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Mycoplasma pneumonia as a cause of neuromyelitis optica?

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Sirs: Until recently neuromyelitis optica (NMO) was regarded as a severe form of multiple sclerosis (MS). But characteristic serologic and neuroradiological findings and particularly the discovery of the specific NMO antibody by Lennon and colleagues [8] indicate that NMO is an autoimmune disease different from MS.

In a few patients, typical NMO is associated with viral infection like HIV [3], Dengue fever [10], varicella infection [1], infectious mononucleosis [12] and hepatitis A virus [6]. The only bacterial agent that has been associated with NMO is *Mycobacterium tuberculosis* [2].

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On the other hand, several neurological manifestations have been described following *Mycoplasma pneumonia* [4, 5] infection, a common bacterium of the respiratory tract, including acute transverse myelitis (ATM) [11].

Here we present a patient with typical NMO after *M. pneumonia* infection that may represent an underestimated etiology for NMO. A previously healthy 32-year-old woman developed fever and a non-productive cough. A chest x-ray showed an infiltrate in the right inferior lobe. Respiratory symptoms improved with erythromycin treatment. Ten days later she experienced paresthesia and weakness in both legs, urinary retention and was admitted to our department.

On neurological examination she was alert. Cranial nerves were normal, but there was tetraparesis with tetrahyperreflexia and hypaesthesia with a sensory level at the 4^{th} thoracic level. No signs of meningism were present. Sphincter tone was reduced on rectal examination. The night after admission, the patient had to be transferred to our intensive care unit because of respiratory failure requiring intubation. MRI investigation revealed a severe myelitis (Fig. 1A and B).

CSF investigation showed 15 white blood cells per µL, 37 % polymorphonuclear neutrophils. There was no quantitative intrathecal immunoglobulin production.

Serologic examinations showed a highly positive complement fixation test (CFT) to *M. pneumonia* (1:5120). An indirect immunofluorescence assay was used to search for *M. pneumonia* antibodies in CSF and serum. This investigation revealed an elevated titer of IgG antibodies specific to *M. pneumonia* in the CSF. In combination with an antibody specificity index of 9.5 these results indicate an intrathecal production of IgG antibodies specific to *M. pneumonia*. Neither in CSF nor in serum were there signs of another acute infection or autoimmune disorder. NMO-IgG anti-aquaporin-4 antibodies [8] were negative. Within 4 days the tetraparesis progressed to tetraplegia. Sensory level of hypesthesia moved up to C4 and bilateral blindness occurred. An immunosuppressive therapy with methylprednisolone and later with plasma exchange and mitoxantron was initiated in addition to the initial antibiotics therapy. Blindness resolved slowly within the following months. After 1 year, the patient had regained almost full function of both upper extremities. Visual function was normal, but she was still paraspastic and -plegic. CFT to *M. pneumonia* had decreased to 1:120 and spinal MRI revealed an atrophy (Fig. 1C).

In this case, the development of symptoms after pneumonia and associated increase of *M. pneumonia* antibody titres both in serum and CSF strongly suggests that the mycoplasma infection is involved in this NMO syndrome.

Several neurological complications including ADEM and ATM have been described after *M. pneumonia* infection [5, 9]. Both direct CNS infection and an autoimmune mechanism triggered by *M. pneumonia* are possible. Since direct PCR evidence for *M. pneumonia* is only seldom found in CSF [11], it is often difficult to differentiate between both possibilities [5]. The clinical syndrome with bilateral optic neuritis and longitudinally extensive myelitis is typical for NMO and, to the best of our knowledge, has not been reported to date in association with *M. pneumonia* infection. Overall, an autoimmune parainfectious pathogenesis seems more likely than a direct infection since the symptoms started late after the pneumonia, progressed in spite of an adequate antibiotic treatment, and since CSF analysis

