Myelin oligodendrocyte glycoprotein-antibody (MOG-IgG) associated disease with centrally located long spinal cord lesion in a 14-month old child

Mohamad Syafeeq Faeez Md Noh1,2

1Department of Radiology, Universiti Putra Malaysia (UPM) Teaching Hospital, Persiaran MARDI-UPM, Serdang, Selangor, Malaysia. 2Department of Imaging, Level 3, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia (UPM), Serdang, Selangor, Malaysia.

ABSTRACT: Myelin oligodendrocyte glycoprotein-antibodies (MOG-IgG) are associated with acquired inflammatory demyelinating syndromes, seen predominantly in children and young adults. The overlapping clinical and radiological features of the heterogenous spectrum of demyelinating central nervous system (CNS) diseases makes the detection of MOG-IgG antibodies important for prognosis and treatment decisions. Herein, we describe the occurrence of MOG-IgG associated disease presenting as acute disseminated encephalomyelitis (ADEM), with spinal MRI findings of centrally located long cord lesion in a 14-month old child.

KEYWORDS: Myelin oligodendrocyte glycoprotein-antibody (MOG-IgG) associated disease, acute disseminated encephalomyelitis (ADEM), long cord lesion (LCL), demyelination, magnetic resonance imaging (MRI)

Introduction

Acute disseminated encephalomyelitis (ADEM) is an autoimmune, non-vasculitic, demyelinating disease of the central nervous system (CNS) which predominantly affects children. Population-based studies quote the incidence of ADEM to be 0.3 to 0.6 per 100 000 per year.1,2,3 Albeit uncommon in adults, a second peak is quoted to occur in those over 60 years old.2 The signs and symptoms include fever, encephalopathy, seizures, and multifocal neurological manifestations. Due to the overlapping neurological signs and symptoms, other possible etiologies including meningitis, infective encephalitis, multiple sclerosis (MS), transverse myelitis, and neuromyelitis optica spectrum disorder (NMOSD) need to be ruled out, to confirm the diagnosis. Though traditionally considered a monophasic illness, some patients may present with a multiphasic illness, possibly revising the diagnosis to MS—as per the International Pediatric Multiple Sclerosis Study Group.4

Spinal lesions in ADEM have been reported to occur in up to 30% of cases.5 A centrally located long cord lesion (LCL) is seen as hyperintensities on T2 weighted/fluid attenuated inversion recovery (FLAIR) sequences on MRI, appearing as an “H” sign; a finding that is usually attributed to NMOSD. Other possible causes of this finding include tumors, infections, vascular pathologies, autoimmune diseases, and ADEM.6 We report the occurrence of MOG-IgG associated ADEM in a 14-month old child, with spinal MRI findings of a centrally located long cord lesion.

Case report

A 14-month old child, born full term, with no significant antenatal history as well as history of recent vaccination presented to us with fever, cough, and rapid breathing for the past 1 week. On the day of presentation, upon review, the child had 1 episode of seizure, manifesting as a tonic clonic movement of the right upper limb, which aborted spontaneously. Upon examination, the child was lethargic. The recorded temperature was 37°C, with blood pressure reading of 113/60 mmHg, oxygen saturation of 97% under room air, with fair hydration. Mild intercostal and subcostal recessions were noted. The respiratory rate was 40 breaths per minute. No murmurs were noted on auscultation of the heart. Minimal crepitations of the left lung base was heard. Abdominal examination was unremarkable. Neurological examination noted an unsustained clonus of the right lower limb; otherwise, the tone, power, and reflexes of the remaining limbs were normal. The Babinski’s reflex was equivocal. No more episodes of fitting were reported apart from the episode at presentation. Upon further questioning, the parents reported an episode of “flu” approximately 3 weeks prior to current presentation, which resolved with medication. Biochemical tests including a full blood count, renal profile, and blood cultures were negative. Serum anti-aquaporin 4 (AQP4) antibody and oligoclonal bands were negative. However, serum for MOG-IgG using cell based assay (indirect fluorescence test) came back positive (titer 1:1000). A lumbar puncture was pursued, which revealed negative cerebrospinal fluid (CSF) cultures, Ziehl–Neelsen staining, negative Indian ink stain, with normal glucose, chloride, and protein levels. No lymphocytic pleocytosis was seen. Both AQP4 and oligoclonal bands were also sent from CSF, with negative results. An urgent MRI of the brain and spine was scheduled, which showed multiple ill-defined T2/FLAIR hyperintense white matter lesions which were located in the subcortical and deep white matter regions.
of bilateral centrum semiovale, right frontal, bilateral parietal and occipital regions, splenium of the corpus callosum, left cerebral and cerebellar peduncle with extension to the left cerebellum, as well as the right thalamus (Figure 1). Abnormal high T2/FLAIR signal intensities were also noted in the spinal cord, with long segment involvement from T2 to T5 levels, as well as at the conus medullaris. On the axial images, these were restricted to the central aspect of the cord, with an “H” sign (Figure 2a). All these abnormal signal intensities of the brain and spinal cord exhibited no diffusion restriction, no blooming on gradient echo (GRE) sequence, and no enhancement post gadolinium administration. Based on the clinical history, encephalopathy, neurological findings, supplemented by biochemical and radiological findings, a final diagnosis of MOG-IgG associated ADEM with central long cord spinal involvement was made, after fulfilling the diagnostic criteria.

