CASE REPORT

Idiopathic acute transverse myelitis: Complete recovery after intravenous immunoglobulin

Pavlou E[1], Gkampeta A[1], Kouskouras K[2], Evangeliou A[3], Athanasiadou- Piperopoulou F[1]

[1] 2nd Department of Pediatrics, Aristotle University of Thessaloniki, "AHEPA" Hospital
[2] Department of Radiology, Aristotle University of Thessaloniki, "AHEPA" Hospital
[3] 4th Department of Pediatrics, Aristotle University of Thessaloniki, "Papageorgiou" Hospital

Abstract
Idiopathic acute transverse myelitis is a focal inflammatory disorder of the spinal cord of unknown etiology diagnosed according to established criteria. As it occurs rarely in children herein we report a case of a 4 year old boy who developed clinical and radiological manifestations of myelitis, 10 days after a recent respiratory tract infection. Diagnostic workup failed to reveal a causative factor. After the administration of corticosteroids a clinical deterioration was observed and intravenous immunoglobulin was administered. Symptoms resolved within a 48-hour period, suggesting an immune-mediated pathogenetic mechanism. Hippokratia 2012; 16 (3): 283-285

Key Words: idiopathic, acute transverse myelitis, children, intravenous immunoglobulin

Corresponding author: Pavlou Evagellos, Assistant Professor of Pediatric Neurology, 2nd Pediatric Department, AHEPA Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece, e-mail: eepav@yahoo.gr, tel: +306945391839

Acute transverse myelitis (ATM) is a focal inflammatory disorder of the spinal cord. The main etiologic factors include systemic autoimmune diseases, multiple sclerosis, localized nonpyogenic infections, post-infectious and post-traumatic events, neoplastic and paraneoplastic diseases, spinal cord ischemia or hemorrhage and rarely iatrogenic causes[1,2]. When adequate diagnostic workup fails to reveal the causative factor of the lesion, the cases are referred as "idiopathic". The Transverse Myelitis Consortium Working Group proposed inclusion and exclusion criteria in order to distinguish idiopathic ATM cases from disease-associated ATM and facilitate research regarding a common pathogenesis[3]. An antecedent respiratory or gastrointestinal infection or immunization is usually referred in most cases of idiopathic ATM but causality cannot be established.

In the following case, a 4 year old boy developed clinical and radiological manifestations of acute transverse myelitis, 10 days after a recent respiratory tract infection. Diagnostic workup failed to reveal a causative factor. Due to clinical deterioration after corticosteroids, intravenous immunoglobulin was administered and symptoms resolved within a 48-hour period, suggesting an immune-mediated pathogenetic mechanism.

Case Report

A 4-year-old boy presented at the emergency room with asymmetric upper and lower extremities flaccid weakness and dysphagia. Symptoms developed the last 24 hours and an antecedent upper respiratory tract infection with cough and low fever 10 days before presentation has been reported from the parents. Fever lasted 24 hours but cough persisted until presentation.

On admission, his vital signs were as follow: blood pressure 100/65 mm/Hg, pulse rate 95/min and body temperature 36.7°C. On examination he was cooperative with a normal state of consciousness. The chest was clear on auscultation and there was no heart murmur. His abdomen was painless to pressure and no signs of peritoneal irritation were present. Neurological examination revealed sensory loss in upper and lower extremities with an incomplete cervical sensory level. Tendon reflexes were reduced mainly in lower extremities. Muscle strength was diminished and the patient had great difficulty standing and walking. Extensor plantar responses initially were not elicited in both legs and sphincter tone also seemed to be initially reserved.

The patient had an unremarkable past medical history and developmentally he had reached his milestones normally. His immunization was current and his last immunization had taken place almost 6 months ago.

