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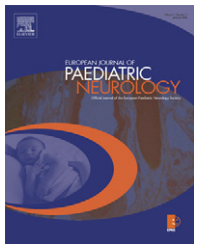

Case study

Lyme disease with lymphocytic meningitis, trigeminal palsy and silent thalamic lesion ☆

Joachim Köchling[a,*], *Hans J. Freitag*[c], *Thomas Bollinger*[b], *Alexander Herz*[a], *Jürgen Sperner*[a]

[a]*Klinik für Kinder- und Jugendmedizin, Universitätsklinikum Schleswig-Holstein, Campus Lübeck, Ratzeburger Allee 160, D-23538 Lübeck, Germany*
[b]*Institut für Medizinische Mikrobiologie und Hygiene, Universitätsklinikum Schleswig-Holstein, Campus Lübeck, Ratzeburger Allee 160, D-23538 Lübeck, Germany*
[c]*Zentrum für Radiologie, Neuroradiologie und Nuklearmedizin, Tesdorpfhaus, Mengstrasse 66-70, D-23552 Lübeck, Germany*

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ABSTRACT

We describe a follow-up in a 15-year-old boy with neuroborreliosis diagnosed by clinical symptoms, CSF and serum analysis. MRI revealed a thalamic lesion and an enhancement of the right trigeminal nerve clinically associated with mild hypasthesia in the right maxillary region. Both, clinical symptoms and radiological findings disappeared within 2 months after treatment. *Borrelia burgdorferi* specific IgM and IgG in CSF and IgG in serum became negative between 6 and 12 months after diagnosis. We show that neuroborreliosis at an early stage may present only with moderate neurological deficits and that at this stage MRI reveals distinct cerebral lesions which might even precede clinical manifestation. Thus, early diagnosis and treatment of neuroborreliosis may prevent persistent neurologic lesions.

1. Introduction

Lyme disease is caused by the tick borne spirochete *Borrelia burgdorferi* and its incidence is correlated with the geographic distribution of ixodic ticks. It may affect the lymphatic system, skin, joints, heart, eyes and the nervous system.[1] Central nervous system presentations occur in about 10–15% of patients and include lymphocytic meningitis, radiculoneuritis and cranial neuritis.[2] A summary of clinical presentation, diagnosis, genetic heterogeneity and therapy of lyme neuroborreliosis has recently been published by Pachner and Steiner.[3] While the most frequently reported neurological features are headache and facial palsy associated with neuritis of the seventh cranial nerve, involvement of other cranial nerves is rare.[1,4,5] Neuroimaging findings in children or adolescents have been described only by a few authors.[4–8] Furthermore, there exist only few follow-up reports about immunological and radiological findings in children with neuroborreliosis. Here we present a unique pediatric case of neuroborreliosis with thalamic and trigeminal nerve lesions, which resolved completely within 2 months after the antibiotic treatment.

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*Corresponding author. Tel.: +49 451 500 2545; fax: +49 451 500 6222.
E-mail address: koechling@paedia.ukl.mu-luebeck.de (J. Köchling).
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2. Case report

A 15-year-old boy was referred to the hospital because of a history of progressive headache on the right side for 6 weeks, dizziness, loss of appetite and progressive fatigue. There was no history of tick bite or erythema migrans. Physical examination revealed a distinct loss of sensitivity within the right maxillary region, but no fever nor neck stiffness. Routine blood tests and EEG were normal. Ophthalmoscopy did not reveal a papilledema. Lumbar puncture showed an opening pressure of 21 cm H_2O. Analysis of CSF revealed a pleocytosis (448/μl), predominantly lymphocytes, an elevated protein level (1.51 g/l) and a slightly elevated lactate level (2.41 mmol/l). The CSF culture was sterile. The elevated albumin-CSF/serum ratio (21×10^{-3}) showed an impairment of the blood brain barrier. Furthermore, the Borrelia-IgM-CSF/serum ratio (56×10^{-3}) indicated intrathecal synthesis of specific antibodies. Oligoclonal IgG bands were present in isoelectric focusing electrophoresis. In serum and CSF IgM was positive and IgG intermediates for *B. burgdorferi* using the ELISA and immunoblot. The antibody specificity index was significantly positive: 26 (positive >2, highly positive >4).[6] In contrast, PCR for *B. burgdorferi* in CSF was negative. Cerebral MRI scans were performed using a 1.5 T unit (Magnetom Symphony Siemens, Germany) and axial flair sequences without contrast medium and T1-weighted images after intravenous injection of 0.1 mmol gadolinium/kg bodyweight (5 mm), coronal T1-weighted images with and without gadolinium (2 mm) and sagittal T2-weighted images (3 mm). Prior to the treatment the flair sequences showed a small hyperintense lesion within the right thalamic nucleus (Fig. 1A). The T1-weighted images showed an isolated enhancement of the right trigeminal nerve (Fig. 2A).