The child was treated with IV Rocephin, IV acyclovir, as well as IV methylprednisolone (for 5 days) before being converted to oral prednisolone. After 1 week of hospital admission, the child recovered with no neurological deficits, and was discharged well, pending next outpatient review.

Discussion

ADEM is an autoimmune, non-vasculitic, demyelinating disease of the CNS which predominantly affects children, although occurrence across all age groups is also possible. It is typically a monophasic disorder; occurring once with no recurrence. When two attacks occur within 4 weeks of one another, it is called multiphasic disseminated encephalomyelitis (MDEM)—usually difficult to differentiate with recurrent episodes of MS. Further history in cases of ADEM usually reveals a prior episode of fever, with upper respiratory tract

Figure 1. Axial brain MRI images, in fluid attenuated inversion recovery (FLAIR) sequence showing; (A) Abnormal high signal intensity is noted at the left cerebellar peduncle, with extension to the left cerebellar hemisphere. (B) Abnormal high signal intensity of the splenium is seen (arrow). Notice multiple foci of abnormal signal intensities at the right temporal cortex and bilateral occipital regions.

Figure 2. Sagittal (A,B) and axial (C) T2 weighted spine MRI images, showing; (A) Long segment abnormal high signal intensity noted from the level of T2 to T5 vertebra (arrow), with no obvious cord expansion. (B) Abnormal high signal intensity is seen involving the conus medullaris, with cord expansion. (C) The abnormal high signal intensity is noted to be confined centrally (in the gray matter), with sparing of the periphery (“H” sign). This is at the level of T5 vertebra.
symptoms, which may be bacterial or viral in origin. This may be found in up to 72–77% of patients.\(^7,6\)

The pathogenetic mechanisms underlying ADEM are incompletely understood, with multiple theories put forth. One of the most common theories proposes common antigenic determinants that are shared by myelin autoantigens, such as proteolipid protein, myelin basic protein, and myelin oligodendrocyte with that of an infecting pathogen.\(^8\) It has been reported that in patients with ADEM, the frequency of T cell reactivity to myelin basic protein is as high as 10 times, in comparison to those with encephalitis, or normal controls.\(^10\)

Other diagnoses to consider when patients present with overlapping neurological signs and symptoms include meningitis, encephalitis, and demyelinating diseases such as MS and NMOSD. Thus, a high index of suspicion needs to be maintained, when other diagnoses have been ruled out. There are no specific laboratory or biochemical tests to diagnose ADEM. However, in light of the possible differential diagnoses, specific laboratory tests to rule out demyelinating diseases such as MS and NMOSD, as well as CSF studies to look for evidence of meningitis and encephalitis need to be pursued.

MOG-IgG associated disease is a relatively new clinical entity, which may present clinically as ADEM, NMOSD, optic neuritis, encephalitis other than ADEM, and myelitis. It is seen predominantly in children and young adults. The prevalence of MOG-IgG antibodies can be seen in up to 30% of children with acquired demyelinating syndromes.\(^11\) Some studies have suggested an increased risk of relapse in patients with persistence of MOG-IgG seropositivity during follow up, hence the need for prompt diagnosis, for long term follow up and prognostication. Our patient fulfilled the diagnostic criteria for ADEM, and had high serum MOG-IgG titer (1:1000), hence the need for long term follow up to monitor persistence or abridgment of seropositivity.