Initial laboratory tests showed a white blood cell (WBC) count of 6590/mm^3 (normal range 4-10.000/mm^3), (55,1% neutrophils, 35,5% lymphocytes, 7,10% monocytes, 1,8% eosinophils, and 0,5% basophils) haemoglobin of 11,5 g/dl (normal range 12-16,0 g/dl), platelet count of 375,000/mm^3 (normal range 150.000-400.000/mm^3), erythrocyte centimentation rate of 27 mm/h (normal range 0-20 mm/h), C-reactive protein of 0,01 mg/dl (normal range 0,0-0,38 mg/dl) and CPK of 76 U/L (normal range 0-190 U/L). Liver and renal function tests and urinalysis were normal. An ECG and chest x-rays showed no abnormalities. An urgent CT scan of the brain was normal and

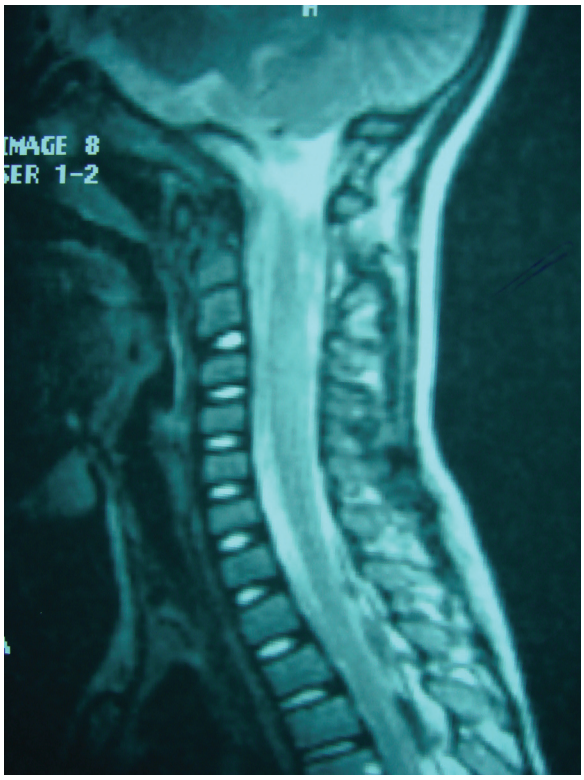

Figure 1: Spinal magnetic resonance imaging (MRI) exhibiting high T2 signal and swelling extending from A2 to A5.

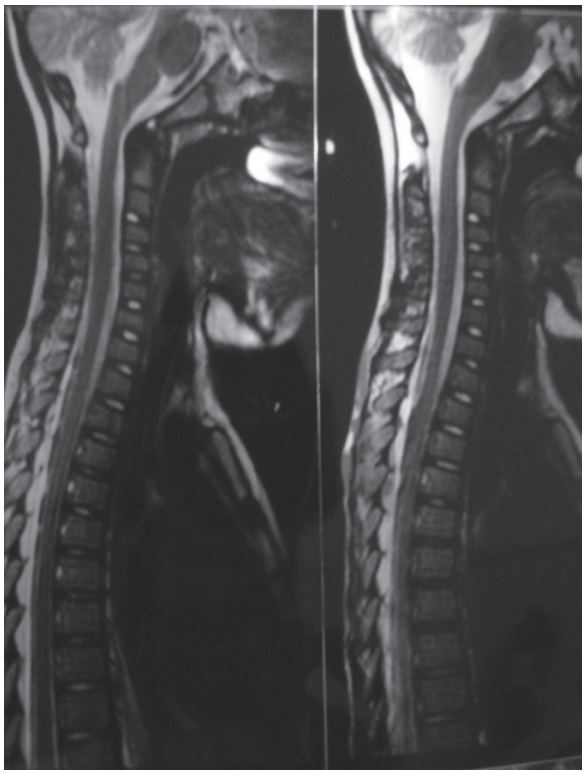

Figure 2: New spinal MRI scan four weeks later showing complete resolution of the lesion.

lumbar puncture revealed a leukocyte count of 24 cells/μL (67% lymphocytes) (normal range 0-5 cells/μL), protein 84mg/dl (normal range 18-58 mg/dl) and glucose 55mg/dl (normal range < 300 mg/dL). The CSF Gram stain and routine bacterial culture were negative. Polymerase chain reaction of the cerebrospinal fluid for herpes simplex virus types 1 and 2, coxsackie virus, echovirus and M. pneumoniae were negative. Serological studies (enzyme linked immunosorbent assay – ELISA) showed elevated M.pneumoniae – specific IgA antibodies (200U/ml, normal < 65U/ml) and IgG antibodies (65U/ml, normal < 40U/ml), but undetectable IgM antibodies. Enzyme linked immunosorbent assays – ELISA were negative for Epstein Barr, and CMV. Serological studies were also negative for antinuclear antibody (ANA), anti dsDNA antibodies, extracellular nuclear antibody (ENA), Rheumatoid Factors (RFs), and antiphospholipid antibodies.

