Case Report

Anti-NMDA Receptor Encephalitis Presenting with Status Epilepticus: Brucellosis as a Possible Triggering Factor: A Case Report

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Abstract

Brucellosis is a common zoonotic infection caused by bacterial genus *Brucella*, a Gram-negative bacterium, and continued to be a health problem in endemic areas. Anti-*N*-methyl-d-aspartate receptor (NMDAR) encephalitis is an autoimmune disease which can lead to status epilepticus. A 19-year-old male patient was referred to our hospital with status epilepticus. The diagnosis of brucellosis was confirmed about 2 weeks before**.** The brain magnetic resonance imaging was normal. Lumbar puncture was performed, and cerebral spinal fluid (CSF) was in normal limits. The patient was treated with antiepileptic, anti-brucellosis agents. Two weeks after discharge, the patient readmitted to hospital with status epilepticus again. Extensive workup was negative except that NMDAR antibodies were detected in serum and CSF. The diagnosis of anti-NMDAR encephalitis was established. Brucellosis as a triggering factor for NMDAR encephalitis should be considered.

Keywords: *Anti-NMDA receptor, brucellosis, encephalitis, epilepsy, status epilepticus*

Introduction

Brucellosis is a common zoonotic infection caused by bacterial genus *Brucella*, a Gram-negative bacteria, and continued to be a health problem in endemic areas.[1] Most of the Brucella cases occur in the developing countries, which >500,000 new cases have been reported per year in the world.[2] This infection also is one of the most prevalent endemic disease in Iran.[3] Brucellosis can involve any system and organ body; hence, this infection also known as a great imitator.[4] Anti-*N*-methyl-d-aspartate receptor (NMDAR) encephalitis is a disorder that has been characterized in adults, frequently young women with teratomas of the ovary. The clinical presentation often includes seizures, decreased level of consciousness, dyskinesias, and autonomic instability.[5] The authors describe a case with anti-NMDAR encephalitis, which demonstrates that synthesis of NMDAR antibodies began after Brucella infection.

Case Report

A 19-year-old male patient was referred to the emergency department with seizure. He had a history of fever and generalized weakness about 2 weeks before. According to having the history of consuming continuously dairy products made from unpasteurized milk, the serologic Brucella tests including wright, 2ME, and coombs wright were checked. Serum SAT test was positive at titer of 1/1,280, and with the diagnosis of brucellosis, the doxycycline and streptomycin were prescribed for him since about 2 weeks before admission. Two weeks later, the patient referred to our hospital with seizure. Convulsion was generalized, tonic, and colonic lasting about 5 min. He had no history of recent drug usage (except for treatment of brucellosis), alcohol consumption, and smoking. No history of head trauma was declared. Vital signs and general examination were not remarkable. He was afebrile. Complete blood cell count was in normal limits. HBS-Ag, HCV-Ab, HIV test, and serum toxic panel were all negative.

Brain computed tomography scan was performed, which was with no abnormality. The lumbar puncture (LP) was performed. Cerebral spinal fluid (CSF) revealed no abnormality; it was colorless and clear; glucose = 67, protein = 15 mg/dL, red blood cell = 0, and white blood cell = 0. The CSF was also sent for Brucella and herpes simplex (HSV 1 and 2) polymerase chain reaction (PCR) studies. Status

How to cite this article: Hakamifard A, Naghibi SN, Hashemi Fesharaki SS. Anti-NMDA receptor encephalitis presenting with status epilepticus: Brucellosis as a possible triggering factor: A case report. Int J Prev Med 2019;10:119.

