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Reversible Splenial Lesion Syndrome (Resles) in a Patient with Clinically Mild Tick-Borne Encephalitis and Hyponatremia

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Abstract

Introduction: Reversible splenial lesion syndrome (RESLES) is a clinicoradiological syndrome of varied etiology, characterized by transient lesions involving the splenium of the corpus callosum (SCC). Clinical presentation is non-specific and depends on etiology. In the case of infectious disease the syndrome is also called mild encephalitis with reversible splenial lesion (MERS). Hyponatremia is often described in patients with RESLES. Here we present a patient case of RESLES/MERS in a patient with tick-borne encephalitis (TBE) accompanied by mild hyponatremia.

Case Presentation: A 46-year-old man presented with malaise, fever, headache, discrete nuchal rigidity, brain stem symptoms (disturbance of ocular movements, gait ataxia) and mild cognitive and psychomotor impairment. Cerebrospinal fluid analysis at two different time points showed a lymphocytic pleocytosis and seroconversion for anti-TBE-IgM/-IgG, serum biochemical analysis a mild hyponatremia. Magnetic resonance imaging (MRI) of the brain on day four after admission revealed a distinct signal hyperintensity on T2/FLAIR sequences in the SCC associated with diffusion restriction and low apparent diffusion coefficient (ADC) values on diffusion-weighted sequences. On T1-weighted images no contrast enhancement was detectable. Until the diagnosis of TBE the patient was treated with intravenous ceftriaxone, ampicillin and acyclovir. The patient recovered completely within three weeks. The T2/FLAIR hyperintense and diffusion-restricted lesion of the SCC was completely resolved ten days after the first MRI.

Conclusion: TBE accompanied by hyponatremia may lead to RESLES/MERS, a clinicoradiological syndrome with reversible non-enhancing lesion of the SCC and excellent prognosis. Neuroradiological findings in RESLES are very similar to findings described in patients with osmotic demyelination syndromes like central pontine myelinolysis or extrapontine myelinolysis.

Keywords: Reversible splenial lesion syndrome; Mild encephalitis with reversible splenial lesion; Tick-borne encephalitis; Hyponatremia

Abbreviations: ADC: Apparent Diffusion Coefficient; CNS: Central Nervous System; CPM: Central Pontine Myelinolysis; CSF: CerebroSpinal Fluid; DWI: Diffusion-Weighted Imaging; EBV: Epstein Barr Virus; EPM: Extrapontine Myelinolysis; TBE: Tick-Borne Encephalitis; MERS : Mild Encephalitis With Reversible Splenial Lesion; MRI: Magnetic Resonance Imaging; RESLES: Reversible Splenial Lesion Syndrome; SIAD: Syndrome Of Inappropriate Secretion Of Antidiuretic Hormone; SCC: Splenium Of The Corpus Callosum

Introduction

Reversible splenial lesion syndrome (RESLES) involving the splenium of the corpus callosum (SCC) is a clinicoradiological syndrome described in a variety of disorders including central nervous system (CNS) infections, seizures, anticonvulsive drug withdrawal, high-altitude cerebral edema and metabolic disturbances like hyponatremia [1,2]. RESLES is defined as transient, non-contrast enhancing, T2/FLAIR hyperintensity associated with diffusion-restriction and low apparent diffusion coefficient (ADC) values on diffusion-weighted imaging (DWI), indicating cytotoxic edema. In rare cases high ADC values consistent with vasogenic edema were reported [1]. In cases with clinically mild encephalitis (viral as well as bacterial) the syndrome is also named MERS (mild encephalitis with a reversible splenial lesion) [3]. Reported causative pathogens are epstein barr virus (EBV), influenza type A/B [4], Salmonella enteritis, mumps virus and mumps vaccination virus [5], varicella zoster virus [3], adenovirus [6], parvovirus B19 [7], HHV 6 [8] and rubella virus [9].

The pathophysiology of RESLES, especially the reversibility of a localized homogenous diffusion-restriction, remains largely unknown. It is assumed that a transient vasogenic, intramyelinic and/or interstitial edema in tightly packed fibers or an edema due to an inflammatory process might be important mechanisms [3,10,11]. An accompanying hyponatremia is frequently described [2,5,12,13]. On a molecular and biochemical level it was observed that serum and CSF levels of interleukin-6 (IL-6) and IL-10 were significantly elevated in RESLES patients [14-17]. Further, increased CSF levels of 8-hydroxy-2'-deoxyguanosine (8-OHdG) and hexanoyl-lysine in MERS patients may indicate augmented oxidative stress levels [17]. As RESLES complicates different disorders, Polster et al. [10] suggested that such a transient lesion in SCC occurs as a nonspecific endpoint of various disease processes leading to a vasogenic edema. Here we present a patient case of RESLES in a patient with clinically mild tick-borne encephalitis (TBE) and mild hyponatremia.