Remarkably, a few hours after lumbar puncture headache disappeared. The patient was treated with ceftriaxone for 21 days. Two days after initiation of the treatment hypesthesia within the right maxillary region disappeared. Four weeks after the antibiotic treatment we performed a follow-up MRI which showed a complete recovery (Figs. 1B and 2B). Six months after the initial diagnosis serum IgM was still positive and IgG intermediates for *B. burgdorferi* as shown by the immunoblot. Twelve months after initial diagnosis the patient was admitted to the hospital a second time because of acute headache. Again, headache disappeared after lumbar puncture which showed an elevated opening pressure of 25 cm H_2O. Clinical examination and analysis of routine blood and CSF revealed normal findings. While both ELISA and immunoblot showed that IgM and IgG in CSF and IgG in serum were negative, only serum IgM remained positive for *B. burgdorferi* as shown by the immunoblot.

3. Discussion

Neuroborreliosis in our patient was diagnosed by clinical symptoms, CSF and serum analysis. In serum and CSF, IgM was positive and IgG intermediates for *B. burgdorferi* using the

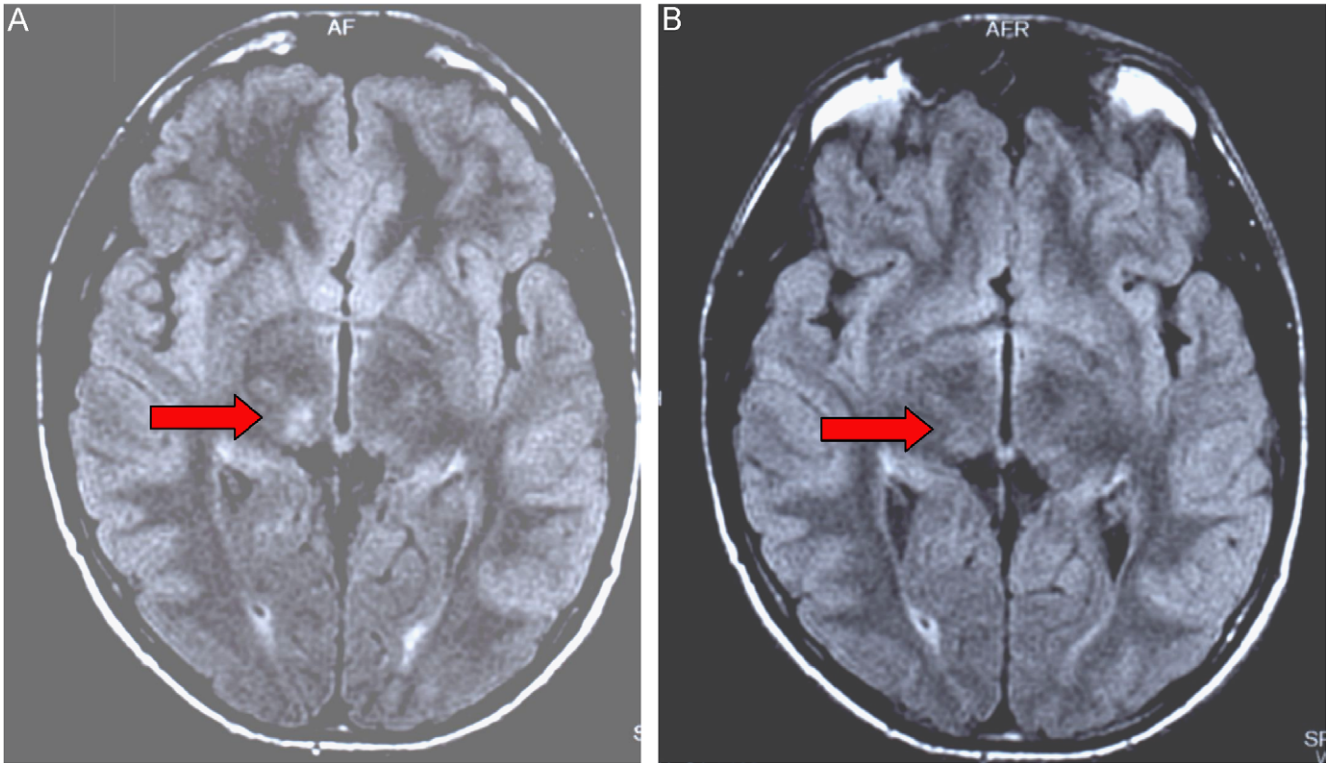

Fig. 1 – Axial MRI flair sequences (5 mm slice thickness) of a 15-year-old boy with neuroborreliosis suffering from headache and mild, right facial hypesthesia show a right thalamic lesion (A). Disappearance of the lesion 7 weeks later (B) after IV treatment with ceftriaxone for 3 weeks.

