

SHORT REPORT

Severe tick borne encephalitis with simultaneous brain stem, bithalamic, and spinal cord involvement documented by MRI

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A case of tick borne encephalitis (TBE) is reported, with simultaneous brain stem, spinal cord, and bilateral thalamic involvement confirmed by magnetic resonance imaging (MRI). After exposure to a TBE endemic region, the patient developed a biphasic clinical course with initial flu-like symptoms followed by a severe brain stem syndrome. The diagnosis of TBE was confirmed serologically. Repeated MRI scans showed brain stem, bithalamic, and spinal cord involvement. The outcome was favourable. TBE cases with concomitant myelitis tend to have a more severe clinical course and more likelihood of needing intensive care support. They should therefore be identified early in order to be prepared for life threatening respiratory complications.

The tick borne encephalitis (TBE) virus causes the most important arthropod transmitted (tick bite) disease in central and eastern Europe. TBE virus causes a generalised infection primarily affecting the CNS. The most common presentation is meningitis (49%), followed by meningoencephalitis (41%) and meningoencephalomyelitis (10%).¹ Polio-like syndromes with a predominantly polyradiculitic course have also been described.² In endemic areas, TBE has an incidence of 1.2 per 100 000 and a mortality of about 1%.³ Like other flavivirus infections (for example, Japanese encephalitis), TBE can lead to bilateral thalamic lesions that are visible on magnetic resonance imaging (MRI), though neuroradiological abnormalities are found only in a minority of cases.

We present a severe TBE case with neuroradiological proof of simultaneous thalamic, brain stem, and spinal cord involvement but a favourable outcome.

CASE REPORT

A 29 year old, previously healthy young man from southern Germany who had not had TBE immunisation fell ill for two days with flu-like symptoms one week after a short mountain bike trip to Austria in August 2003 (to Oetz in the Tyrol, where there have been documented cases of TBE). He had had contact with ticks (he had noticed them on his clothing but did not recall being bitten). Three weeks later he developed acute headache, nausea, and vomiting (day 1). On the next day, he began to have dysarthria, diplopia, gait ataxia, and clumsiness in both hands. On day 3 he was admitted to hospital.

At this time his consciousness was impaired (Glasgow coma scale, 11) and he had moderate meningism and fever (38.5°C). Laboratory findings (normal values in brackets) were abnormal: increased C reactive protein (22.1 mg/dl (<0.5)) with low leucocytes ($4.4 \times 10^9/l$ (4.0 to 11.0)) and raised values for creatine kinase (2301 U/l (<180)), alanine

aminotransferase (62 U/l (<35)), and aspartate aminotransferase (73 U/l (<33)). Procalcitonin, a marker for severe systemic bacterial infection, was normal (0.1 ng/ml (<0.5)).

Initial cranial computed tomography (CT) without contrast showed diffuse infra- and supratentorial brain oedema, which necessitated postponement of a lumbar puncture (fig 1A). As meningoencephalitis could not be ruled out, intravenous antibiotic and antiviral therapy with ceftriaxone, ampicillin, and acyclovir was initiated. In addition, heparin was given intravenously for possible sinus venous thrombosis. The patient received antioedema treatment with mannitol and elevation of the upper part of the body. Because his clinical condition deteriorated, he had to be intubated and ventilated.

MRI of the brain on day 6 revealed abnormalities (hyperintense signals on T2 weighted images) throughout the brain stem and bilaterally in the thalamus and basal ganglia (fig 1, panels B–D). There was no pathological contrast enhancement and less brain oedema. Lumbar puncture showed a lymphomonocytic (100%) pleocytosis (65 cells/ μ l (normal <5)) with a slightly increased protein content (65 mg/dl (<45)) and a normal CSF/serum glucose index. CSF and blood cultures remained sterile. Oligoclonal IgG bands were positive in the CSF but not in the serum. As CSF findings and MRI abnormalities were also compatible with cerebral listeriosis, and as TBE serology was not yet available, tobramycin was added to the antibiotic regimen.

Serological testing of the CSF and serum showed raised IgM and negative IgG against TBE virus. This investigation was repeated on day 26, when there was an increase in serum IgG concentrations and a raised TBEV-IgG CSF/serum index of 28.7 (>4 confirms intrathecal specific antibody production). After the diagnosis of TBE was established, antibiotic therapy was discontinued.

