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Case Report

MOG-IgG Associated Brainstem Encephalitis in a Chinese Boy: Complication of *Mycoplasma pneumoniae* Infection

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Abstract MOG-IgG associated disorder is uncommon in children. It has a wide range of presentation which may make diagnosis difficult. The triggering factor for the disease is not well reported. We reported a 5-year-old Chinese boy with slurred speech and unsteady gait, presented ten days after *Mycoplasma pneumoniae* infection, and he was later diagnosed to have MOG-IgG associated brainstem encephalitis.

Key words *Brainstem encephalitis; MOG-IgG associated disorder, Mycoplasma pneumoniae*

Introduction

MOG-IgG associated disorder (MOGAD) is an uncommon acquired immune mediated demyelinating disease, and is recently recognised as a distinct clinical entity. Myelin oligodendrocyte glycoprotein antibody (MOG-Ab) targets the myelin oligodendrocyte glycoprotein (MOG) on the outer surface of the myelin sheath and plasma membrane of oligodendrocyte, leading to a spectrum of demyelinating syndromes, such as acute disseminated encephalomyelitis (ADEM), optic neuritis (ON) and transverse myelitis.[1] While demyelinating disease was well-known to be triggered by viral infection or immunisation, to our knowledge, only one case of MOG-associated ADEM was reported following *Mycoplasma pneumoniae* infection in paediatric population.[2] Our case demonstrated different clinical features and treatment strategy that was worth reporting.

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We described a 5-year-old Chinese boy, who developed slurred speech and unsteady gait following *Mycoplasma pneumoniae* infection was finally diagnosed to have MOG-IgG associated brainstem encephalitis.

Case Report

In June 2019, a 5-year-old locally born Chinese boy with good past health was first admitted to our hospital with 5-day history of fever and dry cough. On examination, his temperature was 38.5°C, blood pressure 94/59 mmHg, pulse rate 109 beats per minute and respiratory rate of 32 per minute. Examination of chest revealed bilateral basal crepitation with no respiratory distress. Cardiovascular, abdomen and neurological examinations were unremarkable.

Complete blood count, liver function test and renal function tests were normal. C-reactive protein (CRP) was elevated at 17.3 mg/L (<9.9 mg/L). Nasopharyngeal swab for *Mycoplasma pneumoniae* DNA polymerase chain reaction (PCR) was positive. It was negative for influenza A, influenza B, adenovirus, parainfluenza virus and enterovirus/rhinovirus. Chest X-ray showed no consolidation and pleural effusion. Patient was treated as *Mycoplasma pneumonia* with Azithromycin. Fever settled and cough improved, hence he was discharged three days after admission.

Ten days after fever onset, patient was readmitted to

our department for slurred speech and unsteady gait. There was no drowsiness, focal weakness, headache and seizure. Physical examination revealed that he was afebrile. The blood pressure was elevated, up to 150/75 mmHg. The patient was fully conscious and showed mild slurred speech with associated gurgling sound. Examination showed mild truncal ataxia with wide-based gait. Other cerebellar signs were negative. Otherwise, examination of the cranial nerves was unremarkable and the gag reflex was present. He had normal motor tone, full muscle power and normal deep tendon reflexes with bilateral down going plantar response. Chest, cardiovascular and abdominal examinations were unremarkable.

Repeated blood tests showed thrombocytosis with platelet count of $576x10^9$/L ($150-384x10^9$/L). The white cell count and haemoglobin were normal. The previously elevated CRP was normalised. Previous *Mycoplasma pneumoniae* came back to be 23S rRNA Gene positive. Chest X-ray showed no interval change. Magnetic resonance imaging (MRI) brain showed fluffy T2 hyper-intense signals over the medulla oblongata, central and posterior portion of pons, substantia nigra and periaqueductal region (Figure 1). There was neither associated restricted diffusion nor abnormal contrast enhancement.

Lumbar puncture was performed and cerebral spinal fluid (CSF) yielded normal white cell count and no red blood cell. The protein and glucose levels were normal. There was no bacterial growth. Latex agglutination showed negative for *Escherichia coli* K1, *Streptococcus* group B, *Neisseria meningitidis*, *Streptococcus pneumoniae*, *Haemophilus influenzae* type B, *Cryptococcus antigen*. PCR was negative for herpes simplex virus DNA, enterovirus RNA, varicella zoster virus DNA, human herpesvirus 6 DNA and Japanese encephalitis. CSF for *Mycoplasma pneumoniae* PCR was not performed as validated test was not available locally.