The imaging findings of ADEM are best investigated via MRI. MRI of the brain utilizing T2 weighted/FLAIR sequences typically show bilateral symmetrical (but may also be asymmetrical) abnormal signal intensities, in the deep and subcortical white matter, usually non-enhancing, with no restricted diffusion—these were seen in our patient. Spinal cord lesions are usually long segment (involving >3 vertebral bodies) and involves both gray and white matter; isolated involvement of the gray matter, as seen in this case, is more commonly attributable to MOG-IgG associated disease. Additionally, one study reported an increased risk of clinical recurrence, when spinal lesions are seen in ADEM.\(^12\)

The treatment of ADEM involves high-dose steroids, the most commonly reported first line therapy. However, other options may include the use of intravenous immunoglobulin (IVIg), whether on its own or in combination with steroids. When steroid therapy fails, some authors recommend the use of plasma exchange.\(^13\)

### Conclusion

ADEM is an important clinical entity to be considered when children present with non-specific neurological manifestations, after other causes have been excluded. Traditionally monophasic, the possibility of either MDEM or even MS needs to be taken into consideration, when symptoms recur. The recent finding of MOG-IgG also necessitates this disease entity to be considered in pediatric acquired demyelinating syndromes. Thorough history and clinical examination, with targeted biochemical tests and MRI of the brain and spine aid accurate and swift diagnosis, allowing early institution of treatment, with good long term neurological outcome.

### Author Contributions

MSF is responsible for the data and preparation of the manuscript for publication.

### Informed Consent

Written informed consent was obtained from the parents for the publication of this case and all accompanying images/data.

### ORCID iD

Mohamad Syafeeq Faeez Md Noh  [https://orcid.org/0000-0001-9386-8914](https://orcid.org/0000-0001-9386-8914)

### REFERENCES

1. Pohl D, Alper G, Van Haren K, et al. Acute disseminated encephalomyelitis: updates on an inflammatory CNS syndrome. *Neurology*. 2016;87:538–545.
2. Dale RC, de Sousa C, Chong WK, Coc TC, Harding B, Neville BG. Acute disseminated encephalomyelitis, multiphasic disseminated encephalomyelitis and multiple sclerosis in children. *Brain*. 2000;123:2407–2422.
3. Chen Y, Ma F, Xu Y, Chu X, Zhang J. Incidence of acute disseminated encephalomyelitis in the Jiangsu province of China, 2008-2011. *Mult Scler J Exp Transl Clin*. 2015;1:1–7.
4. Krupp LB, Tardieu M, Amato MP, et al. International Pediatric Multiple Sclerosis Study Group criteria for pediatric multiple sclerosis and immune-mediated central nervous system demyelinating disorders: revisions to the 2007 definitions. *Mult Scler*. 2013;19:1261–1267.
5. Marin SE, Callon DJ. The magnetic resonance imaging appearance of monophasic acute disseminated encephalomyelitis: an update post application of the 2007 consensus criteria. *Neuroradiology Clin N Am*. 2013;23:245–266.
6. Monden Y, Yamagata T, Kuroiwa Y, et al. A case of ADEM with atypical MRI findings of a centrally-located long spinal cord lesion. *Brain Dev*. 2012;34:380–383.
7. Hynson JL, Kornberg AJ, Coleman LT, Shield L, Harvey AS, Kean MJ. Clinical and neuroradiologic features of acute disseminated encephalomyelitis in children. *Neurology*. 2001;56:1308–1312.
8. Tenembaum S, Charosnes N, Feijerman N. Acute disseminated encephalomyelitis: a long term follow-up study of 84 pediatric patients. *Neurology*. 2002;59:1224–1231.
9. Stonehouse M, Gupte G, Wassmer E, Whitehouse WP. Acute disseminated encephalomyelitis: recognition in the hands of general pediatricians. *Arch Dis Child*. 2003;88:122–124.
10. Pohl-Koppe A, Burchert SK, Thiele EA, Hafler DA. Myelin basic protein reactivity to myelin basic protein is as high as 10 times, in comparison to those with encephalitis, or normal controls. *Neurosurg*. 2013;96(suppl 1):A1–A100.
11. Kisseih E, Mamilla D, Kaddurah A. A rare presentation of encephalopathy in a 3-year-old child. *Global Pediatric Health*. 2017;4:1–4.