The patient slowly recovered. On day 14, he was awake and followed commands, but he had developed a flaccid tetraparesis. Electrophysiological and myographic testing revealed abnormal spontaneous activity in all five muscles examined. Paravertebral muscles were more severely affected than distal muscles. Compound muscle action potentials (CMAP) were decreased in all nerves examined, with normal motor conduction velocity, while sensory neurography was normal. This pattern of acute impairment is compatible with an acute motor neuropathy or affection of the anterior horn cells, but would be unexpected in the most likely differential diagnosis of critical illness polyneuropathy. This spinal involvement was confirmed by spinal MRI on day 21, when the signal on T2 weighted and T1 weighted contrast enhanced images within the anterior part of the cervical cord was increased (fig 2). Serological testing for enterovirus and *Borrelia burgdorferi* antibodies as other potential sources of myelitis was negative. Follow up MRI of the brain at the same time revealed a reduction of signal alterations in the brain stem

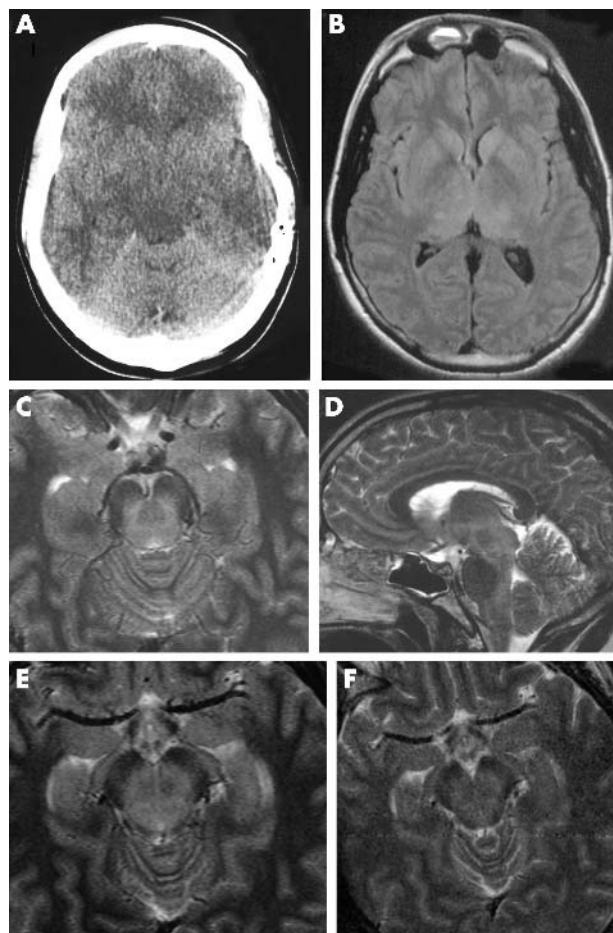


Figure 1 Brain imaging. (A) Computed tomography without contrast media (day 3) showing diffuse brain oedema with effacement of the surface sulci and basilar subarachnoid spaces. (B–D) Native axial and sagittal magnetic resonance imaging (MRI) (day 6), showing abnormal high signal intensities in the brain stem and thalamus ((B) axial fluid attenuated inversion recovery (FLAIR) sequence; (C) axial and (D) sagittal T2 weighted turbo spin-echo sequences). (E, F) MRI (axial T2 weighted images) of the brain on day 6 (E) and day 21 (F), showing improvement of the brain stem lesions.

(fig 1E–F). This neuroradiological finding correlated well with the clinical improvement of the patient. He was extubated on day 31 and transferred to a rehabilitation unit on day 35. At the time of writing (day 173) he was still suffering from weakness in his left arm but was able to walk and had only minimal neuropsychological deficits (Barthel index 90).

DISCUSSION

TBE is usually characterised by a biphasic course with initially flu-like symptoms followed by neurological symptoms—for example, impaired consciousness (31%), ataxia (18%), paresis of the limbs (15%) or the cranial nerves (11%), and tremor (4.3%).¹ As there is no specific treatment and as the illness is associated with significant morbidity and neurological sequelae (27% have sequelae lasting more than three months), active immunisation is the most important way to manage TBE.¹

TBE virus is part of the flavivirus genus, which includes several significant neurotropic human pathogens that cause TBE-like diseases such as Saint Louis encephalitis, Japanese encephalitis, and West Nile virus infection. A common neuroradiological feature of these diseases is diffuse bilateral thalamic high signal on T2 weighted images.^{4–6} Contrast

