



Presentation of a Patient With Neurobrucellosis: A Case Report in Iran

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Abstract

Background: Brucellosis is a common zoonotic infection caused by the bacterial genus *Brucella*. It is one of the infectious diseases transmissible between humans and animals, and its clinical manifestations are very diverse and misleading. One of these manifestations is central nervous system involvement, which occurs in various forms. Better and more accurate identification of these diverse clinical manifestations can help physicians in the timely diagnosis and treatment of the disease.

Case Presentation: In this study, we introduce a sixteen-year-old patient who complained of fever, low back pain, dizziness, and headache for two months. A detailed history of our patient revealed previous contact with sheep and consumption of unpasteurized milk. Further clinical tests confirmed the diagnosis of *Brucella meningitis* in this patient.

Conclusion: Patients with brucellosis can show a wide variety of clinical symptoms, and knowing these different clinical forms can help physicians in the early diagnosis of the disease. In a country like Iran, where brucellosis is endemic, any patient who presents with complex and unexplained neurological complaints, especially those with a history of brucellosis, should be considered for neurobrucellosis.

Keywords: Neurobrucellosis, *Brucella meningitis*, Meningitis, Case report, Iran

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Introduction

Brucellosis is a common zoonotic infection caused by the bacterial genus *Brucella*. It is an infectious disease transmissible between humans and animals that is prevalent in the Mediterranean region, the Middle East, India, Mexico, and some Central and South American countries (1, 2). This disease can have variable symptoms, from mild to moderate and severe. It can affect multiple organs and tissues in the human body (3-5).

The disease is caused by intracellular gram-negative bacteria of the *Brucella* genus (6). It is mainly transmitted to humans through the consumption of contaminated dairy products such as unpasteurized milk, cheese, and ice cream, direct contact with infected animals, inhalation of contaminated particles in the air, and occupational contact with the organism (7-11).

Infection of the human body systems with *Brucella* occurs in various forms. So far, various pulmonary (12), dermatological (13), psychological (14), cardiac (15), musculoskeletal (16), gastrointestinal (17), and

neurological (18) manifestations of this disease have been reported.

Some other clinical manifestations include central nervous system involvement and epididymo-orchitis; however, these manifestations are infrequent, especially at young ages (19, 20).

Brucellosis is an endemic infectious disease in Iran, and its central nervous system involvement can occur in 4% to 13% of patients (8). The neurological symptoms in patients with brucellosis are due to the effect of *Brucella* toxin on the central nervous system (21). However, the manifestations of involvement of the neurological system due to direct invasion of *Brucella* to the central nervous system can occur in 5% of patients. These manifestations include meningitis, encephalitis, meningoenkephalitis, meningovascular complications, parenchymal dysfunction, psychosis, peripheral neuropathy, and radiculopathy (21-26).

In this study, we introduced a case with neurological symptoms who was finally diagnosed with brucellosis.

Case Presentation

A 16-year-old boy, resident of Khalkhal (Ardabil province, Iran), with a body mass index (BMI) of 17.1 and complaints of fever, chills, back pain, headache, dizziness, anorexia, and weight loss of 6 kg (from 50 to 44 kg) during the last two months was referred to our local hospital.

He had a history of contact with sheep and consumption of unpasteurized milk. He also reported a previous history of brucellosis with symptoms of fever, pain in the hands and elbow joint, and tingling in the hands. He had been hospitalized for 6 days in his previous infection.

On the initial physical examination, the oral temperature was 38.2°C, and the patient's fever pattern was remittent. The patient was conscious and had no organomegaly. Physical examination findings, including nuchal rigidity, Kernig's sign, and Brudzinski's sign, were positive. Cardiac and pulmonary auscultation was normal, but the patient complained of pain and a burning feeling on the left side of the chest. The results of initial laboratory tests are shown in Table 1.

After the initial laboratory tests, according to the symptoms and history of the previous disease, an abdominal and pelvic ultrasound was performed for the patient, and no abnormal findings were observed. Due to pain and burning sensation in the left side of the chest and the possibility of endocarditis, echocardiography was requested, and the test result was normal.

Because of the suspicion of *Brucella meningitis* regarding the past medical history (contact with sheep and consumption of unpasteurized milk) and clinical symptoms, the patient underwent lumbar puncture (Table 2). In addition, a brain computed tomography (CT) scan was done, and no significant abnormal findings were observed. The 2-mercaptoethanol (2ME) and Coombs-Wright tests were also performed, and the

results were positive, confirming brucellosis.

