever. Prior to this illness the child could walk with support but now cannot stand. There was no history of trauma. He was developmentally age appropriate up to 11 months of age. This child had no history of perinatal events. There is no consanguinity and no family history of such type of illness. He is immunized as per EPI schedule. On examination; he was conscious, cooperative, interested to surroundings. His Vitals were normal. Anthropometrically well thriving. Nervous system examination shows bulk of muscle was normal, tone was increased lower limbs, deep tendon reflex were exaggerated and planter was bilaterally extensor. His basic metabolic screening was normal. Brain MRI shows bilateral symmetrical periventricular white matter hyperintensity. Ophthalmologic evaluation shows bilateral optic atrophy. This patient was treated with supportive management. Parents were counseled about the outcome of the disease. They were also advised to avoid head trauma, stressful condition she was advised for regular follow up.

**Discussion**

Vanishing white matter disease (Childhood ataxia and central nervous system hypomyelination) is a slowly progressive disorder of white matter. At first, Dr. Hanefeld and Dr. Schiffmann and their colleagues identified the disease in 1993-94. The precise incidence and prevalence of VWM is unknown, but it is one of the most prevalent childhood leukodystrophies. Van der Knapp et. Al(YEAR), described the age of onset of VWM as an infantile form (onset age 1 year), an early childhood onset form (onset age 2-4 years), a late childhood/juvenile onset form (onset age 5-15 years), and an adult onset form (onset age >15 years). One of our reported patients presented with infantile form and another one had late childhood onset form. Infantile form is one of the fewer forms of the VWM. Infantile form constituted 8.2% of the 85 cases with mutation proved VWM(Ref). Early childhood form 57.6%, late childhood/juvenile form 29.4%, adult form 4.7% respectively. Patient usually presents with cerebellar ataxia, spasticity, optic atrophy with loss of vision and epilepsy. Cognition is often better preserved. Both of our patient presented with typical clinical features including ataxia, spasticity and optic atrophy with preserved cognitive function and one also had epilepsy. Van der Knapp et. al, proposed a diagnostic criteria for ease of diagnosis of the disorder-(a) Normal or near normal Initial psychomotor development, (b) Episodic and chronic progressive neurological deterioration,(c) Spasticity and cerebellar ataxia (epilepsy and optic atrophy may also occur), (d) Magnetic resonance imaging findings of symmetrical and bilateral involvement of the cerebral white matter, with parts or all of the white matter demonstrating signal intensities similar to that of CSF over time. Both of our patient had initial normal developmental periods followed by a chronic progressive neurological deterioration after an episode of febrile event. Some stressful conditions including fever, head trauma, and fright etc. are considered as provoking factors responsible for onset of the disease and the episodes of neurologic deterioration. During acute illness consciousness may be impaired, from somnolence to coma, and death also may occur. Otherwise acute

![Fig.-1: T2 image showing bilateral symmetrical involvement of white matter with near normal CSF intensity and FLAIR image showing hypointense signal due to cystic degeneration (case 2)](image-url)
decompensation usually follows a slowly progressive course. One of our patients had an episode of acute decompensation followed by mild improvement and then a slowly progressive clinical course. Though not obligatory, optic atrophy is an important feature of this condition and both of our patient developed optic atrophy. It could be a nonspecific marker of the disease progression or may occur due to environmental or genetic susceptibility. MRI of brain is mandatory for diagnosis. MRI abnormalities are present in almost all patients with VWM, even in the asymptomatic at-risk family members. Magnetic resonance imaging typically shows diffuse and symmetrical involvement of the cerebral white matter. Cerebellar white matter and brainstem, especially pontine tegmentum also involved. Inner rim of corpus callosum may be involved early but usually there is sparing of the U fibers. The cortical grey matter is not involved in VMD. Contrast enhancement usually does not occur. Over time there is progressive rarefaction and cystic degeneration of the white matter and eventually it is totally replaced by CSF-like signal intensity. Van der Knapp et al. (Year) established an MRI criteria for diagnosis. MRI findings of both of our patients are consistent with the typical MRI features of vanishing white matter disease showing bilateral symmetric T2 hyperintensities of periventricular white matter with near CSF intensities and FLAIR image shows attenuation. Magnetic resonance spectroscopy (MRS) findings are not specific for VWM and there may be reduction of the normal metabolite peaks with the accumulation of glucose and lactate. Biochemical markers including Cerebrospinal fluid (CSF) analysis may be done in patient with inconclusive MRI features and may demonstrate a decreased asialotransferrin: transferrin ratio. On genetic testing there may be mutation in any of five genes EIF2B1, EIF2B2, EIF2B3, EIF2B4, and EIF2B5. Mutation mostly found in EIF2B5 (68.4%) and disease with EIF2B2 mutations found to have a better course than EIF2B5 mutations. There is no specific management for this condition. Treatment is only supportive and symptomatic as we provide to our patients.

Conclusion
Vanishing white matter disease or childhood ataxia with central hypomyelination (CACH syndrome) is a chronic and progressive white matter disorder, with unique clinical and radiological features. There is no specific treatment, but as it often exacerbated by infection or minor head trauma, avoidance of stressful condition could be important. With comprehensive multidisciplinary care the symptoms of VWM can be managed to improve the quality of life.

References
8. Van der Knaap MS, Breiter SN, Naidu S, Hart AA, Valk J. Defining and categorizing leukoencephalopathies of...