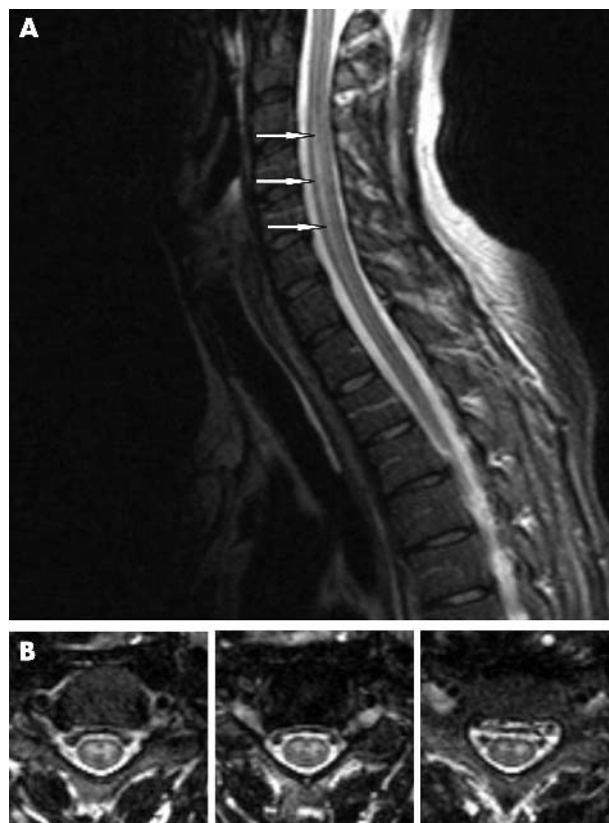


Figure 2 Spinal T2 weighted images showing longitudinal involvement of the anterior part of the spinal cord from the C2 level to the C7 level in sagittal view ((A); arrows mark signal alteration) and on corresponding axial images (B).

enhancement of the affected brain parenchyma is not regularly seen (for a review of MRI abnormalities, see table 1).

Pathological MRI changes can be observed in approximately 20% of patients with manifest TBE. In the most comprehensive series of TBE cases published so far, Kaiser found bilateral involvement of the thalamus in 15 of 18 patients, and changes in the cerebellum, brain stem, and caudate nucleus in the remaining three.¹ These findings have been confirmed by others, mainly in the form of case reports.¹² Data on follow up MRI examinations in TBE are lacking. In the present case, we observed a good correlation between clinical improvement and restitution of the T2 abnormalities of the affected brain parenchyma.

To the best of our knowledge, this is the first published case of simultaneous thalamic, brain stem, and especially spinal cord involvement, both clinically and on MRI. Beer *et al* described a rare case of a TBE patient who had an isolated anterior horn lesion of the C3 to the T1 level.¹³ Considering that the location of the spinal cord lesion in our patient was nearly identical, we suggest an accurate clinical, electrophysiological, and neuroradiological investigation of the cervical spinal cord when tick borne encephalomyelitis is suspected.

Like Beer *et al* and Kuntzer *et al*,^{8,13} we also observed a progression of the neurological deficits after initiating antibiotic treatment, including ceftriaxone. This might have been caused by activation of persisting TBE virus by cephalosporins, as Malenko *et al* showed in an animal model.¹⁴

With increasing intercontinental travel over the past decades, flavivirus infections such as TBE are posing a growing global health threat. This is reflected by a recent outbreak of West Nile virus infection in the New York City

Table 1 Comparison of MRI findings (increased signal on T2 weighted images, rarely combined with pathological contrast enhancement) in flavivirus infections

	Cortex	Thalamus	BG	Brain stem	SC	References
Tick borne encephalitis	Unilateral	Bilateral	Bilateral	Bilateral	Bilateral	1, 4, 7, 8
St Louis encephalitis	No data	No data	No data	Bilateral	No data	6
Japanese encephalitis	Unilateral	Bilateral	Bilateral	Bilateral	No data	5
West Nile virus encephalitis	No data	Bilateral	Bilateral	Bilateral	Bilateral	9, 10, 11

BG, basal ganglia; SC, spinal cord.

area.¹⁵ Such infections therefore remain a diagnostic challenge to health care professionals, even outside typical endemic areas. As these viruses seem to lead to a comparable pattern of abnormalities on thalamic and basal ganglia MRI, it is probable that other cases of non-TBE flavivirus infection with brain stem and spinal cord involvement will be found. This hypothesis is supported by a recent paper reporting five cases of acute paralytic poliomyelitis associated with West Nile virus infection.¹¹

Conclusions

In cases of suspected encephalitis in association with bilateral lesions in the thalamus or with brain stem involvement, the possibility of a flavivirus infection such as TBE should be considered. Patients with concomitant spinal cord involvement may be affected more severely and should therefore be identified early by means of clinical, electrophysiological, and radiological examinations, in order prepared for the likelihood that they will need mechanical ventilation.

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