The patient was diagnosed with *B. meningitis* and treated with gentamicin, cotrimoxazole, and rifampin. The patient's fever stopped after five days of receiving the drugs. Loss of appetite, headache, dizziness, back pain, and neck stiffness disappeared after ten days of treatment.

Discussion

Brucellosis is a bacterial infection caused by *Brucella* spp., a gram-negative coccobacillus from the *Brucellaceae* family (27). This infection is considered zoonotic due to its ability to infect non-preferential hosts such as humans. Additionally, it can affect any organ and body site of the host (28, 29). However, the disease has been eradicated in many parts of the world but is still endemic in developing countries like Iran (30, 31).

The clinical manifestations of this disease are very different and variable, and the severity of symptoms depends on the stage of the disease and involved organs (32). Arthralgia, fatigue, and fever are common symptoms of brucellosis. In some cases, brucellosis can be appeared as a systemic disorder and cause significant complications. Various body systems can be involved, such as the musculoskeletal system, hematological system, nervous system, and digestive system (33). The diverse manifestations of brucellosis, along with overlapping symptoms with other diseases, lead to misdiagnosis and late treatment (34).

Neurobrucellosis (nervous system involvement with *Brucella*) is an inflammation caused by the direct action of bacteria and the indirect effects of cytokines and endotoxins on the central and peripheral nervous system (31, 35-40). Sometimes neurological findings may be the only symptoms of brucellosis. According to studies, the incidence of neurological complications in patients with brucellosis is 2% to 5%. Clinical diagnosis of neurobrucellosis is difficult because of various clinical forms of central nervous system involvement, including meningitis, meningoencephalitis, myelitis, radiculitis, meningovascular complications, parenchymal dysfunction, psychosis, peripheral neuropathy, and radiculopathy (7, 25, 41-43). The most common neurological complication is meningitis, which is not easily distinguishable from other meningitis. Neck stiffness is seen in less than 50% of cases (3, 44).

Table 1. Results of the Initial Laboratory Examination

Laboratory Tests	Number
White blood cell count	7300
Red blood cell count	5300
Hemoglobin level	10.5
Platelet count	266000
Erythrocyte sedimentation rate (ESR)	8
C-reactive protein (CRP)	+3
Total bilirubin	0.5
Direct bilirubin	0.2
Alanine transaminase (ALT)	46
Aspartate transaminase (AST)	8
Alkaline phosphatase (ALP)	251
Creatine phosphokinase (CPK)	39
Lactate dehydrogenase (LDH)	499

Table 2. The Results of Lumbar Puncture

Color and Appearance of CSF	Colorless/Clear
WBC/cumm	10
Lymphocytes%	90
Neutrophils, %	5
Monocytes, %	5
Protein, mg/dL	54
Glucose, mg/dL	53

In our study, we presented a patient with symptoms of meningitis and positive physical examination findings, including nuchal rigidity, Kernig's sign, and Brudzinski's sign. The initial analysis of cerebrospinal fluid (CSF) indicated a bacterial process (high WBC count, slightly low glucose concentration, and high protein level). However, lymphocytic pleocytosis in the CSF was not a typical manifestation of bacterial meningitis. These findings were consistent with previous studies that reported laboratory findings of neurobrucellosis (44, 45). Therefore, two additional tests (i.e., 2ME and Coombs Wright tests) were requested, and their positive results helped us diagnose *B. meningitis*.

In the mentioned case, based on a three-drug treatment regimen (gentamicin, cotrimoxazole, and rifampin), the patient's fever stopped after five days of treatment. Loss of appetite, headache, dizziness, back pain, and neck stiffness improved after 10 days of treatment, and a weight gain of approximately 2 kg was observed after 15 days of treatment. After one month of hospitalization and receiving the treatment with the three mentioned drugs, the patient was discharged with continuing the drug regimen and a one-year follow-up.

Conclusion

In conclusion, patients with brucellosis can show a wide variety of clinical symptoms, and knowing these different clinical forms can help physicians in the early diagnosis of the disease. In a country like Iran, where brucellosis is endemic, any patient who presents with complex and unexplained neurological complaints, especially those with a history of brucellosis, should be considered for neurobrucellosis.

Authors' Contribution

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Competing Interests

The authors declare that they have no conflict of interest.

Data Availability Statement

The authors announce that data supporting the findings of the present case study are available within the article.

Ethical Approval

The present study was approved by the Ethics Committee of Guilan University of Medical Sciences, Rasht, Iran (IR.GUMS.REC.1401.300).

