

## Acute transverse myelitis in Lyme neuroborreliosis

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### Abstract

**Introduction** Acute transverse myelitis (ATM) is a rare disorder (1–8 new cases per million of population per year), with 20% of all cases occurring in patients younger than 18 years of age. Diagnosis requires clinical symptoms and evidence of inflammation within the spinal cord (cerebrospinal fluid and/or magnetic resonance imaging). ATM due to neuroborreliosis typically presents with impressive clinical manifestations.

**Case presentation** Here we present a case of Lyme neuroborreliosis-associated ATM with severe MRI and CSF findings, but surprisingly few clinical manifestations and late conversion of the immunoglobulin G CSF/blood index of *Borrelia burgdorferi* sensu lato.

**Conclusion** Clinical symptoms and signs of neuroborreliosis-associated ATM may be minimal, even in cases with severe involvement of the spine, as shown by imaging studies. The CSF/blood index can be negative in the early stages and does not exclude Lyme neuroborreliosis; if there is

strong clinical suspicion of Lyme neuroborreliosis, appropriate treatment should be started and the CSF/blood index repeated to confirm the diagnosis.

**Keywords** Lyme · Neuroborreliosis · Transverse myelitis

### Introduction

Acute transverse myelitis (ATM) is an inflammatory myelopathy with an incidence of 1–8 cases per million of population per year. Of all affected patients, 20% are younger than 18 years of age [1]. Diagnosis is based on clinical symptoms, cerebral spinal fluid (CSF) findings and spinal neuroimaging results. In addition to the inflammatory myelopathies, demyelination, infection (e.g. polymyelitic enteroviral infection) and other inflammatory disorders (i.e. systemic lupus erythematosus, neurosarcoidosis) must be considered in the differential diagnosis [2, 3]. In adults, multiple sclerosis and neuromyelitis optica together with infectious/parainfectious aetiologies are the most frequent causes of ATM [4], while in children the aetiology is mainly postinfectious [5]. Clinical features consist of sensory disturbances in most of the patients, followed by weakness and—especially in childhood—urinary tract dysfunction. Children suffer from more severe clinical impairment than adults. In the series of Pidcock et al., 89% of the paediatric patients were bed- or wheelchair bound or required assisted ventilation, whereas the majority of adults showed only mild impairment [1, 6]. Outcome is generally favourable. Chronic bladder dysfunction has been shown to be the main sequelae [1].

ATM due to Lyme neuroborreliosis has rarely been reported. However, those cases that have been documented, the majority of patients presented with impressive clinical