Patient was empirically started on IV Cefotaxime and IV Levofloxacin on admission. He was also put on intravenous immunoglobulin (IVIG) of total 2 gram/kg for 2 days for suspected post infectious immune mediated encephalitis. Patient responded well to the treatment. He was given a dose of hydralazine for elevated blood pressure, which was subsequently normalised. The patient was also assessed by speech therapist and confirmed to have dysphagia. Feeding was gradually stepped up from soft diet under the guidance of speech therapist. He then tolerated normal diet 3 days after completion of IVIG. Slurred speech and unsteady gait gradually improved after IVIG and fully resolved 3 days afterwards.

Pre-IVIG sample later came back showing the serum anti-MOG was positive. Serum anti-aquaporin-4, anti-NMDA-receptor, anti-GQ1b, anti-GM1, anti-GD1b, anti-CASPR2, anti-LGI1, anti-AMPAR1/2, anti-DPPX, anti-

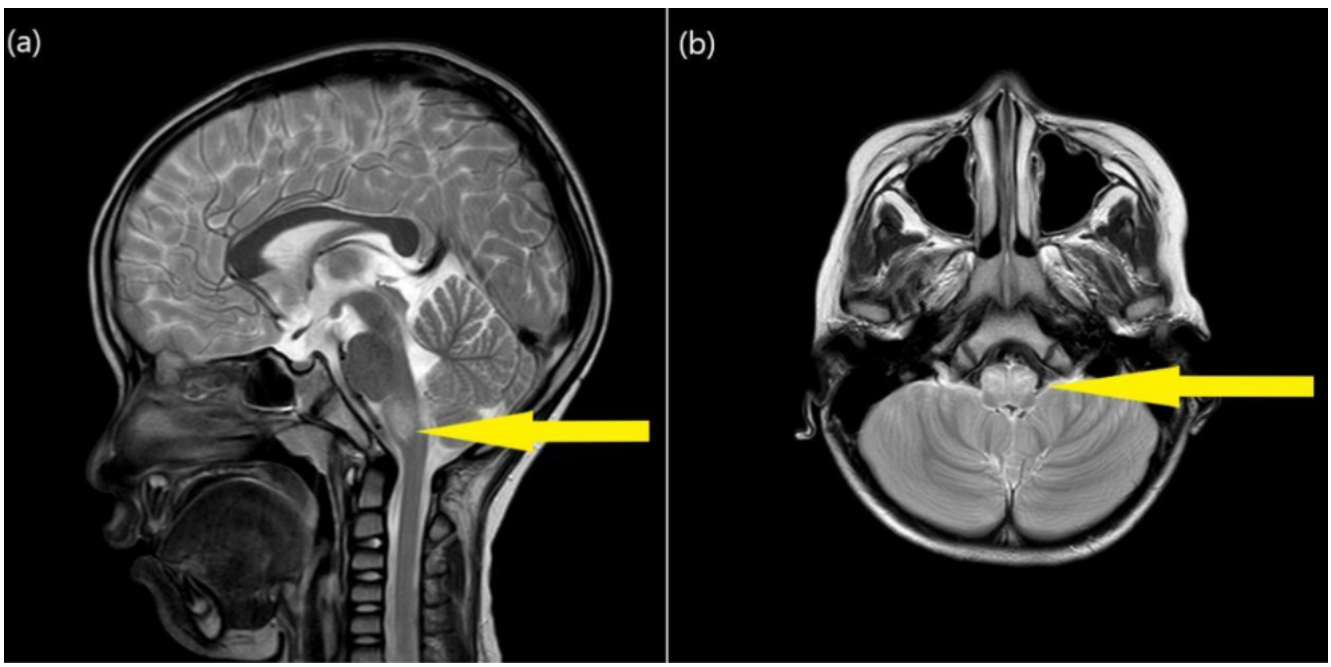

Figure 1 Magnetic resonance imaging brain showing fluffy T2 hyper-intense signals over the brainstem. (a) Sagittal plane (b) Axial plane.

GABAR B1/B2 were all negative. CSF anti-NMDA-receptor was also negative. Patient was diagnosed as MOG-associated brainstem encephalitis, as sequelae of *Mycoplasma pneumoniae* infection.

Visual evoked potential three months later was normal. MRI brain showed resolution of brainstem encephalitic change. Repeated serum test for anti-MOG 6 months later was negative. Patient had no relapse but he defaulted follow up after six months.

