CASE REPORT / OLGU SUNUMU

DOI: 10.4274/mjima.galenos.2024.24246.22
Mediterr J Infect Microb Antimicrob 2024;13:24246.22
Erişim: http://dx.doi.org/10.4274/mjima.galenos.2024.24246.22

Neurobrucellosis Cauda Equina Syndrome: Rare of Rarity

Nörobruselloza Bağlı Kauda Ekuina Sendromu: Nadirin Nadiri

Hassan Mohammed Abdel RAHMAN[1,2]*, Omar Mohammed ALNASHIWATY[3], Abdallah Abdelkader ELSAYED[4], Rabab Mahmoud AHMED[5], Farouk Mostafa FARIS[6]

[1]Madinah Cardiac Center, Associate Consultant of Infectious Disease, Al Madinah, Kingdom of Saudi Arabia
[2]Kafr El-Sheikh Fever Hospital, Consultant of Infectious Disease, Kafr El-Sheikh, Egypt
[3]King Abdullah Medical City, Internal Medicine and Infectious Disease Consultant, Mecca, Kingdom of Saudi Arabia
[4]Madinah Cardiac Center, Department of Nephrology, Al Madinah, Kingdom of Saudi Arabia
[5]Cairo University, Kasralainy Faculty of Medicine, Department of Internal Medicine, Cairo, Egypt
[6]Cairo University, Kasralainy Faculty of Medicine, Department of Critical Care, Cairo, Egypt

Abstract

We have reported here a case of a 68-year-old female patient with hypertension and a history of spinal fixation 4 years ago. She was admitted to the intensive care unit for sepsis. She presented with lower back pain, sciatica in her left lower limb, saddle hypoesthesia, urine incontinence, and an inability to walk or stand. Three days before her admission, she had developed a fever. A review of her medical history revealed repeated consumption of unpasteurized milk and cheese. Blood culture tested positive for *Brucella* infection, which was supported by the results of the positive Rose Bengal test and tube agglutination test. The spine magnetic resonance imaging revealed an abnormal enhancement of the cauda equina. The patient received treatment with gentamicin, rifampicin, and doxycycline for 6 months, which yielded an excellent response. After 6 months, laboratory data and radiological findings normalized and neurological signs resolved completely.
Keywords: Neurobrucellosis, cauda equina syndrome, fever

Öz

Dört yıl önce omurga fiksasyonu ve hipertansiyon öyküsü olan 68 yaşında bir kadın hasta bildirilmiştir. Hasta sepsis nedeniyle yoğun bakıma yatırıldı. Bel ağrısı, sol alt ekstremitede siyatik tarzı ağrı, eyer terzi hipoestezisi, idrar tutamama ve yürüyememe-ayakta duramama şikayetleriyle başvurdu. Yatmadan üç gün önce ateşinin çıktığı öğrenildi. Mevcut hastalığın geçmişini incelerken, hastanın tekrarlayıcı olarak pastörize edilmemiş süt ve peynir tükettiği öğrenildi. Pozitif Rose Bengal testi ve tüp aglütinasyon testi ile desteklenen kan kültürü sonuçları *Brucella* tanısını doğruladı. Spinal manyetik rezonans görüntülemede kauda ekuinada anormal kontrast tutulumu saptandı. Hastaya altı ay boyunca gentamisin, rifampisin ve doksisiklin tedavisi uygulandı ve mükemmel bir yanıt alındı. Altı ay sonra laboratuvar verileri ve radyolojik bulgular normale döndü ve nörolojik belirtiler tamamen düzeldi.
Anahtar Kelimeler: Nörobruselloz, kauda ekuina sendromu, ateş

Cite this article as: Rahman HMA, Alnashiwaty OM, Elsayed AA, Ahmed RM, Faris FM. Neurobrucellosis Cauda Equina Syndrome: Rare of Rarity. Mediterr J Infect Microb Antimicrob. 2024;13:24246.22