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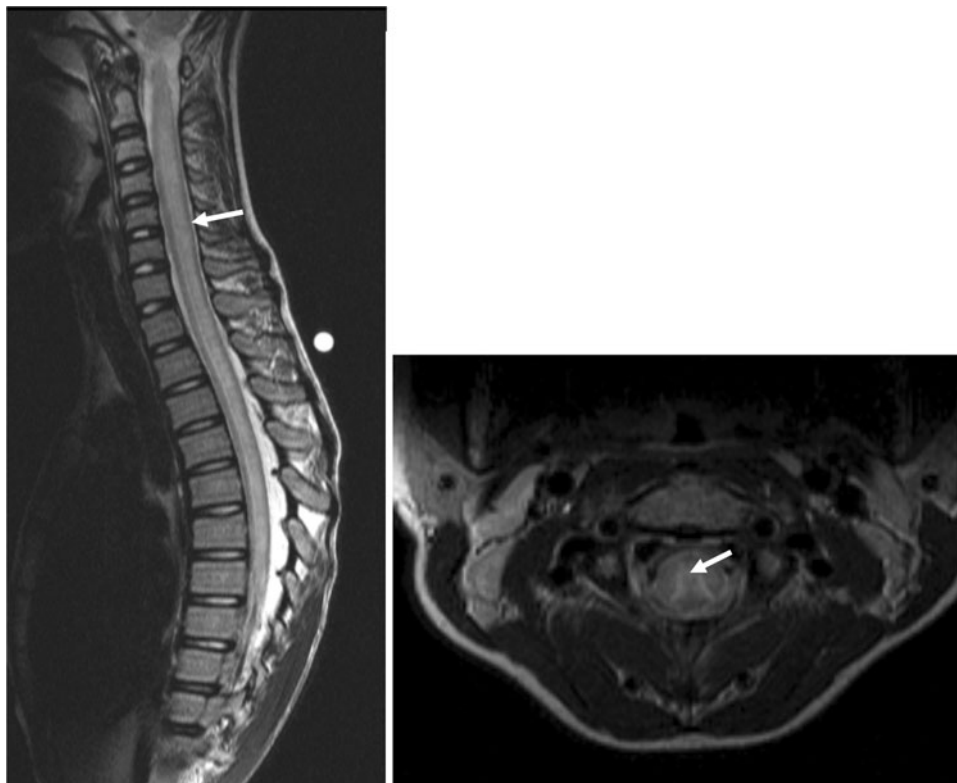
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**Fig. 1** *Left* T2-weighted sagittal scan of the cervicothoracic spine. There is an extensive centromedullary hyperintensity (*arrow*) and swelling as an expression of the spinal cord edema. *Right* T2-weighted axial scan at the level of the cervical spine. The edema involving the gray and white matter is discernible. The hyperintensity of the gray matter (*arrow*) is particularly prominent



symptoms [7–9]. Here, we report a case of ATM due to Lyme neuroborreliosis, which—despite severe neuroimaging (magnetic resonance imaging, MRI) and CSF findings—was characterized by surprisingly few clinical signs.

### Case report

A 12.5-year-old boy presented to our emergency department in November with a >4-week history of increasing frontal headache that got worse in the evening. He noted intermittent subfebrile temperatures. Additional complaints were fatigue, diffuse non-radicular back/neck pain and nausea. There was no vomiting. In this period, a weight loss of 2–3 kg was documented. Three weeks before admission he had been immunized (dT<sub>ap</sub> = diphtheria, tetanus, acellular pertussis) according to the recommended Swiss vaccination schedule. His personal history is unremarkable. There was no tick bite reported, and no an erythema migrans.

On admission, the general physical condition of the patient was slightly lower than would normally be expected, he was afebrile, and the results of a general clinical examination were normal. His neurological examination was remarkable only for nuchal rigidity. In particular, there

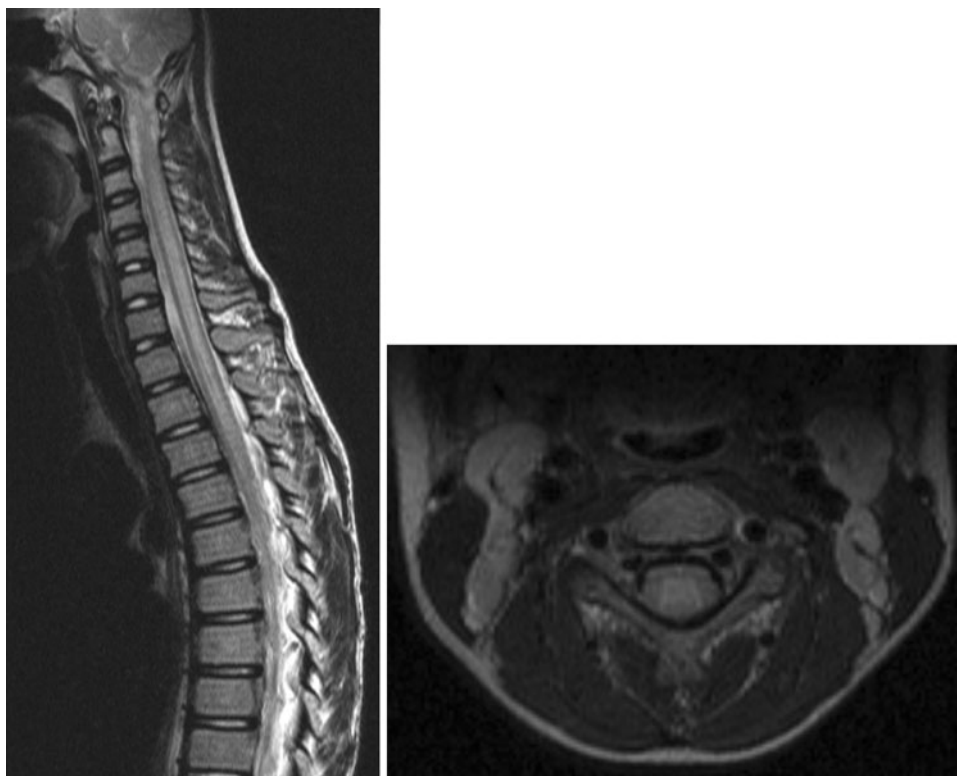
was no bladder dysfunction, and there was no sensory disturbance or weakness.