Discussion

MOGAD is a rare disease entity in paediatric population, with a higher incidence compared to adults (0.31 versus 0.16 per 100,000 populations).[3] The development of highly specific cell-based assay allowed the detection of MOG-Ab in one third of the paediatric patients with acquired demyelinating syndrome.[1] MOG-Ab was found to be encephalitogenic and a wide variety of clinical manifestations have been described in these patients. Hence, MOGAD is now emerged as a new neuroinflammatory disease distinct from other acquired demyelinating syndromes of the central nervous system like neuromyelitis optica spectrum disorder and multiple sclerosis. MOGAD can present as different clinical phenotypes initially, which changes with age from ADEM in children to optic neuritis and myelitis in adults. Brainstem manifestation was quite infrequent at any age.[4] Isolated attack of brainstem was reported down to 1.8% in a cohort. Although up to one third of patient can be asymptomatic, they can develop hypoventilation, dysarthria, dysphagia, balance difficulties, limbs weakness and ataxia.[5] In our patient, he was tested positive for MOG-IgG, and the MRI brain showed involvement of the midbrain (periaqueductal region, substantia nigra), pons and medulla oblongata that could account for the unsteady gait, elevated blood pressure, slurred speech and dysphagia. We hence diagnosed our patient suffered from an exceedingly rare complication following *Mycoplasma pneumoniae* infection in paediatric population, which is MOG-IgG associated brainstem encephalitis.

Mycoplasma pneumoniae infection is a common cause of community-acquired pneumonia. It was well known that infection can be complicated by encephalitis, which can either caused by direct invasion or immune-mediated mechanism. These mechanisms are not mutually exclusive. Despite CSF *M. pneumoniae* DNA was not performed in our patient, the utility of the test in identifying the true pathogenic mechanism might be limited as *M. pneumoniae* DNA was usually not detectable in either of the cases.[6] Instead, our patient's symptoms arose after fever settled, together with the presence of anti-MOG, this would favour a greater contribution of the indirect type of nervous system damage by autoantibodies. It was hypothesized that molecular mimicry between some *M. pneumoniae* component and host myelin glycolipids contribute to auto-antibodies formation, which causes damage to splenium of corpus callosum or adjacent white matter, leading to encephalitis.[6] An example of autoantibodies would include anti-MOG, which was reported to cause neuroinflammatory disease like ADEM.[2] In looking back to our case, brainstem encephalitis could have been caused by indirect type of nervous system damage secondary to MOG-Ab formation following *M. pneumoniae* infection. However, further study is required to accurately delineate the relationship between *M. pneumoniae* infection and anti-MOG associated disorder.

The optimal acute treatment for both MOGAD and neurological complications of *M. pneumoniae* infection are debated. Antibiotic treatment is the cornerstone of all *M. pneumoniae* related neurological disease. Studies reported antibiotics help prevent direct central nervous system damage and interrupt autoimmunity. However, the effectiveness of corticosteroids, IVIG and immunosuppressive drugs are still unclear but they can be considered in selective cases.[6] As for MOGAD, there is lack of controlled trials in paediatric population. Intravenous high dose corticosteroid was considered as first line treatment. For patients with poor response to corticosteroid, IVIG or therapeutic plasma exchange was considered as second line therapy.[7] For our patient, he was started on antibiotics with subsequent IVIG and showed good response. Interestingly, animal study showed that IVIG reduced autoantibodies associated demyelination by interfering with the complement cascade instead of blocking of the anti-MOG antibodies.[8] The effectiveness of IVIG in our case would serve as a reference for future study on treatment of MOGAD, particularly after *M. pneumoniae* infection.

Serial testing of MOG-Ab might be useful in patients with MOGAD. 70-80 percent of children with MOGAD develop monophasic disease and hence their antibodies likely to disappear over time, with a median of 12 months.[9] Children with persistent MOG-Ab are at risk of developing relapsing acquired demyelinating disease like multiphasic ADEM. Testing patient for conversion to seronegative

might have prognostic implication, hence, it was recommended to recheck MOG-Ab 6-12 months after acute attack.[10] Our patient with good recovery showed negative MOG-Ab at 6 months after initial attack. However, the lack of long term data in children warrants continuous follow up for relapse of the disease.

In conclusion, MOGAD can be a complication of *Mycoplasma pneumoniae* infection. Physician should be alert of this disease entity, especially for patients presenting with neurological symptoms following *Mycoplasma pneumoniae* infection. Once diagnosis is made, appropriate treatment can be offered and our case also highlighted the potential use of IVIG as first line treatment.

Declaration of Interest

There are no conflicts of interests.

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