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Case Report

CT and MRI findings in infantile vanishing white matter ^{☆,☆☆,★}

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ABSTRACT

Infantile vanishing white matter disease is an uncommon cause of developmental delay and seizures in children. Presented here is a case of vanishing white matter disease diagnosed at 6 months of age. Imaging findings demonstrated widespread white matter abnormalities throughout the supratentorial and infratentorial brain. The diagnosis of infantile vanishing white matter disease was confirmed via molecular analysis which revealed a rare mutation in the gene responsible for this disorder.

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Introduction

Vanishing white matter disease is a rare autosomal recessive leukodystrophy that results in demyelination of the central nervous system. It was first characterized in the 1960s, however, it wasn't until 1988 that the infantile form was described in a group of native Indian infants in northern Quebec and Manitoba [1]. The disease can present at any stage of life. The most severe type of vanishing white matter disorder is the infantile form. It presents in the first year of life and

most commonly starts with deterioration of motor function followed by seizures. Most patients with infantile vanishing white matter disease die within the first few years of life [2].

Vanishing white matter disease occurs more commonly in early childhood between the ages of 1-5 years. The presentation of the childhood form is similar to the infantile form with the addition of ataxia [3].

Although vanishing white matter disease is thought to be one of the more common leukodystrophies, the incidence is rare. The incidence is estimated to be 1 in 80,000 live births in one study [4]. Given that the infantile form is even less

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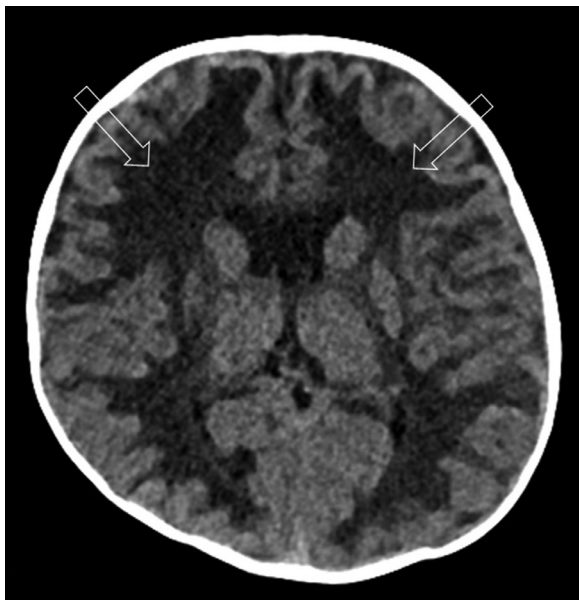


Fig. 1 – Axial CT of the head shows diffuse low attenuation throughout the white matter (arrows)

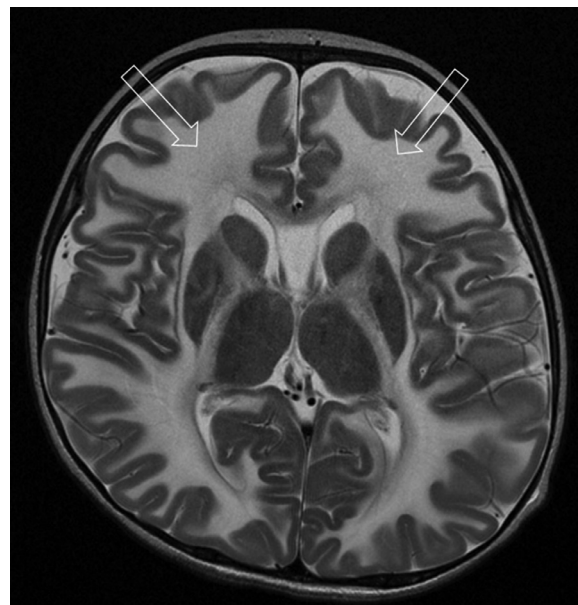


Fig. 2 – Follow-up axial T2-weighted MRI of the brain demonstrates diffuse increased T2 signal throughout the white matter (arrows)

common, there are only limited reports. Presented here is a case of infantile vanishing white matter disease with imaging findings that represent this disease.

Case report

The patient was a 6-month-old female who presented to the emergency department exhibiting decerebrate posturing with intermittent flexion of her upper extremities. It was reported that this had happened several times in the week prior to presentation raising concern for status epilepticus. Her history was notable for chorioamnionitis and maternal marijuana use during pregnancy. Her family history was unremarkable for neurologic disease. She had a 4-vessel cord, was small for gestational age, and had small kidneys for age. Mild left sensorineural hearing loss had been diagnosed at birth.