Address for Correspondence/Yazışma Adresi: Hassan Mohammed Abdel RAHMAN MD, Madinah Cardiac Center, Associate Consultant of Infectious Disease, Al Madinah, Kingdom of Saudi Arabia
E-mail: dr.gobara22@gmail.com **ORCID ID:** orcid.org/0000-0002-7002-2550
Received/Geliş Tarihi: 19.07.2024 **Accepted/Kabul Tarihi:** 18.11.2024

Epub: 19.11.2024
Published: 26.12.2024

Introduction

Brucellosis (also known as "undulant fever", "Mediterranean fever", or "Malta fever") is the most common zoonosis worldwide and is considered an important public health concern in several resource-limited settings; it is transmitted to humans from infected animals (such as cattle, sheep, goats, camels, and pigs) via ingestion of food products (such as unpasteurized dairy products) or by coming in contact with infected tissues or fluids. It can also occur by inhalation of infected aerosolized particles. Accordingly, the microbiology laboratory is notified if *brucellosis* is suspected considering that the organism is a biohazard to laboratory personnel[1-3].

This disease affects approximately 500,000 cases worldwide annually[4]. The prevalence is in progression because of growing international tourism, trade, and migration[5,6].

The usual neurological symptoms resulting from the involvement of both the central nervous system (CNS) and the peripheral nervous system occur due to a direct impact on the nervous system or indirectly due to toxic-febrile neurobrucellosis. These symptoms are reported in 3-12% of all brucellosis cases in most large-scale series[7-9].

Cauda equina syndrome-which is characterized by lower back pain, sciatica, saddle hypoesthesia, lower extremity motor weakness, and bowel or bladder dysfunction-can be a rare and atypical manifestation of neurobrucellosis[10,11].

The incidence or prevalence of cauda equina syndrome associated with brucellosis has only been published in a few case reports[12,13]. Despite the challenging diagnosis of cauda equina syndrome with brucellosis, successful antibiotic treatment has been reported to achieve stable neurological conditions, often without needing surgical intervention.

Case Presentation

The present case was a 68-year-old, Saudi, hypertensive female, who arrived at the emergency department. She fulfilled the sepsis criteria. Her medical history revealed back pain, anorexia, fatigue, nausea, and limited mobility due to sciatica and left leg pain in the past 3 months. Three days prior, she developed intermittent fever, night sweats, and urine incontinence. The patient reported frequent consumption of unpasteurized milk and raw cheese. Four years earlier, she had undergone bilateral knee arthroplasty, laminectomy for lumbar disc prolapse, and decompression and fixation of L4-S1.

Further examination revealed that the patient appeared irritable and depressed, morbidly obese (weight=103 kg, height 158 cm, body mass index=41.3 kg/m^2), Glasgow Coma Scale=15. The patient could not stand up without assistance and could not walk easily due to severe pain, primarily in her left lower limb. Her vital signs included a temperature of 38.3 °C, pulse of 117 beats/min, blood pressure of 100/52 mmHg, and a respiratory rate of 26 breaths/min. Oxygen saturation was 92% on room air. Local tenderness over the lumbar and sacral vertebrae was noted, with no signs of meningeal irritation. Although the neurological examination was challenging, muscle tone and strength remained intact, along with preserved reflexes.

Examination of the surgical site indicated no signs of cellulitis, purulent discharge, redness, or warmth.

Laboratory results revealed white blood cell count: 13.2x10^3/mm, hemoglobin: 11.6 g/dL, platelet count: 354x10^3/mm, erythrocyte sedimentation rate (ESR): 90 mm/h, C-reactive protein (CRP): 89.5 mg/L, alanine transaminase: 20 U/I, aspartate transaminase: 27 U/I, alkaline phosphatase: 88 U/I, gamma glutamic transferase: 102 U/I, total bilirubin: 0.89 mg/dL, direct bilirubin: 0.27 mg/dL, albumin: 2.86 g/L, total protein: 75 g/L, creatinine: 2.73 mg/dL; urea: 95 mg/dL, lactate: 5.4 mmol/L, Na: 139 mEq/L, K: 4.5 mEq/L.

