Acute brainstem encephalitis associated with Mycoplasma pneumoniae in an adult

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Abstract

Brainstem encephalitis (BE) associated with Mycoplasma pneumoniae in adults is rare and the diagnosis is challenging. We diagnosed BE associated with M. pneumoniae through increasing IgM level using EIA with clinical feature. This method of clinical diagnosis would be helpful to treat with macrolide antibiotics earlier and showed good outcomes.

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Conflict of Interest

None of the authors have any conflicts of interest to disclose.

Key Clinical Message: Brainstem encephalitis (BE) associated with *Mycoplasma pneumoniae* in adults is rare and the diagnosis is challenging. We diagnosed BE associated with *M. pneumoniae*through increasing IgM level using EIA with clinical feature. This method of clinical diagnosis would be helpful to treat with macrolide antibiotics earlier and showed good outcomes.

Keywords: Brainstem encephalitis, *mycoplasma pneumoniae* , Enzyme-Immunoassay, diagnostic method

1. Introduction

The etiologies of brainstem encephalitis (BE) can be divided into infectious and autoimmune. The most common infectious causes are listeria, enteroviruses, and herpes viruses.[1] Among these causes, central nervous system (CNS) infection with*Mycoplasma pneumoniae* is rare in adults than in pediatric patients. As CNS manifestations related to *M.* pneumoniae are variable and a positive serological result in adults may simply reflect carriage or previous encounters with *M. pneumoniae* , making the diagnosis of BE associated with *M. pneumonia* particularly challenging in adult patients.[2]

We report a case of BE associated with *M. pneumoniae* in an immunocompetent adult patient, diagnosed based on an increased level of specific IgM antibody against *M. pneumoniae* through enzyme immunoassays (EIAs), as comparing levels between the acute phase and the convalescent sera. The patient recovered without any sequelae despite initial severe neurological deficits.

2. Case report

A 43-year-old, otherwise healthy woman visited our emergency room with high fever and a sore throat. She was discharged initially after symptom control, but after three days re-visited with an altered, drowsy mental status (Glasgow coma scale, 4). The body temperature was 38. The initial laboratory tests showed mild leukocytosis with slightly elevated C-reactive protein. A lumbar puncture was performed and cerebrospinal fluid (CSF) analysis showed minimal pleocytosis (white blood cells, 3cells/mm^3) with slightly elevated protein concentration of 46 mg/dL. The brain MRI (T2-weighted and fluid-attenuated inversion recovery) displayed diffuse swelling in the bilateral cerebral regions involving the bilateral pons (Fig. 1). We immediately administered intravenous (IV) ceftriaxone, vancomycin, acyclovir, and dexamethasone. On hospital day 3, IV immunoglobulin was also administered since autoimmune encephalitis such as NMDA encephalitis could not be ruled out. On hospital day 4, the patient's mental status recovered, but diplopia remained. The specific serological IgM test via EIA (DIESSE Diagnostica, Italy) for *M .pneumoniae* was positive (1.5 [cutoff value: 0.9]) and that for IgG was negative. The antibiotics regimen was changed to clarithromycin due to infection with *M . pneumoniae* . Routine CSF gram stain and bacterial cultures, and polymerase chain reaction tests (PCR) showed negative results for herpes simplex, varicella zoster, cytomegalovirus, Epstein-Barr virus, and Mycobacterium. The tests for autoimmune antibodies (anti-NMDAR, -LGI1, -CASPR2, -AMPA1, -AMPA2, -GABAB-R, -Hu, -Yo, -Ri, -Ma2, -CV2/CRMP5, and -amphiphysin) in the CSF and serum were negative. Also, serum anti GQ1b, GM1 and GD1b IgM antibodies were negative. On hospital day 10, serum IgM value for *M. pneumoniae* increased by up to 2.1-and the IgG test still was negative. After one month, the patient fully recovered from the neurological deficits and a follow-up brain MRI was completely improved.

Written informed consent was obtained from the patient for publication of the case and any accompanying images.

3. Discussion

In this case report, we present a middle-aged adult patient with BE associated with *M. pneumoniae* infection, diagnosed via positive IgM tests and increased levels in acute and convalescent sera with an EIA. The patient was successfully treated with clarithromycin and intravenous immunoglobulin.

M. pneumonia is well known to cause respiratory tract disease and extrapulmonary manifestations are also common[3]. It is frequently associated with encephalitis, especially in children. Lerer and Kalavsky found that 53 % of patients with CNS disease associated with *M. pneumoniae* were aged between 6 and 20 years[4]. In adults above middle ages, only a few cases have been reported, and one of these patients took an immunosuppressive agent[5-7]. Encephalitis caused by *M. pneumoniae*cannot be reliably diagnosed in adults, because the incidence rate is low and there are no clinical or radiologic signs indicating a mycoplasma etiology of CNS disease in addition to the absence of a clear diagnostic marker in CSF. The detection rate of *M .pneumoniae* by PCR in the CSF of *M . pneumoniae*encephalitis patients is relatively low (0–14 %), and serologic tests are indispensable[2]. In addition, due to the high prevalence of *M . pneumoniae* infection, one measurement of high serum antibody titers may simply indicate carriage or a previous infection[8]. A reliable diagnosis may be achieved by using paired patient sera in order to detect seroconversion and/or increase in antibody titers. The gold standard is a four-fold increased Ig titer in partial agglutination assays or complement fixation tests.[2] An EIA test can detect IgG and IgM separately to distinguish current from past infections. Several commercial EIA kits are now available and in some studies, the EIA method had moderate to high sensitivity and specificity.[2] Furthermore, correlation of *M. pneumoniae* IgM values obtained by various IgM assays with particle agglutination assay titers was also noted.[9] In our case, the level of IgM was increased in paired sera and the diagnostic value of an increasing titer should be validated in additional

validation studies.

The pathogenesis of encephalitis associated with the respiratory pathogen *M. pneumoniae* is not well understood. A direct infection of the CNS and an immune-mediated process have been discussed.[2] Considering several cases of Guillain-Barré syndrome[10], Bickerstaff brainstem encephalitis[11], and N-methyl-D-aspartate receptor associated with *Mycoplasma spp.* Infection[12], the immune response to *M. pneumoniae* in the CNS can be an important factor that contributes to encephalitis.[6] Therefore, the development of new diagnostic tools, such as the detection of antibodies against *M. pneumoniae* in the CSF is necessary.

M . pneumoniae lacks a cell wall and beta-lactate antibiotics are not suitable to treat the infection. Doxycycline, a macrolide can be used and corticosteroids may be beneficial according to a recent review of severe cases.[2]

We diagnosed BE associated *M. pneumoniae* infection through EIA with an increasing titer of IgM in acute and subacute paired sera. The early treatment with macrolide antibiotics resulted in a good outcome for our patient. IV immunoglobulin was administrated for five days and might have supported the recovery. Considering the pathogenesis of immune-mediated processes, it will be necessary to conduct further studies on the efficacy of immunomodulatory treatment.

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Author contribution

WMG and SJW participated in the management of this patient as well as in the preparation of this manuscript. WMG drafted the initial manuscript, and SJW reviewed and revised manuscript.

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Figure Legends

Fig 1. T2 FLAIR axial images demonstrating the diffuse swelling in the bilateral cerebral swelling that involved the bilateral pons at admission

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