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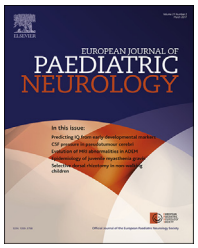

Case study

An unusual neuroimaging finding and response to immunotherapy in a child with genetically confirmed vanishing white matter disease

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ABSTRACT

Background: We present an unusual neuroimaging finding in a young girl with genetically confirmed vanishing white matter disease and a possible response to immunotherapy.
Methods and results: 2.5 yr old girl, presented with acute onset unsteadiness and encephalopathy following a viral illness. MRI showed global symmetric white matter abnormality, with symmetric enhancement of cranial nerves (III and V) and of cervical and lumbar roots. She received immunotherapy for her encephalopathic illness with white matter changes. Follow up neuroimaging showed resolution of white matter edema and resolution of the change in the brainstem.

Genetic testing confirmed a diagnosis of vanishing white matter disease (VWMD).
Conclusion: Craniospinal nerve enhancement and possible response to immunotherapy has not been described in vanishing white matter disease.

1. Introduction

We present an interesting case of a young girl who presented with involvement of craniospinal nerves on neuroimaging of vanishing white matter disease (VWMD) and a possible clinical response to immunotherapy, which is unusual for this condition.

2. Case report

A 2.5 yr old girl presented with a history of unable to weight bear and leg weakness 3 weeks after an episode of presumed viral illness, with gastroenteritis. On examination, there was high tone in lower limbs, no obvious abnormal cranial neuropathy, and exaggerated reflexes with truncal ataxia and she

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was irritable, drowsy and agitated on approach to examination had intermittent lucid periods and latterly had an electroencephalogram (EEG) demonstrating a diffuse generalised slowing.

Initial MRI performed pre-lumbar puncture demonstrated diffuse symmetric high T2 and low T1 signal within the white matter of both cerebral hemispheres with white matter swelling. These changes extended globally from the periventricular to the subcortical regions, involving all lobes, with involvement of the U-fibres. The changes extended to the corpus callosum, capsular white matter, brainstem and deep cerebellar hemispheres (Fig. 1 top row). Fine linear strands were seen in the abnormal white matter, somewhat reminiscent of the striped or 'tigroid' pattern seen in metachromatic leukodystrophy (MLD). On FLAIR images, there was some suppression of the white matter changes in the deep frontoparietal regions, suggesting cystic change. Diffusion weighted imaging demonstrated restricted diffusion at the deep and peripheral margins, and additionally in the basis pontis, along the corticospinal tracts. Of interest, post-gadolinium imaging demonstrated abnormal contrast enhancement of the oculomotor and trigeminal nerves (Fig. 1 top row), and additionally of the cervical and lumbar nerve roots diffusely.

There was no intrinsic spinal cord abnormality and the grey matter structures in brain were normal. MR spectroscopy showed reduced NAA but did not reveal any elevation of lactate or abnormal peaks. The overall pattern of symmetric diffuse white matter abnormality suggested a primary white matter disorder or leukodystrophy, as opposed to an acquired demyelinating process. MLD was one of the considerations, given some features such as the tigroid stripes and cranial nerve enhancement, but the changes were unusually extensive with cystic changes in the white matter and involvement of the U-fibres, all of which were felt unusual for MLD and raised the possibility of other leukodystrophies such as VWM.

CSF was acellular with normal protein, lactate and without any oligoclonal bands. There was no evidence of any neuronal or glial antibodies (NMDAR, Aquaporin 4, and MOG) in CSF or blood. CSF was negative for Herpes simplex Virus, Enterovirus.

Blood aryl sulphatase A and galactocerebrosidase levels were normal. She was treated for acute encephalopathy with intravenous immunoglobulin (IVIG) and corticosteroids initially. Clinically she was less encephalopathic, within 48 h of starting therapy. She continued to have ataxia with evolving spasticity. She was continued on oral steroids (2 mg/kg) for two weeks and tapered over 2–3 wks.