Laboratory investigations on admission included a normal complete blood cell count, inflammatory markers (C-reactive protein), liver enzymes and kidney function parameters.

Because of the clinical constellation (neck stiffness in an afebrile patient), MRI of the brain was performed to exclude a haemorrhagic or space-occupying lesion. The brain scan was normal, but there were signal alterations (T2w hyperintensities) within the medulla down to cervical spine. A consecutive MRI of the spinal cord was added to the tests, which revealed a longitudinal signal alteration (T2w hyperintensities) from the pons to the conus, accentuated centromedullarily with a patchy enhancement (Fig. 1). The myelon was swollen, especially in the cervical region. There was no tumor or cerebral or meningeal enhancement on the MRI scan.

There was marked CSF pleocytosis (787 cells/ $\mu$ l; 734 mononuclear cells), elevated protein (6.24 g/l) and decreased glucose (1.79 mmol/l), with a glucose CSF/plasma ratio of 0.28. Microbiological investigation revealed increased serum immunoglobulin G (IgG) and IgM for Epstein–Barr virus (EBV) (EBV viral capsid antigen-IgM and -IgG, anti-early-antigen IgG p54) and *Borrelia burgdorferi* sensu lato. Serological testing for

**Fig. 2** *Left* T2-weighted sagittal scan of the cervicothoracic spine. The centromedullary edema is regressive but still visible. *Right* T2-weighted axial scan at the level of the cervical spine. Central hyperintensity with accentuation in the central grey matter was present, but was less marked than in the initial scan



*B. burgdorferi* was performed using a recomWell enzyme-linked immunosorbent assay (ELISA; IgM and IgG; Mikrogen, Neuried, Germany) and confirmed by recomBlot (Mikrogen; IgM and IgG). The Western blot revealed that the patient had borrelia-specific positive IgM and IgG bands that were distributed as follows: anti-OspC IgM (*B. burgdorferi* sensu lato); anti-p41 flagellin IgM; anti-p41 intern IgM (*B. afzelii*); anti-VisE IgG (*B. afzelii*); anti-p41 flagellin IgG; anti-p41-intern IgG (*B. garinii*); anti-p41-intern IgG (*B. afzelii*). The EBV DNA PCR of the CSF and the CSF/blood index for *B. burgdorferi* sensu lato IgM and IgG were negative. The CSF/blood index was performed using the IDEIA test (Oxoid, Cambridge, UK) for Lyme neuroborreliosis. The results of the CSF PCR for herpes simplex virus (HSV) and enteroviruses were negative.

