Mycoplasma pneumoniae-associated transverse myelitis with unexpected rapid response to macrolide therapy: a case report

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SUMMARY: Tezer H, Kara A, Haliloğlu G, Devrim İ, Karlı-Oğuz K, Sül D. *Mycoplasma pneumoniae*-associated transverse myelitis with unexpected rapid response to macrolide therapy: a case report. Turk J Pediatr 2008; 50: 585-588.

A seven-year-old boy admitted with the complaints of fever, weakness in legs, sensory loss in lower limb, and difficulty in voiding lasting for two weeks. His initial symptoms also included cough and fever. His spinal magnetic resonance imaging scan demonstrated acute transverse myelitis, and *Mycoplasma pneumoniae*-specific IgM and IgG antibodies were found to be positive in cerebrospinal fluid (CSF) and serum samples. He was treated with a single high-dose intravenous immunoglobulin (2 g/kg/dose) and clarithromycin.

***Mycoplasma pneumoniae* is a frequent cause of upper and lower respiratory tract infections in children. Central nervous system (CNS) manifestations are among the most frequent extrapulmonary complications during the course of the disease. They occur most frequently in children, usually within three weeks after the onset of respiratory illness, with an incidence of approximately 1 in 1,000 patients.**

In this report, we present a seven-year-old boy with transverse myelitis during the course of *Mycoplasma pneumoniae* infection with serological confirmation both in serum and CSF samples.

Key words: Mycoplasma pneumoniae, transverse myelitis, clarithromycin, intravenous immunoglobulin.

Mycoplasma pneumoniae is a common cause of acute respiratory tract infections and atypical pneumonia, particularly in children and young adults[1,2]. Although the main presentation of *M. pneumoniae* infection is respiratory system involvement, there has been increasing evidence of extrapulmonary manifestations due to *M. pneumoniae,* with the wide spectrum including neurologic, cardiac, dermatologic, musculoskeletal, hematologic, and gastrointestinal manifestations[3].

The most serious nervous system complications of *M. pneumoniae* infections are acute transverse myelitis and acute disseminated encephalomyelitis[4,5]. Pathogenesis of central nervous system (CNS) disease caused by *M. pneumoniae* is incompletely understood but autoimmune phenomena seem to have a major role in the development of myelitis[6].

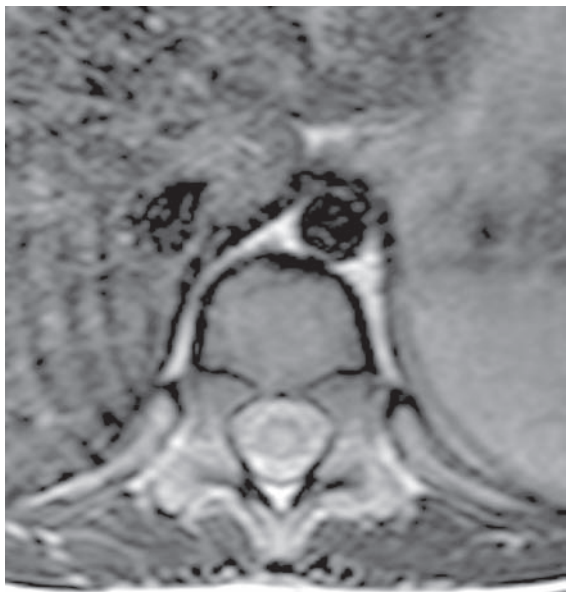
Acute transverse myelitis is characterized by motor, sensory and autonomic dysfunction due to demyelinization of the spinal cord and neuronal damage following focal inflammation. Parainfectious causes account for 30-60% of the cases. Differential diagnosis includes vascular, infectious, neoplastic, autoimmune, collagen vascular and demyelinating conditions. An idiopathic group has also been defined since they are not related to any systemic diseases and etiology could not be defined.

We report our experience in a seven-year-old boy with acute transverse myelitis due to *Mycoplasma pneumoniae* infection, with rapid improvement after macrolide therapy.

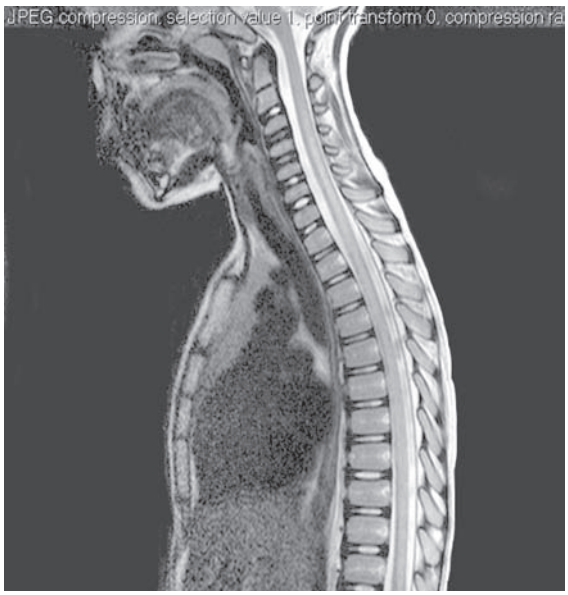
Case Report

A seven-year-old boy with an unremarkable medical history was referred to our hospital with the complaints of fever, weakness in legs, sensory loss in lower limb, and difficulty in voiding lasting for two weeks. His initial symptoms included cough and fever. On physical examination, his vital signs were unremarkable. His neurological examination

