Case Report

A Case of Combined Infection with Tick-Borne Encephalitis and Lyme Borreliosis with Severe Meningoencephalitis and Complete Recovery

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Abstract

Here, we present a case of severe meningoencephalitis caused by combined infection with tick-borne encephalitis (TBE) and Lyme borreliosis (LB) in a 25-year-old woman in a rural area of Zhambyl region, Kazakhstan. She presented with fever, nausea, vomiting, weakness, sweating, severe headache, arthralgia, and malaise. The course of illness was further complicated by encephalitis with symmetric lesions of the midbrain cerebral peduncles and serous meningitis. TBE and LB co-infection were established by a two-fold increase in serum IgG titers between day 21 and day 25 of illness. Both infections responded well to combined therapy with human TBE immunoglobulins, antibiotics, antiviral drugs, glucocorticoids, and diuretics. The outcome of the disease was favorable and the patient recovered completely.

Keywords: *Borrelia burgdorferi* s. l, Kazakhstan, lyme neuroborreliosis, meningoencephalitis, tick-borne encephalitis, tick-borne encephalitis virus

Introduction

In Central Europe and many parts of Asia, tick-borne encephalitis virus (TBEV) and *Borrelia burgdorferi* sensu lato (s. l.), the causative agents of tick-borne encephalitis (TBE) and Lyme borreliosis (LB) are the two most important tick-borne pathogens that can lead to severe neurological complications.[1] Although several cases of co-infection with TBE and LB have been reported, there are limited data on the severe cases with prolonged meningoencephalitis followed by complete recovery of the patient.[1-3] Here, we describe a case of severe TBE and Lyme neuroborreliosis (LNB) co-infection in a woman from the Zhambyl region of Kazakhstan.

Case Report

A 25-year-old woman presented with a fever lasting 9 days. She was inactive, had nausea, vomiting, weakness, sweating, severe headache, arthralgia, and malaise. Low titers of antibodies to *Brucella* bacteria were noted in the indicative Haddlson (+) and confirmatory Wright (1:50) agglutination reactions. Urinalysis showed elevated protein levels and the presence of leukocytes and erythrocytes [Table 1]. A presumptive diagnosis of brucellosis was made, and the patient started empiric treatment with nonsteroidal anti-inflammatory drugs, glucocorticoids, and kanamycin.

On day 13, the patient showed convulsions, unconsciousness, stupor, mild neck muscle stiffness, and clonic muscle spasms of the upper and lower limbs. Magnetic resonance imaging (MRI) examination revealed brainstem encephalitis with symmetric lesions in the midbrain cerebral peduncles, dyscirculatory encephalopathy, and signs of increased intracranial pressure. Analysis of the cerebrospinal fluid (CSF) showed mild pleocytosis with high lymphocyte counts and protein concentrations. Blood and CSF culture results were

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Table 1: Laboratory findings

Test	Illness days								Normal range
	Day 10	Day 12	Day 15	Day 18	Day 21	Day 30	Day 37	Day 39	
Blood tests									
WBCs (×10³/μL)	8.8	-	-	-	12.9	-	-	12.3	4.5-13.5
Band neutrophils (%)	2	-	-	-	10	-	-	4	0-5
Segmented neutrophils (%)	68	-	-	-	62	-	-	85	40-60
Monocytes (%)	7	-	-	-	14	-	-	6	2-11
Lymphocytes (%)	23	-	-	-	14	-	-	5	20-40
ESR (mm/h)	8	-	-	-	23	-	-	3	<15
Total protein (mg/dL)	68.5	-	-	-	61.8	-	65.2	-	60-83
Glucose (mg/dL)	-	-	-	-	73	-	-	-	70-100
Creatinine (mg/dL)	-	-	-	-	16.0	-	-	-	0.45-1.05
Urine tests									
Total protein (mg/24 h)	-	-	-	-	198	-	-	132	<100
RBCs (/hpf)	1	-	-	-	1	-	-	2	≤2
WBCs (/hpf)	2	-	-	-	3	-	-	7	≤2–5
Squamous epithelial cells (/hpf)	2	-	-	-	2	-	-	1	≤15-20
CSF tests									
WBCs (cells/ml)	-	-	85.2	13.2	-	9.6	-	-	0-5
Lymphocytes (cells/ml)	-	-	81.6	13.2	-	3.6	-	-	1-7
Total protein (mg/dL)	-	-	165.0	49.5	-	66.0	-	-	15-60
Pandy's test	-	-	3+	1+	-	1+	-	-	Negative
Culture tests									
CSF culture	Negative	Negative	-	-	-	-	-	-	Negative
Blood culture	Negative	Negative	-	-	-	-	-	-	Negative

WBCs: White blood cells, ESR: Erythrocyte sedimentation rate, RBCs: Red blood cells, CSF: cerebrospinal fluid, hpf: High power field

negative [Table 1]. On day 16, pupils were constricted and fixed to the center. Acute meningoencephalitis of unknown etiology was diagnosed and treatment was supplemented with intravenous medovir and ofloxacin.