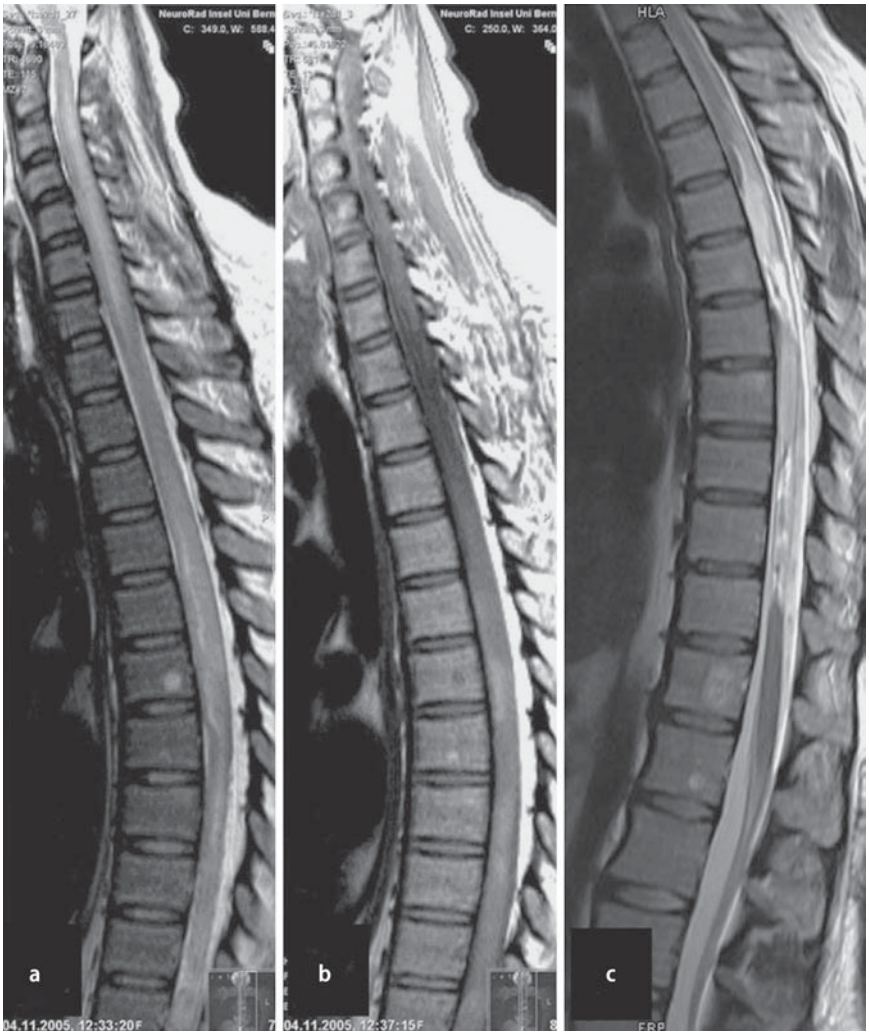

Fig. 1 Spinal MRI. **A** Sagittal T2-weighted TSE images reveal progressive T2-hyperintense and progressive swelling of the spinal cord at the level of C2-Th1 and Th4-Th9 16 days after symptoms onset. **B** T1-weighted SE images show hemorrhagic transformation at the level of Th5–Th9. **C** Follow-up examination after 10 months reveal severe atrophy of the thoracic cord

revealed only weak inflammatory signs in spite of a strong anti-mycoplasma antibodies titre. In this case, the recently published revised diagnostic criteria for NMO are fulfilled [13] even though the anti-aquaporin-4 antibodies [7], which have a 90 % specificity for NMO, were not detected in the CSF or blood.

We postulate that this case represents an anti-aquaporin-4 antibody negative NMO syndrome following *M. pneumonia* infection. We propose that in patients with NMO syndrome, especially cases with rapid symptom onset, a comprehensive search for possible infectious etiologies including *M. pneumonia* infection should be performed.

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