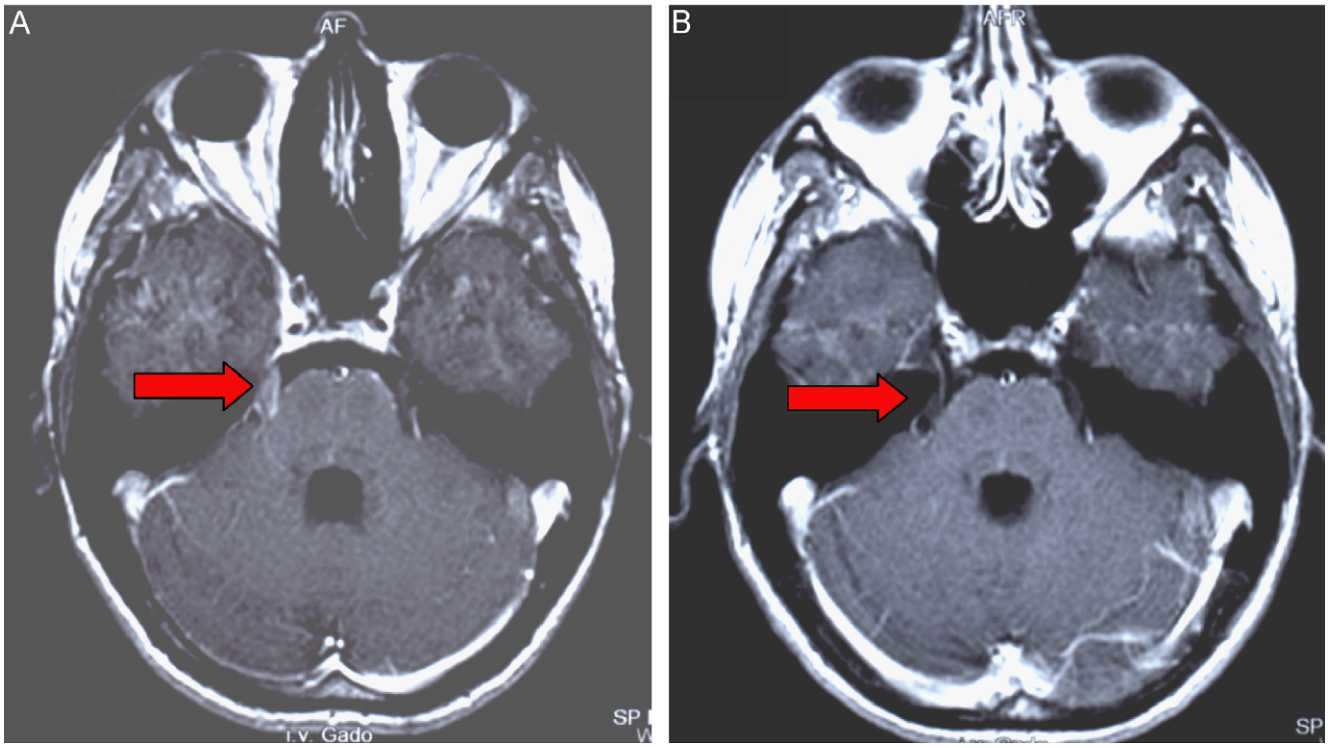

Fig. 2 – Axial T1-weighted MRI (5 mm slice thickness) of the same patient shows enhancement of the right trigeminal nerve (A) and normalization seven weeks later (B) after IV treatment with ceftriaxone for 3 weeks.

ELISA and immunoblot. The antibody specificity index was significantly positive for *B. burgdorferi*. In addition, Borrelia-IgM-CSF/serum ratio was elevated and showed intrathecal synthesis of specific antibodies as well as oligoclonal-IgG bands in isoelectric focusing electrophoresis. These results strongly argue for neuroborreliosis.[9,10]

The negative CSF PCR in our patient does not surprise since *B. burgdorferi* CSF PCR has been shown a sensitivity of 5% and a specificity of 99% in North American children with Lyme meningitis.[11] In addition, two European studies which focused primarily on the diagnostic sensitivity of Lyme PCR in children also reported sensitivities of 25% or below.[12,13]