Spinal magnetic resonance imaging (MRI) exhibited high T2 signal and swelling extending from A2 to A5 (figure 1). Brain MRI and visual evoked potentials were reported as normal. Nerve conduction studies showed normal peripheral nerves velocities and F-waves of lower limbs were obtainable.

Based on history, clinical, and MRI findings, the diagnosis of a parainfectious acute transverse myelitis was considered and the patient was initially treated with intravenous ceftriaxone (100mg/kg/day), clarithromycin (30mg/kg/day), acyclovir (30mg/kg/day) and a 3-day course of intravenous methylprednizolone (20mg/kg/day). Despite intervention, there was clinical deterioration and on day 4 the patient showed breathing problems, reduced consciousness, inability to sit and stand, and urinary and bowel dysfunction with loss of sphincter tone. Ceftriaxone and acyclovir were discontinued as the culture of CSF for bacteria and the PCR for herpes simplex virus types 1 and 2 were negative. A single dose of intravenous immunoglobulin was administered in a dose of 2 gram/kg infused over 24 hours. Clinical improvement became obvious 48 hours later (on day 6 after admission) with improvement of alertness and sphincter control. On day 9 the patient was able to sit and stand again and on day 10 after admission he was able to take a few steps. On day 14 after admission, new serological studies showed no increase of M.pneumoniae – specific IgA and IgG antibodies and no detection of IgM antibodies. The patient was discharged from hospital on day 18 and a new spinal MRI scan four weeks later showed complete resolution of the lesions (figure 2). At 3 months follow up the patient remained in a good condition with no residual symptoms.

Discussion

Acute transverse myelitis is characterized by abrupt onset of progressive weakness of the limbs, sensory impairment with a sensory level and rectal and bladder sphincter dysfunction[3]. A potential causal link between various infectious agents, vaccinations and ATM has been described and when the extensive diagnostic workup succeeds to reveal a clear etiological factor, the cases are referred as "dis-

ease associated" ATM[3]. When the diagnostic search fails to reveal such a cause, "idiopathic" ATM is defined[3,4].

ATM rarely occurs in children. Several studies have showed one pick of the incidence in the age group of 10-19 years and another pick in the age group of 30-39 years[5]. In a recent center-based analysis of 47 pediatric cases, the age of onset clustered between 0-2 years and 5-17 years[6]. 47% of the patients had preceding history of febrile illness and 28% had a recent history of vaccination[6].

In the index case, a 4 year old boy developed clinical and radiological manifestations of acute transverse myelitis, 10 days after a recent respiratory tract infection. Inflammation within the spinal cord was demonstrated by CSF pleocytosis and spinal MRI findings. Diagnostic workup failed to reveal a causative factor suggesting the diagnosis of idiopathic ATM.

Serologic studies remain clinician's primary method in order to diagnose Mycoplasma infection despite their limitations and detection of IgM antibodies with ELISA shortly after the acute stage has been reported in few ATM cases[7]. Positive PCR testing for M. pneumoniae in CSF has also been reported in two acute transverse myelitis cases[8,9]. The combination of ELISA IgM antibodies and throat-swab PCR has been reported as the most sensitive laboratory method in diagnosing Mycoplasma infection during the acute stage[10]. At the same study it has been reported that the detection of M.pneumoniae specific IgA antibodies is not relevant for the diagnosis in children**.** The failure to detect specific IgM antibodies in two different serum specimens excluded the hypothesis of a recent M.pneumoniae infection in our patient.

Systemic inflammatory disorders (i.e, SLE) were also excluded by serological testing. Ischemic etiology seemed unlikely from the history, as the progression of symptoms took more than 24 hours to reach maximal severity. Vascular myelopathy usually shows a rapid (<4 hours) progression to nadir and a spinal cord imaging corresponding to vascular territories[1]. Visual evoked potential and brain MRI did not show demyelination and excluded the possibility of acute disseminated encephalomyelitis, neuromyelitis optica (Devic's disease) and multiple sclerosis.

