Paediatric MOG antibody-associated disease and movement disorder – a case report

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Abstract:

MOG-Ab are a well-recognised cause of acquired demyelinating syndromes in both adult and children. Despite basal ganglia involvement on imaging, movement disorder is not a cardinal feature. We describe a 2-year-9-month-old girl who presented with sever encephalopathy with aphasia, seizures, and a complex movement disorder with dystonic posturing and tonic eye deviation. Neuroimaging revealed subtle asymmetrical predominantly white matter signal changes. MOG-Ab were positive in the serum. Other known pathogenic autoantibodies including NMDAR-Ab were negative. The patient made a complete recovery following 2-week corticosteroid treatment. This case highlights the need for MOG-Ab testing in children with suspected autoimmune encephalopathies.

Introduction:

Myelin oligodendrocyte glycoprotein antibodies (MOG-Ab) are seen in up to 50% of children with acquired demyelinating syndrome (ADS).[1] Patients with an ADS and MOG-Ab positivity identified acutely at first presentation are more likely to have a favorable clinical outcome and less likely to have a multiple sclerosis course in contrast to children lacking MOG antibodies.[2] In addition, this group of patients usually responds quickly to first-line treatments.[3]

MOG-Ab associated disease commonly presents with optic neuritis (ON) or transverse myelitis in adults[3] and as ON or acute disseminated encephalomyelitis (ADEM) in children[2]. Expected MRI findings in children are confluent, bilateral white matter changes with a distinct enhancement pattern.[4]

More recently, reports of patients with acute onset of seizures[5,6] and MRI changes limited to the cortex[6] has expanded the phenotype of MOG-Ab associated disease beyond the white matter, to also include grey matter encephalitis.

Here we report a paediatric case of MOG-Ab associated disease presenting as ADEM associated with a movement disorder and seizures, mimicking autoimmune encephalitis.

Written informed consent for the publication of the case description and video was obtained.

Case report:

A previously well 2-year-9-month-old girl with a normal antenatal and developmental profile presented with a four-day history of fever and vomiting, followed by acute onset of lethargy and progressive encephalopathy. On initial examination she was drowsy with eye opening to voice and a normal response to pain, she was aphasic and did not seem to recognize her parents. She had four limb weakness and was unable to walk or sit unsupported. On day six of illness she had a brief right-sided focal seizure which responded to buccal midazolam. She was then started on phenytoin maintenance and did not have any further seizures. She was also noted to have repetitive and frequent stereotyped dystonic episodes characterized by tonic eye deviation to the right, mouth opening, jerky tongue movements, flexion of lower limbs at the hips, extension of right arm and flexion of the right wrist (Video 1).

Brain MRI (on day three of admission) demonstrated bilateral asymmetrical lesions in the deep white matter, brainstem and cortex, with no contrast enhancement (Figure 1-A). Repeat imaging on day six demonstrated no change in the brain with normal spinal-cord. There was no evidence of optic nerve involvement. A prolonged 16-hour EEG showed continuous high amplitude slow rhythmic activity not timely related with the stereotyped movements captured. There were also occasional epileptiform discharges seen over the frontal/central regions, right more than left, but these were also not related to clinical events (Figure 1-B). CSF showed 4 white blood cells, normal protein, glucose and lactate. CSF culture and viral PCR for HSV1/2, VZV and Parechovirus were negative. Serum MOG antibodies were positive. NMDAR-Ab (serum and CSF) and CASPR2, LGI1, AMPAR, $GABA_A$ $GABA_B$ antibodies in the

serum were negative. Serum and CSF oligoclonal bands were both positive but there were additional bands in the CSF.

The patient was initially treated with triple antimicrobial (IV ceftriaxone, IV acyclovir and enteral azithromycin) which were stopped after negative culture and virology results. The patient completed three days of intravenous methylprednisolone (30mg/kg) followed by oral prednisolone (2mg/kg) weaning course over 2 weeks.

She made a good clinical recovery and one week after steroid treatment initiation she was able to sit up from lying position, sit unsupported for short periods and take a few steps with light truncal support. Her verbal communication also improved, and she was able to speak in short sentences appropriate to context. At one month review she had recovered completely, with normal mobility and no focal neurology other than using her left hand more, previously she was right handed. We were still unable to repeat serum MOG antibodies as the girl is extremely needle phobic.

Discussion:

In this case the subtle white matter changes in an encephalopathic child made us suspect an immune-mediated encephalopathy. Although consistent with a diagnosis of ADEM, some of the features were not typical in particular the movement disorder, more frequently seen in anti-NMDAR encephalitis.[7]

The discovery of pathogenic autoantibodies that bind to extracellular proteins of neuronal and glial proteins, resulted in a paradigm shift in the diagnosis and management of encephalitis in children[1,8]. The most common autoimmune encephalitis in children is anti-NMDAR encephalitis. Children typically present with a polysymptomatic recognizable disease syndrome featuring psychiatric features, agitation, movement disorders, mutism, seizures and encephalopathy.[9] Interestingly, our patient did not have irritable insomnia, frequently seen in patients with anti-NMDAR encephalitis and in fact showed increased somnolence.

Contrary to MOG-Ab associated disease[4], brain MRI in anti-NMDAR encephalitis is usually normal. Also, while patients affected with anti-NMDAR encephalitis frequently show a slow response to steroid treatment and may require second and third line treatment options[10], there is usually a quick response to first line immunotherapy treatment in MOG-Ab associated disease[2] as seen in our case.

Despite basal ganglia involvement frequently described in patients with MOG-Ab associated disease[4], movement disorders or tonic eye deviation are not a well described feature.[2]

Tonic eye deviation can be caused by symptomatic lesions in the context of CNS demyelination, but this has been more frequently reported in paediatric patients with seizures, ischemic events, tumours or vestibular, brainstem or cerebellar disorders. Our patient had a prolonged video EEG that confirmed episodes of tonic eye deviation and stereotyped movements were not epileptic, however occasional unrelated epileptiform discharges were seen.

Dyskinesia is an uncommon but reported side-effect of phenytoin treatment. This is usually only present when serum drug levels are within toxic levels. We believe that it is very unlikely for this to be the cause for our patient's abnormal movements as these stopped immediately after the intravenous methylprednisolone treatment while she was continued on maintenance phenytoin.

In conclusion, this case highlights the need to test for MOG-Ab in children presenting with acute encephalopathy even when the clinical phenotype extends beyond what is typically expected for ADEM. With a wide differential diagnosis in children presenting with acute encephalopathies, which includes both inflammatory and non-inflammatory conditions, prompt diagnosis has management, treatment and prognostic implications.

References

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Figure and video captures:

Figure 1-A: Axial T2-weighted images at the level of the midbrain, genu of corpus callosum & centrum semiovale and one coronal FLAIR image at the level of the cingulate gyrus anterior to the genu of the corpus callosum; demonstrating the bilateral and asymmetric distribution of multiple non-enhancing poorly marginated lesions. These are present in the midbrain (small arrow head), genu of the corpus callosum (thin arrow) and centrum semiovale (thick arrows). The cortical disease is demonstrated in the left cingulate girus in the coronal image (large arrow head).

Figure 1-B: EEG taken at day 5. Widespread, high amplitude semi-rhythmic 1-1.5 Hz activity which was persistent and did not alter with clinical events.

Video 1: Video clip captured during EEG recording at day 5. As seen in the video, the child had frequent episodes of tonic eye deviation to the right side, abduction of the right arm, wrist flexion, bilateral lower leg flexion at the hips and knees and mouth opening. EEG activity did not alter during these episodes.