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Informed Consent

Informed consent was obtained from the patient before the initiation of the study.

References

- Sanjuan-Jimenez R, Morata P, Bermúdez P, Bravo MJ, Colmenero JD. Comparative clinical study of different multiplex real time PCR strategies for the simultaneous differential diagnosis between extrapulmonary tuberculosis and focal complications of brucellosis. *PLoS Negl Trop Dis*. 2013;7(12):e2593. doi: [10.1371/journal.pntd.0002593](https://doi.org/10.1371/journal.pntd.0002593).
- Hendaus MA, Qaqish RM, Alhammadi AH. Neurobrucellosis in children. *Asian Pac J Trop Biomed*. 2015;5(2):158-61. doi: [10.1016/s2221-1691\(15\)30160-x](https://doi.org/10.1016/s2221-1691(15)30160-x).
- Schutze G, Jacobs R. *Brucella*. In: Kliegman RM, Behrman RE, Jenson HB, Stanton BF, eds. *Nelson Textbook of Pediatrics*. Philadelphia, PA: WB Saunders Company; 2007.
- Sasan MS, Nateghi M, Bonyadi B, Aelami MH. Clinical features and long term prognosis of childhood brucellosis in northeast Iran. *Iran J Pediatr*. 2012;22(3):319-25.
- Kassiri H, Amani H, Lotfi M. Epidemiological, laboratory, diagnostic and public health aspects of human brucellosis in western Iran. *Asian Pac J Trop Biomed*. 2013;3(8):589-94. doi: [10.1016/s2221-1691\(13\)60121-5](https://doi.org/10.1016/s2221-1691(13)60121-5).
- Liu D. *Brucella*. In: *Molecular Medical Microbiology*. Elsevier; 2015. p. 1781-8.
- Ay S, Tur BS, Kutlay S. Cerebral infarct due to meningovascular neurobrucellosis: a case report. *Int J Infect Dis*. 2010;14 Suppl 3:e202-4. doi: [10.1016/j.ijid.2009.07.012](https://doi.org/10.1016/j.ijid.2009.07.012).
- Tajdini M, Akbarloo S, Hosseini SM, Parvizi B, Baghani S, Aghamollai V, et al. From a simple chronic headache to neurobrucellosis: a case report. *Med J Islam Repub Iran*. 2014;28:12.
- Vigeant P, Mendelson J, Miller MA. Human to human transmission of *Brucella melitensis*. *Can J Infect Dis*. 1995;6(3):153-5. doi: [10.1155/1995/909404](https://doi.org/10.1155/1995/909404).
- Najafi N, Ghassemian R, Davoody AR, Tayebi A. An unusual complication of a common endemic disease: clinical and laboratory aspects of patients with *Brucella* epididymo-orchitis in the north of Iran. *BMC Res Notes*. 2011;4:286. doi: [10.1186/1756-0500-4-286](https://doi.org/10.1186/1756-0500-4-286).
- Tuncel D, Uçmak H, Gokce M, Utku U. Neurobrucellosis. *Eur J Gen Med*. 2008;5(4):245-8.
- Uluğ M, Can-Uluğ N. Pulmonary involvement in brucellosis. *Can J Infect Dis Med Microbiol*. 2012;23(1):e13-5. doi: [10.1155/2012/164892](https://doi.org/10.1155/2012/164892).
- Karaali Z, Baysal B, Poturoglu S, Kendir M. Cutaneous manifestations in brucellosis. *Indian J Dermatol*. 2011;56(3):339-40. doi: [10.4103/0019-5154.82505](https://doi.org/10.4103/0019-5154.82505).
- Shoaei SD, Bidi N. Serologic evaluation of brucellosis in patients with psychiatric disorders. *Caspian J Intern Med*. 2012;3(4):557-8.
- Gatselis NK, Makaritsis KP, Gabranis I, Stefos A, Karanikas K, Dalekos GN. Unusual cardiovascular complications of