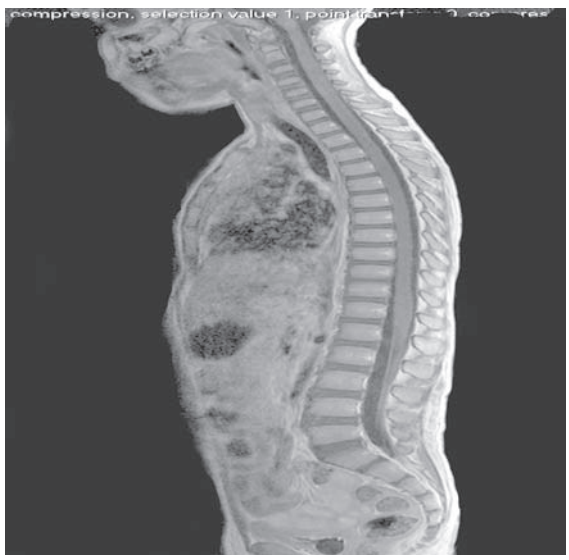
revealed a fully oriented boy. Deep tendon reflexes at lower extremities were absent bilaterally and there was marked proximal and distal muscle weakness. Babinski sign was positive bilaterally. Sensory examination showed diminished temperature and pain sensation below the level of T_{10}. He had stool and urine incontinence with neurogenic bladder. Other systemic physical examination findings were unremarkable. Laboratory investigation revealed that his white blood cell count, hemoglobin level and platelet count were 6600/mm^3, 12.7 g/dl, and 189000/mm^3, respectively. Initial cerebrospinal fluid (CSF) examination (which was done in another center two weeks before referral to our clinic) revealed 73 leukocytes/µl and CSF biochemical values were as follows: protein 220 mg/dl and glucose 62 mg/dl. CSF examination performed in our hospital at the time of admittance revealed clear CSF with protein value of 32 mg/dl and glucose 54 mg/dl. Electromyography revealed involvement of anterior horn motor neurons in L_3-L_5, S_1 lumbosacral roots. His spinal magnetic resonance (MR) imaging scan demonstrated diffuse involvement of the spinal cord by mild swelling, increased T2 signal intensity (Fig. 1a, b) and patchy contrast enhancement (Fig. 1c) at the level of C_3-T_{11} suggestive of acute myelopathy. There was also contrast enhancement of the caudal roots (Fig. 1c). He was treated with a single high-dose intravenous immunoglobulin (IVIG) (2 g/kg/dose) with the diagnosis of acute transverse myelitis. *Mycoplasma pneumoniae*-specific IgM and IgG antibodies were found to be positive in CSF and serum samples. Clarithromycin was added to his supportive therapy on the second day of hospitalization. His muscle strength increased



(b)



(a)



(c)

Fig. 1. Sagittal (a) and axial (b) T2-weighted (W) turbo spin-echo (SE) (TR/TE; 3800/100 ms) images show diffusely increased signal intensity and subtle enlargement of the spinal cord in a long segment. Patchy mild enhancement of the spinal cord and diffuse enhancement of the caudal nerve roots are seen on sagittal postcontrast T1-W SE (TR/TE; 500/15 ms) (c).

at the tenth day of clarithromycin therapy, and urine and stool incontinence started to resolve after 12 days of treatment. Clarithromycin therapy was stopped at the 14th day. He was discharged with mild lower limb weakness on the 14th day and his follow-up examination was normal after one month.

Discussion

Mycoplasma pneumoniae is a common respiratory pathogen. Extrapulmonary complications of *M. pneumoniae* infection include neurologic complications involving the central and peripheral nervous systems and occur in 0.01-4.8% of *M. pneumoniae*-infected patients[7]. Among the neurologic complications, encephalitis is the most frequently encountered complication of *M. pneumoniae*, followed by acute transverse myelitis and encephalomyelitis[7]. It is characterized by demyelination and focal inflammation of the spinal cord causing neuronal damage[5]. The pathophysiology behind the CNS symptomatology in *M. pneumoniae*-associated diseases remains hypothetical. It is suggested that the complications may result either from direct invasion of *M. pneumoniae* into the neural tissue, a neurotoxin produced by the organism, or an immune-mediated damage[4]. The immune-mediated injury could be caused by cross-reacting antibodies to antigens shared by mycoplasma and the brain, organism-induced immunosuppression, immune complex vasculopathy, or vascular microthrombi[8].

In the majority of the patients who have *M. pneumoniae*-associated transverse myelitis, respiratory system infection develops around 10 days prior to neurological findings[9]. However, it has been shown in various studies that this period may vary from 1 day to 30 days. Clinical findings may range from non-specific upper respiratory tract infections to pneumonia[10]. Likewise, our patient had respiratory system findings such as cough 12 days before presentation to our hospital.