Although corticosteroids have been used in cases of ATM with clinical improvement in almost half of them, it is still unclear whether this improvement was due to corticosteroids treatment or to spontaneous remission. Defresne et al reported a favorable effect of high-dose intravenous (IV) methylprednisolone on the proportion of pediatric patients walking independently at 1 month. Pidcock et al recently stated that treatment with IV steroids does not improve outcome in children but oral steroids may be associated with improvement in the area of mobility[6,11]. Despite these conflicting reports steroids remain the standard first line intervention for ATM. Other treatment modalities include plasmapheresis and IV immunoglobulin but their effectiveness have not been reported consistently. De Seze et al in a recent retrospective and not randomized study with 45 adult cases of idiopathic ATM reports the absence of a clear beneficial effect on clinical outcome of immunosuppressive drugs and IV immunoglobulin in 12 of the 16 treated patients[4]. Only 4 patients showed clinical improvement: two of the four treated with IV immunoglobulin, one of the four treated with azathioprine and one of the eight treated with cyclophosphamide. All of these patients had initially been treated with IV steroids. The authors suggested that these results may have been due to the delay between the onset of the symptoms and the start of the treatment with IV immunoglobulin or immunosuppressive agents which was administrated within 45 (+ 18) days. In our case the evolution of motor and sensory dysfunction had a subacute profile with maximum clinical signs including loss of bowel and bladder control, 4 days after onset and despite pulsed intravenous methylprednisolone administration. Rapid clinical improvement after intravenous immunoglobulin administration within a week of the onset of symptoms supports an immune-mediated pathogenetic mechanism for this case of idiopathic ATM and an early therapeutic approach should be considered in critically ill patients who show no clinical improvement after pulsed methylprednisolone administration. It would be very interesting if further studies test the effectiveness of IV immunoglobulin with or without a high dose of corticosteroids given within a few days after the onset of the disease.

References

1. de Seze J, Stojkovic T, Breteau G, Lucas C, Michon-Pasturel U, Gauvrit JY, et al. Acute myelopathies :clinical, laboratory and outcome profiles in 79 cases. Brain. 2001; 124: 1509-1521.
2. Krishnan C, Kaplin AI, Deshpande DM, Pardo CA, Kerr DA. Transverse myelitis: pathogenesis, diagnosis and treatment. Front Biosci. 2004; 9: 1483-1499.
3. Transverse Myelitis Consortium group. Proposed diagnostic criteria and nosology of acute transverse myelitis. Neurology. 2002; 59: 499-505.
4. de Seze J, Lanctin C, Lebrun C, Malikova I, Papeix C, Wiertlewski S, et al. Idiopathic acute transverse myelitis : Application of the recent diagnostic criteria. Neurology. 2005; 65: 1950-1953.
5. Scotti G, Gerevini S. Diagnosis and differential diagnosis of acute transverse myelopathy. The role of neuroradiological investigations and review of the literature. Neurolo Sci. 2001; 22, Suppl 2: s69-s73.
6. Pidcock FS, Krishnan C, Crawford TO, Salorio CF, Trovato M, Kerr DA. Acute transverse myelitis in childhood: center-based analysis of 47 cases. Neurology. 2007; 68: 1474-1480.
7. Tsiodras S, Kelesidis T, Kelesidis I, Voumbourakis K, Giamarellou H. Mycoplasma pneumoniae-associated myelitis: a comprehensive review. Eur J Neurol. 2006; 13: 112-124.
8. Abele-Horn M, Franck W, Busch U, Nitschko H, Roos R, Heesemann J. Transverse myelitis associated with Mycoplasma pneumoniae infection. Clin Inf Dis. 1998; 26: 909-912.
9. Goebels N, Helmchen C, Abele-Horn M, Gasser T, Pfister HW. Extensive myelitis associated with Mycoplasma pneumoniae infection: magnetic resonance imaging and clinical long-term follow-up. J Neurol. 2001; 248: 204-208.
10. Souliou E, Almasri M, Papa A, Theodoridou A, Diza E. Laboratory diagnosis of Mycoplasma pneumoniae respiratory tract infections in children. Eur J Clin Microbiol Infect Dis. 2007; 26: 513-515.
11. Defresne P, Hollenberg H, Husson B, Tabarki B, Landrieu P, Huault G, et al. Acute transverse myelitis in children: clinical course and prognostic factors. J Child Neurol. 2003; 18: 401-406.