The arterial blood gas analysis revealed a PaO_2 of 61 mmHg, a $PaCO_2$ of 49 mmHg, a pH of 7.3, and an HCO_3^- level of 17 mEq/L. The Acute Physiology and Chronic Health Evaluation II (APACHE II) score on admission was 16 points. The Sequential Organ Failure Assessment (SOFA) score on admission was 5 points, with an estimated mortality of ≤33%.

After the patient was admitted, dehydration and electrolyte imbalances were corrected, appropriate hydration was provided, and kidney function recovered.

Brucella testing in the serum was found to be positive by 2 tests (Rose Bengal test and Tube Agglutination Test); the titer was 1/640 as per protocols. The requested spine magnetic resonance imaging (MRI) was not performed because the patient was not cooperative, morbidly obese, and sick; initially, the clinical situation was unclear, the impression and provisional diagnosis was brucella spondylodiscitis, especially positive results of brucella serology, epidemiological history, and clinical presentation s/p lumbosacral decompression fixation 4 years ago. Two sets of blood cultures were drawn as a part of septic work that later came positive for *Brucella*. Other serological tests (such as hepatitis B surface antigen, hepatitis C virus antibodies, human immunodeficiency virus, rheumatoid factor, anti-cyclic citrullinated peptide, antinuclear antibodies, and QuantiFERON) were negative, and urine examination was unremarkable.

Accordingly, the patient received a triple regimen of doxycycline 100 mg twice daily, rifampicin 600 mg orally daily, and gentamycin 5 mg/kg intravenously once daily for 10 days, with proper monitoring to doses with trough and peak levels strictly to achieve clearance of bacteremia. The patient responded

dramatically, and her fever subsided. She regained the ability to stand with support and began walking; a lumbosacral MRI conducted 10 days later revealed the following: the patient had undergone posterior laminectomy with internal fixation at L4, L5, and S1 levels, mild retrolisthesis of L3 over L4 (grade I), with subsequent mild thecal sac compression, and bilateral neural foraminal narrowing. At the L3-4 level, a central disk herniation extending into the superior vertebral endplate of L4 was noted; it formed a small Schmorl node. Subtle abnormal contrast enhancement of the cauda equina nerve roots was noted, with tethering at the L4 level (Figure 1). Spondylodiscitis and mass effect were ruled out.

Additional imaging of the pelvis, left hip, and knee showed no significant abnormalities. The patient declined lumbar puncture. However, based on her clinical presentation, history of *Brucella* endemicity in Saudi Arabia, frequent consumption of raw milk and cheese, positive blood cultures and serology tests, and, finally, lumbosacral MRI, the final diagnosis was neurobrucellosis complicated by bacteremia.

Echocardiography did not reveal any signs suggestive of endocarditis, and a systemic workup eliminated other focal brucellosis.

After completing a 10-day course of gentamicin, the patient was discharged to the ward. The treatment plan included continuing with doxycycline and rifampicin for 6 months. The plan was to continue on the same regimen as the patient showed marked improvement clinically and her bacteremia was cleared. However, 2 months later, rifampicin was replaced with ciprofloxacin (500 mg orally every 12 h) due to elevated liver enzymes. The patient showed clinical improvement and could walk unsupported. After 6 months, all neurological signs improved, laboratory data and radiological findings resolved, and clinical signs completely resolved. The ESR decreased to 30 mm/h, CRP decreased to 0.314 mg/L, and the brucella titer became negative. Repeated imaging revealed no evidence of infection or loosening of fixation screws, with no paraspinal soft tissue collection.