Case Presentation

In October 2014 a 46-year old man presented with symptoms of

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a meningoencephalitis (malaise, fever of 39,3°C, sinus tachycardia of 113/min, nuchal rigidity, occipital headache, phonophobia, pain during ocular movement and myalgia), brain stem symptoms including binocular diplopia, upward gaze palsy, horizontal gaze-evoked nystagmus as well as slight gait ataxia and mild neurocognitive deficits and psychomotor impairment. Blood white cell count of 17000 cells/µl was accompanied by normal C-reactive protein level. Hyponatremia of 133 mmol/l (normal 135-145 mmol/l) was seen one day after admission. Sodium blood concentration showed normalization within six days. Cerebrospinal fluid (CSF) analysis showed granulocytic pleocytosis (111 cells/µl) and moderately increased protein content (859 mg/l) and lactate (2,76 mmol/l). A detailed serological and microbiological examination – including ELISA and PCR from serum and CSF probes – for *Borrelia burgdorferi*, *Listeria monocytogenes*, *Leptospira interrogans*, *Treponema pallidum*, *Mycobacterium tuberculosis*, HSV 1/2, TBE-virus and EBV revealed a positive blood anti-TBE-IgM/IgG-titer, but not in CSF. Eight days later we saw a shift to a lymphocytic pleocytosis (162 cells/µl, Figure 1A) with further increased protein level (1069 mg/l) in CSF and a seroconversion of CSF anti-TBE-IgM/IgG (antibody index for TBE-IgG of 14,1, normal <1,6). Blood and CSF ELISA and PCR for all other pathogenic agents remained negative. In cerebral MRI four days after admission a non-T1-contrast enhancing, T2/FLAIR hyperintense lesion in the SCC with distinct diffusion-restriction and low apparent diffusion coefficient (ADC) values in diffusion-weighted imaging (DWI) was detected (Figure 1B). In neuropsychological examination cognitive deficits in verbal working memory, attention and concentration could be found. There was no evidence of hemispheric disconnection. Starting on the day of admission, patient was treated intravenously with ceftriaxon 2 g once daily for two weeks and acyclovir 750 mg three times daily until negative result of HSV 1/2-PCR in CSF could be acquired. Supportive therapy included intravenous rehydration as well as antipyretic and analgesic substances as paracetamol and ibuprofen.

After three weeks the patient presented with complete clinical recovery without any neurological or neuropsychological deficit. A follow-up MRI ten days after first MRI demonstrated normalization of the T2/FLAIR hyperintense and diffusion-restricted lesion within the SCC (Figure 1B). This indicates an initial cytotoxic edema in the sense of a reversible splenial lesion syndrome (RESLES). Because of the infectious etiology (TBE-virus infection) the syndrome is also called mild encephalitis with a reversible splenial lesion (MERS).

Discussion

This is the second reported patient case with clinically mild TBE and RESLES [12]. TBE was confirmed by seroconversion for IgG/IgM-TBE in CSF and high antibody index. Brain MRI in the first week after symptom onset showed the typical signs of RESLES. The patient recovered within three weeks without neurocognitive sequelae or defects in MRI. Thus, we came to the diagnosis of RESLES in TBE.

Both patient cases with clinically mild TBE and RESLES were accompanied by a mild hyponatremia (this case and [12]. Hyponatremia is an often reported finding in patients with RESLES/MERS [2,5,12,13] as well as in patients with TBE [18]. Hyponatremia in TBE is often caused by hypovolemic dehydration, less common by the syndrome of inappropriate secretion of antidiuretic hormone [18]. This raises the question, whether hyponatremia is a part of pathophysiology of RESLES or only an accompanying circumstance.

Interestingly, similar MRI findings as are typically described in RESLES can be shown in several patients with osmotic demyelination syndromes like central pontine myelinolysis (CPM) or extrapontine myelinolysis (EPM) [19]. Hyponatremia and rapid correction of sodium blood-concentration are known risk factors for developing CPM/EPM [19]. In CPM/EPM rapid improvement of ADC values predicts a good clinical recovery [20], which is also characteristic in RESLES. Weather

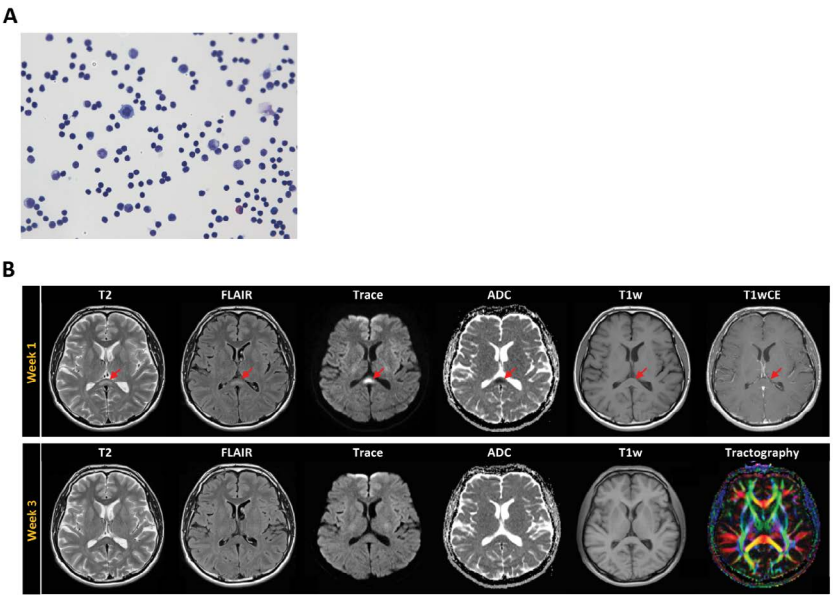

Figure 1: (A) Cytology of second cerebrospinal fluid analysis. CSF-analysis revealed a lymphocytic pleocytosis. (B) Brain MRI in week 1 and week 3 after symptom onset. Brain MRI four days after admission showed a distinct signal hyperintensity on T2/FLAIR sequences in the SCC associated with diffusion restriction and low ADC values on diffusion-weighted sequences. Further a discrete hypointensity on T1 sequences without gadolinium enhancement was detectable. Follow-up MRI ten days later demonstrated complete normalization of the SCC lesion.

RESLES and CPM/EPM have a similar pathophysiology or RESLES is a specific type of EPM remains to be elucidated in future studies.

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