Upon examination in the emergency department, the upper extremities were both shaking, and the lower extremities were stiff. Anti-seizure medications were given, the patient was admitted, and the patient was somnolent during the admission. Review of her medical history revealed that she had unrecognized developmental regression for 1-2 months prior to presentation. At 4 months of age, she was smiling spontaneously, cooing, tracking, reaching for toys, and pushing buttons on toys. By the time of presentation at 6 months, she was less interactive, was no longer vocalizing, was not tracking, and was no longer interested in toys.

Computed tomography was obtained which showed diffuse white matter hypoattenuation (Fig. 1). A follow-up magnetic resonance imaging demonstrated widespread increased T2 signal involving the white matter diffusely (Figs. 2 and 3) with associated diffusion restriction throughout the



Fig. 3 – Axial T2-weighted MRI also shows T2 hyperintensity of the deep cerebellar white matter and medulla (arrows)

white matter tracts (Fig. 4). A diagnosis of leukodystrophy was suggested by the interpreting radiologist.

Video electroencephalography captured multiple events in which abnormal movements were depicted without electrographic correlate. It is thus not known if these abnormal movements were seizures or if they were merely sequela of leukoencephalopathy.

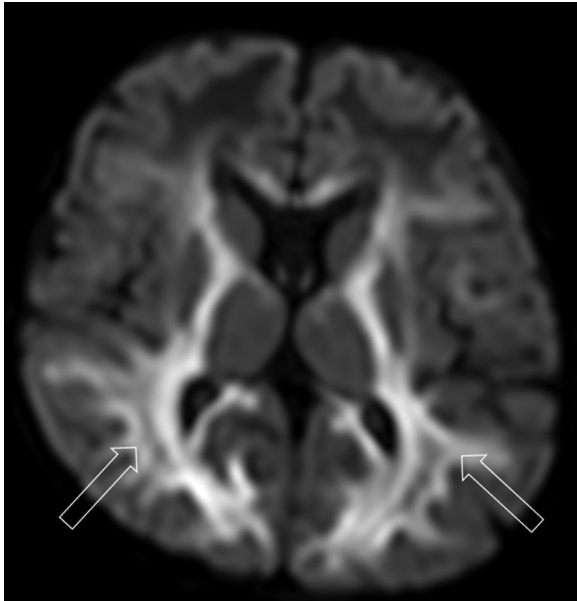


Fig. 4 – Axial diffusion-weighted image shows widespread diffusion restriction throughout the central white matter tracts (arrows)

The diagnosis of infantile vanishing white matter disease was confirmed via the molecular identification of 2 pathogenic eukaryotic initiation factor 2B (EIF2B5) mutations. The patient was found to be heterozygous for EIF2B5 c. 584G>A, p. (Arg195His) and c. 436T>C, p. (Ser146Pro). The child passed away at 9 months of age.

Discussion

Vanishing white matter disease is caused by a variety of mutations in one of the 5 subunits of EIF2B [5]. The mutations cause a partial loss of function of the protein and during periods of cellular stress such as infection or trauma, the unfolded protein response is activated causing selective damage to astrocytes and oligodendrocytes [6,7]. The disease is inherited in an autosomal recessive fashion with the highest rate of carriers located among the Cree Indians, of whom as many as 10% of nonaffected adults are carriers [8].

A previous study of 184 patients with vanishing white matter disease identified mutations in EIF2B5 in 126 patients (68%). The investigators selected the most common mutations and attempted to identify which genotypes were associated

with more or less severe phenotypes [9]. None of the patients in this study were revealed to have the mutation demonstrated in our patient. The unusual mutation in our patient could account for the early presentation, at age 6 months, and rapid progression to death at age 9 months.

The diagnosis of vanishing white matter disease may be considered when a patient, usually younger than the age of 5, has a rapid decline in motor function resulting in ataxia, spasticity, optic atrophy, or seizures. The onset of decline may occur secondary to a stressor such as head trauma or infection. The radiologist can play an important role in the diagnosis of this disease. When magnetic resonance imaging findings are consistent with vanishing white matter disease, genetic testing can be performed as a confirmatory test. Although there is no treatment for vanishing white matter disease, identification of the disease can allow for informing family members of future risk.

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