- brucellosis presenting in two men: two case reports and a review of the literature. *J Med Case Rep.* 2011;5:22. doi: [10.1186/1752-1947-5-22](https://doi.org/10.1186/1752-1947-5-22).
16. Arkun R, Mete BD. Musculoskeletal brucellosis. *Semin Musculoskelet Radiol.* 2011;15(5):470-9. doi: [10.1055/s-0031-1293493](https://doi.org/10.1055/s-0031-1293493).
 17. Aziz S, Al-Anazi AR, Al-Aska AI. A review of gastrointestinal manifestations of brucellosis. *Saudi J Gastroenterol.* 2005;11(1):20-7. doi: [10.4103/1319-3767.33333](https://doi.org/10.4103/1319-3767.33333).
 18. Tarfarosh SF, Manzoor M. Neurological manifestations of brucellosis in an Indian population. *Cureus.* 2016;8(7):e684. doi: [10.7759/cureus.684](https://doi.org/10.7759/cureus.684).
 19. Kanik-Yüksek S, Gülhan B, Ozkaya-Parlakay A, Tezer H. A case of childhood brucellosis with neurological involvement and epididymo-orchitis. *J Infect Dev Ctries.* 2014;8(12):1636-8. doi: [10.3855/jidc.4432](https://doi.org/10.3855/jidc.4432).
 20. Gür A, Geyik MF, Dikici B, Nas K, Cevik R, Sarac J, et al. Complications of brucellosis in different age groups: a study of 283 cases in southeastern Anatolia of Turkey. *Yonsei Med J.* 2003;44(1):33-44. doi: [10.3349/ymj.2003.44.1.33](https://doi.org/10.3349/ymj.2003.44.1.33).
 21. Karsen H, Akdeniz H, Karahocagil MK, Irmak H, Sünnetçioğlu M. Toxic-febrile neurobrucellosis, clinical findings and outcome of treatment of four cases based on our experience. *Scand J Infect Dis.* 2007;39(11-12):990-5. doi: [10.1080/00365540701466199](https://doi.org/10.1080/00365540701466199).
 22. Molins A, Montalbán J, Codina A. Parkinsonism in neurobrucellosis. *J Neurol Neurosurg Psychiatry.* 1987;50(12):1707-8. doi: [10.1136/jnnp.50.12.1707-a](https://doi.org/10.1136/jnnp.50.12.1707-a).
 23. Kochar DK, Kumawat BL, Agarwal N, Shubhakararan, Aseri S, Sharma BV, et al. Meningoencephalitis in brucellosis. *Neurol India.* 2000;48(2):170-3.
 24. Bouza E, García de la Torre M, Parras F, Guerrero A, Rodríguez-Créixems M, Gobernado J. Brucellar meningitis. *Rev Infect Dis.* 1987;9(4):810-22. doi: [10.1093/clinids/9.4.810](https://doi.org/10.1093/clinids/9.4.810).
 25. Shakir RA, Al-Din AS, Araj GF, Lulu AR, Mousa AR, Saadah MA. Clinical categories of neurobrucellosis. A report on 19 cases. *Brain.* 1987;110(Pt 1):213-23. doi: [10.1093/brain/110.1.213](https://doi.org/10.1093/brain/110.1.213).
 26. Pascual J, Combarros O, Polo JM, Berciano J. Localized CNS brucellosis: report of 7 cases. *Acta Neurol Scand.* 1988;78(4):282-9. doi: [10.1111/j.1600-0404.1988.tb03658.x](https://doi.org/10.1111/j.1600-0404.1988.tb03658.x).
 27. Di Bonaventura G, Angeletti S, Ianni A, Petitti T, Gherardi G. Microbiological laboratory diagnosis of human brucellosis: an overview. *Pathogens.* 2021;10(12):1623. doi: [10.3390/pathogens10121623](https://doi.org/10.3390/pathogens10121623).
 28. Mesner O, Riesenberger K, Biliar N, Borstein E, Bouhnik L, Peled N, et al. The many faces of human-to-human transmission of brucellosis: congenital infection and outbreak of nosocomial disease related to an unrecognized clinical case. *Clin Infect Dis.* 2007;45(12):e135-40. doi: [10.1086/523726](https://doi.org/10.1086/523726).
 29. Whatmore AM, Koylas MS, Muchowski J, Edwards-Smallbone J, Gopaul KK, Perrett LL. Extended multilocus sequence analysis to describe the global population structure of the genus *Brucella*: phylogeography and relationship to biovars. *Front Microbiol.* 2016;7:2049. doi: [10.3389/fmicb.2016.02049](https://doi.org/10.3389/fmicb.2016.02049).
