

Case Report

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

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

**Atousa Hakamifard,
Seyed Navid
Naghbi¹,
Seyed Sohrab
Hashemi Fesharaki²**

Department of Infectious Diseases, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran, ¹Department of Neurology, Kashani Hospital Epilepsy Center, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran, ²Pars Advanced Medical Research Center, Pars Hospital, Tehran, Iran

Address for correspondence:

*Dr. Atousa Hakamifard,
Department of Infectious Diseases, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran.
E-mail: a.hakamifard@med.mui.ac.ir*

Access this article online

Website:
www.ijpvmjournal.net/www.ijpvm.net

DOI:
10.4103/ijpvm.IJPVM_417_18

Quick Response Code:



How to cite this article: Hakamifard A, Naghbi 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.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

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-trimoxazole 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 epileptic 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

References

1. Mantur BG, Amarnath S, Shinde R. Review of clinical and laboratory features of human brucellosis. *Indian J Med Microbiol* 2007;25:188-202.
2. Pappas G, Memish ZA. Brucellosis in Middle East: A persistent medical, socioeconomic and political issue. *J Chemother* 2007;19:243-8.
3. Alavi SM, Rafiei A, Nikkhooi AR. The effect of lifestyle on brucellosis among nomads in Iran, Ahvaz. *Pak J Med Sci* 2007;23:358-60.

4. Franco MP, Mulder M, Gilman RH, Smits HL. Human brucellosis. *The Lancet Infectious Dis* 2007;7:775-86.
5. Pappas G, Akritidis N, Bosilkovski M, Tsianos E. Medical progress: Brucellosis. *N E J Med* 2005;352:2325-36.
6. Veciana M, Becerra JL, Fossas P, Muriana D, Sansa G, Santamarina E, *et al.* EEG extreme delta brush: An ictal pattern in patients with anti-NMDA receptor encephalitis. *Epilepsy Behav* 2015;49:280-5.
7. Peery HE, Day GS, Dunn S, Fritzler MJ, Prüss H, De Souza C, *et al.* Anti-NMDA receptor encephalitis. The disorder, the diagnosis and the immunobiology. *Autoimmun Rev* 2012;11:863-72.
8. Finné Lenoir X, Sindic C, van Pesch V, El Sankari S, de Tourchaninoff M, Denays R, *et al.* Anti-Nmethyl-D-aspartate receptor encephalitis with favorable outcome despite prolonged status epilepticus. *Neurocrit Care* 2013;18:89-92.
9. Drislane FW, Blum AS, Lopez MR, Gautam S, Schomer DL. Duration of refractory status epilepticus and outcome: Loss of prognostic utility after several hours. *Epilepsia* 2009;50:1566-71.
10. Dalmau J, Tuzun E, Wu HY, Masjuan J, Rossi JE, Voloschin A, *et al.* Paraneoplastic anti-N-methyl-D-aspartate receptor encephalitis associated with ovarian teratoma. *Ann Neurol* 2007;61:25-36.
11. Florance NR, Davis RL, Lam C, Szerka C, Zhou L, Ahmad S, *et al.* Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis in children and adolescents. *Ann Neurol* 2009;66:11-8.
12. Tüzün E, Zhou L, Baehring JM, Bannykh S, Rosenfeld MR, Dalmau J. Evidence for antibody-mediated pathogenesis in anti-NMDAR encephalitis associated with ovarian teratoma. *Acta Neuropathol* 2009;118:737-43.
13. Moscato EH, Jain A, Peng X, Hughes EG, Dalmau J, Balice-Gordon RJ. Mechanisms underlying autoimmune synaptic encephalitis leading to disorders of memory, behavior and cognition: Insights from molecular, cellular and synaptic studies. *Eur J Neurosci* 2010;32:298-309.
14. Dalmau J, Gleichman AJ, Hughes EG, Rossi JE, Peng X, Lai M, *et al.* Anti-NMDA-receptor encephalitis: Case series and analysis of the effects of antibodies. *Lancet Neurol* 2008;7:1091-8.