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Access this article online

Website: www.ijpvmjournal.net/www.ijpm.ir

DOI: 10.4103/ijpvm.IJPVM_417_18

Quick Response Code:

epilepticus was defined, and patient required intubation and mechanical ventilation. Antiepileptic drugs were started. According to brucellosis, with the clinical suspicious for neurobrucellosis, the treatment including ceftriaxone 2 g every 12 h intravenous (IV), doxycycline 100 mg every 12 h, and rifampin 600 mg daily in addition to IV acyclovir were started. In ICU, the clinical seizure classification was focal and lateralizing signs were right facial and arm clonic and right versive. The electroencephalography monitoring was performed, and the midazolam infusion was started. Brain magnetic resonance imaging (MRI) and magnetic resonance venography (MRV) were both normal. CSF PCR studies for Brucella and HSV, 1 and 2, were reported negative and CSF adenosine deaminase reported 10. Serologic test for brucellosis on CSF were negative. With the probable diagnosis of neurobrucellosis, the treatment with ceftriaxone, doxycycline, and rifampin were continued. Also, 14-day course of IV acyclovir was completed. After 1 month, the patient was stable and treatment with oral doxycycline, rifampin, and co-trimuxazole accompanied with antiepileptic drugs were continued. Two weeks after discharge the patient readmitted to hospital with status epilepticus and was intubated again. The LP was performed, which revealed normal CSF analysis. HSV, 1 and 2, PCR in addition to Brucella PCR were negative in CSF again. The patient underwent renewed brain MRI and MRV and both were normal. Extensive workup did not reveal any cause of the symptoms; however, NMDAR antibodies were positive in both serum and CSF; hence, the diagnosis of NMDAR encephalitis was established. He was started on IV methylprednisolone, which yielded limited improvement. According to intractable epilepsy, the patient's treatment consisting of plasmapheresis and intravenous immunoglobulin was started.

Discussion

We introduce a case of autoimmune encephalitis presenting with status epilepticus with anti-NMDAR antibodies in the CSF and serum possibly triggered by *Brucella* spp. Before antibody testing for anti-NMDAR antibodies became positive, the patient was considered as having probable neurobrucellosis based on positive serology test for brucellosis in serum. The anti-NMDAR encephalitis-associated syndrome includes impaired consciousness, neuropsychiatric symptoms, seizures, and autonomic instability. Timely diagnosis is critical for implementation of treatments.[6,7] This disorder can cause prolonged status epilepticus, which has a high mortality rate.[8,9] According to the association with teratoma, this entity was at first known as a paraneoplastic syndrome, although experience suggests that this disorder classified as neuroautoimmune syndromes, and antibodies formed in response to a number of possible stimuli including infection and tumor.[10,11] Hence, the triggers of the synthesis of anti-NMDAR antibodies consist of tumors, viral infections, and other unknown factors.[12] Patients may have no tumor in evaluations. The prodromal infection may act as the antigenic trigger.[13] CSF abnormality is seen in >90% of patients, including mild-to-moderate lymphocytic pleocytosis, mild increase of CSF protein, and also increase of CSF-specific oligoclonal bands.[14] In our case, the CSF analysis repeatedly was normal completely. In our knowledge, the neurobrucellosis is a rare complication with a variety of manifestation, which may challenge the diagnosis. Few cases of neurobrucellosis with presentation of convulsion or epileptic seizure have been reported. All reported cases with epilepticus seizure due to neurobrucellosis were accompanied with cerebral vein thrombosis, meningitis, encephalitis, meningoencephalitis, or space occupying lesion, such as brain abscess, but none of these were found in our case. In this patient, a coincidental development of both disorders (probable neurobrucellosis and anti-NMDAR encephalitis) is unlikely, although the treatment of neurobrucellosis was continued. If studies for infectious causes became negative, other diagnoses, such as autoimmune causes, must be considered promptly. Brucellosis as a triggering factor for anti-NMDAR encephalitis should always be considered in differential diagnosis. Research is needed to address the issue.

Conclusions

Brucellosis as a triggering factor for anti-NMDAR encephalitis should be considered.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Received: 12 Sep 18 **Accepted:** 31 Jan 19
Published: 05 Jul 19

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