 30. Golshani M, Buozari S. A review of brucellosis in Iran: epidemiology, risk factors, diagnosis, control, and prevention. *Iran Biomed J.* 2017;21(6):349-59. doi: [10.18869/acadpub.ijb.21.6.349](https://doi.org/10.18869/acadpub.ijb.21.6.349).
 31. Bucher A, Gaustad P, Pape E. Chronic neurobrucellosis due to *Brucella melitensis*. *Scand J Infect Dis.* 1990;22(2):223-6. doi: [10.3109/00365549009037906](https://doi.org/10.3109/00365549009037906).
 32. Franco MP, Mulder M, Gilman RH, Smits HL. Human brucellosis. *Lancet Infect Dis.* 2007;7(12):775-86. doi: [10.1016/s1473-3099\(07\)70286-4](https://doi.org/10.1016/s1473-3099(07)70286-4).
 33. Jiang W, Chen J, Li Q, Jiang L, Huang Y, Lan Y, et al. Epidemiological characteristics, clinical manifestations and laboratory findings in 850 patients with brucellosis in Heilongjiang province, China. *BMC Infect Dis.* 2019;19(1):439. doi: [10.1186/s12879-019-4081-5](https://doi.org/10.1186/s12879-019-4081-5).
 34. Long SS, Pickering LK, Prober CG. Principles and Practice of Pediatric Infectious Diseases. LWW; 2003.
 35. Akdeniz H, Irmak H, Anlar Ö, Demiröz AP. Central nervous system brucellosis: presentation, diagnosis and treatment. *J Infect.* 1998;36(3):297-301. doi: [10.1016/s0163-4453\(98\)94279-7](https://doi.org/10.1016/s0163-4453(98)94279-7).
 36. Karsen H, Akdeniz H, Karahocagil MK, Irmak H, Sünnetçioğlu M. Toxic-febrile neurobrucellosis, clinical findings and outcome of treatment of four cases based on our experience. *Scand J Infect Dis.* 2007;39(11-12):990-5. doi: [10.1080/00365540701466199](https://doi.org/10.1080/00365540701466199).
 37. Turkoglu SA, Halicioğlu S, Sirmatel F, Yildiz M, Yildiz N, Yildiz S. Vasculitis and neurobrucellosis: evaluation of nine cases using radiologic findings. *Brain Behav.* 2018;8(4):e00947. doi: [10.1002/brb3.947](https://doi.org/10.1002/brb3.947).
 38. Alqwaifiy M, Al-Ajlan FS, Al-Hindi H, Al Semari A. Central nervous system brucellosis granuloma and white matter disease in immunocompromised patient. *Emerg Infect Dis.* 2017;23(6):978-81. doi: [10.3201/eid2306.161173](https://doi.org/10.3201/eid2306.161173).
 39. Hadda V, Khilnani G, Kedia S. Brucellosis presenting as pyrexia of unknown origin in an international traveller: a case report. *Cases J.* 2009;2:7969. doi: [10.4076/1757-1626-2-7969](https://doi.org/10.4076/1757-1626-2-7969).
 40. Sahin E, Yilmaz A, Ersöz G, Uğuz M, Kaya A. Multiple cranial nerve involvement caused by *Brucella melitensis*. *South Med J.* 2009;102(8):855-7. doi: [10.1097/SMJ.0b013e3181ac0628](https://doi.org/10.1097/SMJ.0b013e3181ac0628).
 41. Bingöl A, Togay-Işıkay C. Neurobrucellosis as an exceptional cause of transient ischemic attacks. *Eur J Neurol.* 2006;13(5):544-8. doi: [10.1111/j.1468-1331.2006.01286.x](https://doi.org/10.1111/j.1468-1331.2006.01286.x).
 42. Adaletli I, Albayram S, Gurses B, Ozer H, Yilmaz MH, Gulsen F, et al. Vasculopathic changes in the cerebral arterial system with neurobrucellosis. *AJNR Am J Neuroradiol.* 2006;27(2):384-6.
 43. Bashir R, Al-Kawi MZ, Harder EJ, Jenkins J. Nervous system brucellosis: diagnosis and treatment. *Neurology.* 1985;35(11):1576-81. doi: [10.1212/wnl.35.11.1576](https://doi.org/10.1212/wnl.35.11.1576).
 44. Gul HC, Erdem H, Bek S. Overview of neurobrucellosis: a pooled analysis of 187 cases. *Int J Infect Dis.* 2009;13(6):e339-43. doi: [10.1016/j.ijid.2009.02.015](https://doi.org/10.1016/j.ijid.2009.02.015).
 45. Pourhassan A. Clinical and laboratory findings in neurobrucellosis: a study of 43 cases. *Arch Clin Infect Dis.* 2007;2(2):71-6.