Six months after initial diagnosis no antibody class switch against *B. burgdorferi* was present, 12 months after diagnosis IgM and IgG in CSF and IgG in serum became negative. Only serum IgM remained positive in the immunoblot. It has been shown that IgM can persist for months or years in spite of sufficient therapy.[9]

In our patient, headache at initial diagnosis as well as 1 year later was associated with a moderately elevated intracranial pressure which disappeared after lumbar puncture. The association of Lyme disease and pseudotumor cerebri has been described by others and our group.[4,14] In contrast to our patient, pseudotumor cerebri is associated in most cases with papilledema. However, there are rare reports of patients with pseudotumor cerebri without papilledema.[15] Nevertheless, we found no evidence of ongoing Lyme disease in our patient and the etiology of the elevated intracranial pressure remains unclear.

The MRI findings are consistent with the clinical diagnosis and showed two different lesions, which resolved completely 4 weeks after treatment with ceftriaxone. While the non-enhancing thalamic lesion was asymptomatic, the isolated enhancement of the right trigeminal nerve was in good correlation with a hypesthesia in the right maxillary region, which resolved within 2 days after initiation of antibiotic treatment. Only few reports described neuroimaging findings in children. Belman et al.[4] performed MRI in 54 of 96 children with neuroborreliosis but found abnormal findings only in 26%. Demaerel et al.[6] described T2-weighted lesions in subcortical white matter and brain stem as well as peripheral and pial gadolinium enhancement. An isolated oculomotor nerve paralysis in Lyme disease was reported by Savas et al.[5] in a 12-year-old girl with a swollen right oculomotor nerve and contrast medium enhancement.

Impairment of the trigeminal nerve due to neuroborreliosis has been reported clinically in 14 patients but MRI scans were not performed.[16–21] although trigeminal neuralgia as a clinical manifestation of Lyme neuroborreliosis has been shown in one patient without abnormal MRI findings it was not mentioned whether MRI was performed with contrast medium.[19] In a 7-year-old boy with Lyme disease and bilateral facial nerve palsy, MRI showed bilateral contrast enhancement of both facial and trigeminal nerves but the enhancement of trigeminal nerves was asymptomatic.[20] Similarly, a 64-year-old woman with neuroborreliosis and diplopia, bilateral third and right sided fifth and seventh cranial nerve enhancement showed no trigeminal palsy.[21] Thus, administration of contrast medium seems to be the only way to diagnose cranial nerve affection by MRI. Nevertheless, trigeminal nerve neuritis diagnosed by contrast enhancement may remain subclinical.[20,21] This strongly suggests that contrast medium enhancement is a sensitive marker of

cranial nerve involvement. Lesions in the cerebral white matter have been described as focal areas of high signal on T2-weighted images.[22,23] These lesions can simulate tumors, acute disseminated encephalomyelitis and vasculitis or may present as a stroke with ischemic lesions in the vertebrobasilar territory.[6,23–25] Involvement of the brain stem with hypermetabolism on PET was described in a 28-year-old male by Kalina et al.[26]

While in our patient MRI is in good correlation with the response to antibiotic therapy, Curless et al.[8] described pontine and cerebrum lesions in a 15-year old with Lyme meningitis whose symptoms resolved after treatment, but had imaging findings that remained. In two other patients contrast enhancing lesions disappeared after 5 months or 2 years, respectively.[24] Six patients were reported with chronic neuroborreliosis and clinical signs of encephalopathy who showed white matter lesions at the time of diagnosis. In three of them the lesions resolved after a mean time of 5.3 months.[22] Follow-up MRI in two children with neuroborreliosis showed in one patient that the peripheral enhancement disappeared, but the subcortical white matter lesions persisted while in another patient the white matter lesions and the pial enhancement disappeared after 86 days.[6] In contrast, no significant changes were seen in three patients with neuroborreliosis and multiple sclerosis like lesions 1–5 yr after antibiotic treatment.[23] Morgen et al.[27] reported about four patients with post-treatment Lyme disease syndrome with focal neurologic deficits, relapsing–remitting disease, and lesions in a distribution typical of MS using whole-brain magnetization transfer ratio measures to identify abnormalities not seen on T2-weighted images.

In conclusion, we show that neuroborreliosis at an early stage may present clinically only with moderate neurological deficits. MRI is very sensitive to detect distinct cerebral lesions caused by Lyme disease. Immediate antibiotic treatment at an early stage of neuroborreliosis can lead to complete clinical recovery and resolution of immunological and radiological findings. We finally suggest that neuroborreliosis should be considered even when only mild neurological deficits are present. To our knowledge this is the first published case of neuroborreliosis with thalamic and trigeminal nerve lesions, which resolved completely 4 weeks after antibiotic treatment.

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