Serological methods are used frequently for the diagnosis of *M. pneumoniae*. Yet, there are patients with negative serology even if positivity is demonstrated with polymerase chain reaction[11]. As in our case, there are a few patients reported in the literature who have positive antibodies along with positive antibodies in CSF[12].

For the diagnosis of transverse myelitis, MR imaging is one of the most reliable methods. MR imaging findings correlate with the development, grading and the prognosis of the disease[13]. Nevertheless, it should be kept in mind that MR imaging is not so helpful in differentiation of the many causes of inflammatory myelopathy[14].

The role of antibiotic therapy in the treatment of *M. pneumoniae*-associated myelitis remains undefined because of unsatisfactory knowledge regarding the pathogenesis and natural history of the disease and of controlled trials assessing such therapy. Antibiotic therapy has been temporally associated with clinical improvement in some cases of *M. pneumoniae*-associated acute transverse myelitis[11]. It should be kept in mind that some patients could improve completely and spontaneously without antibiotics[15]. Although macrolides are regarded as first choice in *M. pneumoniae* infections, the fact that they can not penetrate the blood brain barrier is an important disadvantage of these drugs. Azithromycin, which can pass the blood brain barrier, is an agent that should be preferred in children younger than eight years old and ciprofloxacin in adults[6]. In addition, although immune modulators such as steroids[7,6,17], azathioprine, IVIG[12] and plasma exchange[7,16] were used in treatment, their role still remains to be defined.

Although it was not clear whether or not rapid improvement of our patient was associated with antimicrobial treatment, we suggest anti-microbial therapy in cases with suspected mycoplasma infections associated with transverse myelitis. In conclusion, *M. pneumoniae* should be considered in the differential diagnosis of patients who have CNS findings associated with fever and cough and should be investigated with serological, molecular and culture methods.

REFERENCES

1. Broughton RA. Infections due to Mycoplasma pneumoniae in childhood. Pediatr Infect Dis J 1986; 5: 71-85.
2. Waites KB. New concepts of Mycoplasma pneumoniae infections in children. Pediatr Pulmonol 2003; 36: 267-278.
3. Daxboeck F, Blacky A, Seidl R, Krause R, Assadian O. Diagnosis, treatment, and prognosis of Mycoplasma pneumoniae childhood encephalitis: systematic review of 58 cases. J Child Neurol 2004; 19: 865-871.

4. de Seze J, Lanctin C, Lebrun C, et al. Idiopathic acute transverse myelitis: application of the recent diagnostic criteria. Neurology 2005; 65: 1950-1953.
5. Kerr DA, Ayetey H. Immunopathogenesis of acute transverse myelitis. Curr Opin Neurol 2002; 15: 339-347.
6. Tsiodras S, Kelesidis T, Kelesidis I, Voumbourakis K, Giamarellou H. Mycoplasma pneumoniae-associated myelitis: a comprehensive review. Eur J Neurol 2006; 13: 112-124.
7. Koskiniemi M. CNS manifestations associated with Mycoplasma pneumoniae infections: summary of cases at the University of Helsinki and review. Clin Infect Dis 1993; 17: 52-57.
8. Levine DP, Lerner AM. The clinical spectrum of Mycoplasma pneumoniae infections. Med Clin North Am 1978; 62: 961-978.
9. Lerer R, Kalavsky S. Central nervous system disease associated with Mycoplasma pneumoniae infection: report of five cases and review of the literature. Pediatrics 1973; 52: 658-668.
10. Smith R, Eviatar L. Neurologic manifestations of Mycoplasma pneumoniae infections: diverse spectrum of diseases. A report of six cases and review of the literature. Clin Pediatr 2000; 39: 195-201.
11. Abele Horn M, Franck W, Busch U, et al. Transverse myelitis associated with Mycoplasma pneumoniae infection. Clin Infect Dis 1998; 26: 909-912.
12. Sotgiu S, Pugliatti M, Rosati G, Deiana G, Sechi G. Neurological disorders associated with Mycoplasma pneumoniae infection. Eur J Neurol 2003; 10: 165-168.
13. Holtas S, Basibuyuk N, Fredriksson K. MRI in acute transverse myelopathy. Neuroradiology 1993; 35: 221-226.
14. Isoda H, Ramsey R. MR imaging of acute transverse myelitis (myelopathy). Radiat Med 1998; 16: 179-186.
15. Kornips H, Verhagen W, Prick M. Acute disseminated encephalomyelitis probably related to a Mycoplasma pneumoniae infection. Clin Neurol Neurosurg 1993; 95: 59-63.
16. Pfausler B, Engelhardt K, Kampfl A, et al. Post-infectious central and peripheral nervous system diseases complicating Mycoplasma pneumoniae infection. Report of three cases and review of the literature. Eur J Neurol 2002; 9: 93-96.
17. Parisi A, Filice G. Transverse myelitis associated with Mycoplasma pneumoniae pneumonitis: a report of two cases. Infez Med 2001; 9: 39-42.