Clinical follow up at 2 months revealed persistent cerebellar and long tract signs. Follow-up neuroimaging 6 months later demonstrated resolution of the white matter oedema (Fig. 1 bottom row) and near resolution of the changes within the brainstem (Fig. 1, bottom row) and cerebellum (not shown). However, there was still extensive persistent symmetric white matter abnormality, as seen previously. The cranial nerve enhancement has largely resolved with only mild persisting enhancement seen on follow up and resolution of lumbar nerve root enhancement (Fig. 1, bottom row).

Variant analysis of the EIF2B1, EIF2B2, EIF2B3, EIF2B4 and EIF2B5 genes was undertaken. A heterozygous EIF2B5 variant,

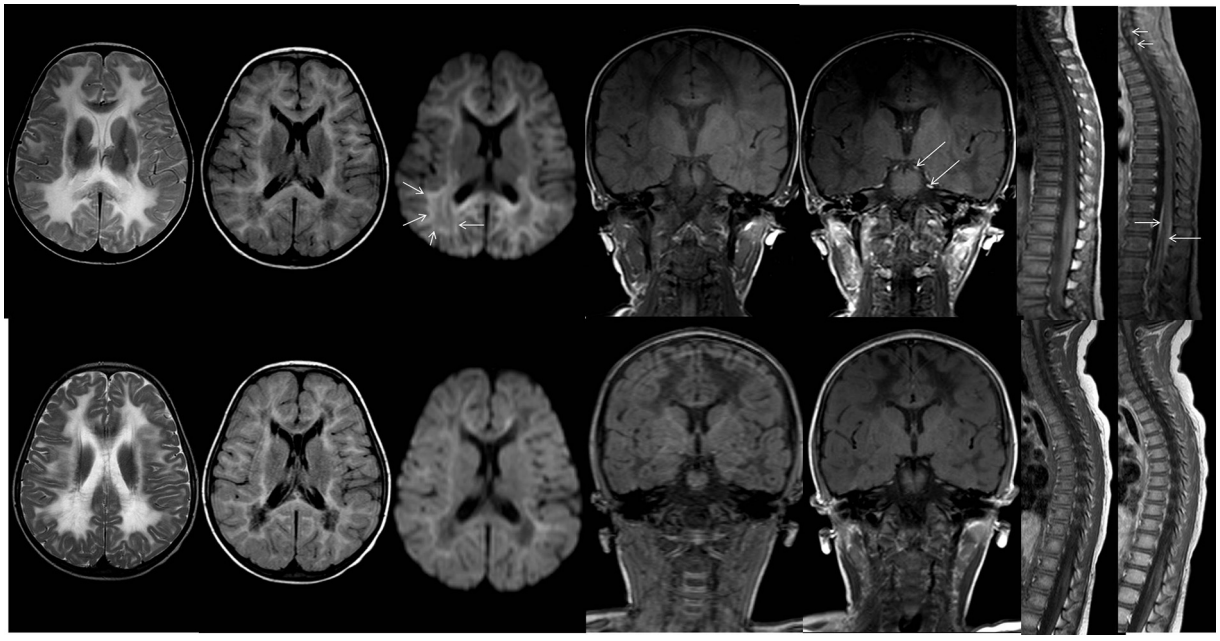

Fig. 1 – Top row – MRI at presentation. T2w axial, FLAIR axial and DWI trace axial images demonstrate diffuse symmetric bilateral cerebral signal abnormality with infratentorial involvement (not shown), with some central cystic changes as seen on FLAIR and a rim of restricted diffusion on DWI (arrows). Pre- and post-gadolinium coronal T1w images of the head and spine demonstrate symmetric diffuse gadolinium enhancement of the oculomotor nerves, trigeminal nerves, cervical and lumbar roots (arrowed on the postcontrast images). Bottom row – corresponding images from a follow up MRI 6 months later showed mild resolution of the white matter swelling and subtle improvement of signal abnormality and also some improvement in the craniospinal neural enhancement.