On day 20, the patient was unable to fix her gaze, opened her mouth with difficulty, and the movement of the eyeballs was limited. Tongue tremors, hypomimia, and extrapyramidal muscle hypertonus were observed. The patient had no control over pelvic functions. On day 21, the serologic analysis revealed negative results for IgM and positive results for IgG antibodies against TBEV and *B. burgdorferi* s. l. On day 25, the serological analysis showed a two-fold increase in IgG titers against both TBEV and *B. burgdorferi* s. l. Human immunoglobulin against TBEV (international nonproprietary name – immunoglobulin encephalitis Ixodidae) and ceftriaxone (14.3 mg/kg × 2 doses for 13 days) intravenously were added to the treatment.

Over the next 12 days, the patient's level of consciousness improved and facial and ocular palsies disappeared. The meningeal symptoms disappeared on day 34, and the patient was completely afebrile on day 38 after the onset of symptoms. She was discharged on day 39 with near complete improvement and underwent long-term rehabilitation. One year after discharge, she had fully recovered and showed no neurologic sequelae.

Discussion

Clinical recognition of combined infections is always complex because of overlapping or distorted manifestations of one or both joint infections. This case illustrates the challenges in establishing a diagnosis in a patient with TBE and LNB co-infection that resulted in severe meningoencephalitis. Acute onset of symptoms, toxemia, meningoencephalitis syndrome, lymphocytic pleocytosis in the CSF, flaccid paralysis, cranial nerve involvement, and facial hypomimia are equally compatible with TBE or LNB.[2] The clinical diagnosis of double infection was supported by a two-fold increase in the titers of IgG antibodies against TBEV and *B. burgdorferi* s. l. in paired serum samples. TBE develops within a few weeks,[4] and the presence of TBE-specific IgM antibodies is usually recommended to confirm the diagnosis of TBE. Interestingly, in our case, IgM antibodies against TBEV were negative despite the acute illness. Several studies have described the same phenomenon.[5] Based on the clinical signs, MRI data, and laboratory findings, we consider the diagnosis of TBE in the patient to be well-established.

Laboratory diagnosis of LB is more difficult because infection with other tick-borne diseases or some viral and bacterial infections can lead to false-positive test results for LB.[6] Encephalitic symptoms caused by LNB occur in the late stage of the disease and may be observed months or even years after primary infection. In these cases, positive IgG and negative IgM results are considered reliable for establishing the diagnosis of LNB.[7] In our case, an increased titer of IgG antibodies to *B. burgdorferi* s. l. in paired sera collected at a short interval supported the diagnosis of LNB.

The establishment of the diagnosis in our case was also challenged by the fact that TBE and LB are not endemic in the Zhambyl region of Kazakhstan.[8] Examination of the patient revealed that she had recently traveled to the endemic areas for TBE and LB, Almaty Region of Kazakhstan.[8] The patient denied a tick bite and symptoms of LB in the past, which is not unusual. It was demonstrated that only 50%60% of patients with TBE and LB report tick bites.[4,7]

In Kazakhstan, TBE frequently causes meningoencephalitis leading to postencephalitic syndrome and long-term neurological morbidity.[4] Around 31.8% of TBE cases with meningoencephalitis results in upper limb paresis.[9] In the presented case, despite the severe form of meningoencephalitis, the outcome was favorable; the patient recovered completely and had no neurologic sequelae. After a diagnosis of co-infection with TBE and LNB was made, the patient was treated with human immunoglobulins against TBEV and ceftriaxone. Ceftriaxone is a preferred drug for LNB therapy.[1] Although there is no specific antiviral treatment for TBE,[4] intravenous human immunoglobulins against TBE have long been used for postexposure prophylaxis and TBE treatment. The efficacy of intravenous immunoglobulins against TBEV has not been demonstrated in clinical trials, several studies have reported their efficacy in the treatment of various clinical forms of TBE.[10] Therefore, we believe that co-infection with TBE and LNB can be successfully treated with a combination of human immunoglobulins against TBEV and antibiotics. Furthermore, this study demonstrates that patients with acute neurologic symptoms traveling to endemic areas should be evaluated for TBE and LB.

The study has several limitations. The TBEV RNA detection in the serum, CSF, or urine during the acute phase of infection was not performed due to the lack of diagnostic resources in the hospital. Furthermore, anti-TBEV antibodies were not tested in CSF, whereas it is recommended to perform for confirmation of the diagnosis.

Research quality and ethics statement

The authors followed applicable EQUATOR Network (http://www. equator-network. org/) guidelines, notably the CARE guideline, during the conduct of this report.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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