With the suspicion of Lyme neuroborreliosis, ceftriaxone therapy for 14 days was started. Antiviral therapy with aciclovir was added at the beginning of the therapeutic regimen and stopped when the negative HSV PCR result became available. Steroids had not been given. The patient recovered almost completely within the first 24 h of therapy, with only residual mild neck stiffness that persisted for 1 week. Eight days after the initiation of therapy, a follow-up MRI of the spinal cord showed improvement with reduced swelling and less signal alteration (Fig. 2).

Three weeks after admission, an outpatient control showed a completely normal clinical examination. In the

follow-up lumbar puncture performed at this time, 27 cells/ $\mu$ l were detected (all mononuclear). Protein and glucose (including CSF/plasma ratio) were normal. Examination of the oligoclonal IgG bands in the CSF/serum revealed an intrathecal IgG production. The IgG CSF/blood index for *B. burgdorferi* sensu lato was 41.73 ( $<0.3$ ), and the EBV DNA PCR of the CSF remained negative.

## Discussion

Lyme neuroborreliosis as a cause of ATM is known, but reports are limited to single cases, both in children and adults. The usual manifestations are severe and often include dramatic signs of motor weakness and bladder dysfunction [7]. In discussing our case, we wish to emphasize two aspects which—to the best of our knowledge—have not been reported to date: the striking discrepancy between the severe imaging manifestations and the minimal clinical signs and symptoms, and the prominent MRI findings involving most of the medulla spinalis in a patient with transverse myelitis of borrelial origin. In pediatric Lyme neuroborreliosis, CNS symptoms are rare—in contrast to symptoms of the peripheral nervous system. Children with CNS symptoms may present with acute myelitis. In all such cases reported so far, the children suffered from acute symptoms due to their myelitis, such as

parese, urinary tract dysfunction and sensory disturbances. All of these symptoms and signs were lacking in our patient, possibly because of the early diagnosis and treatment [10]. The description of an extension to spine involvement in a transverse myelitis of borrelial origin in children is limited to single case reports. In these case reports, the involvement of the spine is limited and mostly cervically [7, 11]. At the moment of first lumbar puncture, our patient had a symptom duration of <6 weeks, which explains the first negative CSF/blood index, as delayed intrathecal antibody synthesis in Lyme neuroborreliosis (positive CSF/blood index) is well known in patients with a symptom duration of <6 weeks. Therefore, the positive CSF/blood index in the follow-up lumbar puncture confirms the assumed diagnosis of Lyme neuroborreliosis, and early detection and treatment may have prevented further progression of the disease. [12–14] In the literature, EBV—in addition to many other occasionally incriminated viruses—is a rare but recognized agent causing ATM [5, 15]. Serologically, our patient had a co-infection with EBV at the time of his CNS manifestation, even though there was no classic mononucleosis (tonsillitis, lymphadenopathy, hepatosplenomegaly) and the EBV DNA PCR of the CFS remained negative over time. We conclude that the ATM was related to Lyme neuroborreliosis and not to the EBV infection. However, this patient most likely has had a recent infection with EBV, which may or may not have paved the way for progression of early, local borreliosis to Lyme neuroborreliosis.

Single cases of ATM after vaccination have been reported, but in these, in contrast to our case, there were no other aetiological findings. Pidcock et al. reported that 28% of the reported children with ATM received immunization or “allergy shots” within 30 days prior to onset, but they could not demonstrate a potential causal link between vaccination and ATM. In our case, the onset of symptoms 1 week prior to vaccination renders a vaccine-related adverse effect unlikely, but the possibility of vaccination supporting the development of Lyme neuroborreliosis because of an already present infection cannot be entirely ruled out or resolved.

In conclusion, we report the case of a patient with ATM caused by Lyme neuroborreliosis with surprisingly few clinical signs—in contrast to the severe MRI and CSF findings. If there is strong clinical suspicion of Lyme neuroborreliosis—irrespective of a history of a recent tick bite or erythema migrans—appropriate treatment should be

started, and the CSF/blood index should be repeated to confirm the diagnosis if the initial results are negative.

**Conflict of interest statement** None.

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