We obtained written informed consent from the patient's first-degree relatives, which included consent for publication. The patient understands that efforts will be made to conceal her identity.

Discussion

Brucellosis is a zoonotic disease that primarily affects animals and secondarily affects humans[14]. Occupational risks contribute to a higher incidence in men than in women[15,16]. In cases of neurobrucellosis, bacterial invasion of the CNS leads to an inflammatory disorder, characterized by the production of pro-inflammatory cytokines and increased matrix metalloproteinases (MMP)[17]. This inflammatory response also triggers the production of mitogen-activated protein kinases, specifically MMP-9[18,19].

In the present case, the primary challenge stemmed from the atypical presentation (neurobrucellosis in the form of cauda

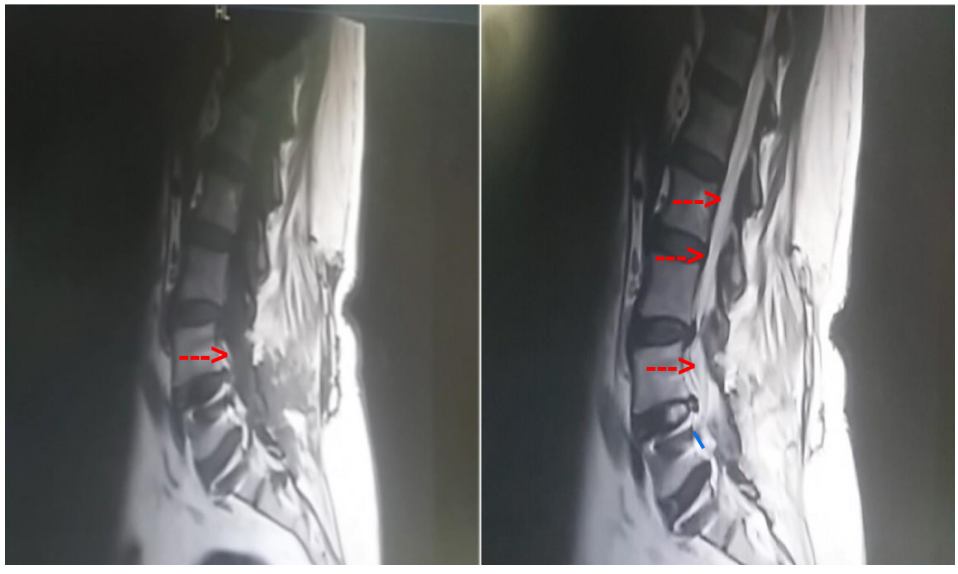

Figure 1. MRI lumbosacral spine. The patient had undergone posterior laminectomy with internal fixation at L4, L5, and S1 levels, mild retrolisthesis of L3 over L4 (grade I), with subsequent mild thecal sac compression, and bilateral neural foraminal narrowing. At the L3-4 level, a central disk herniation extending into the superior vertebral endplate of L4 was noted; it formed a small Schmorl node. Subtle abnormal contrast enhancement of the cauda equina nerve roots was noted, with tethering at the L4 level

MRI: Magnetic resonance imaging

equina syndrome without concurrent spondylodiscitis nor cerebral affection), complicated by signs of sepsis and difficulties in obtaining a comprehensive medical history. Despite the presence of additional comorbidities such as obstructive sleep apnea and acute kidney injury, thorough investigations ruled out surgical site infection and disseminated infection. The patient responded favorably to appropriate antibiotic therapy and supportive measures in the intensive care unit, thereby obviating the need for surgical intervention.

No consensus could be reached regarding the optimal antibiotic therapy and treatment duration for neurobrucellosis. However, early intensive therapy is recommended to prevent severe complications. Also, surgical intervention should be considered in cases of persistent or progressive neurological deficits resulting from nerve root or spinal cord compression[20].

Cauda equina syndrome is an exceptionally rare manifestation of spinal brucellosis, as characterized by challenging early diagnosis due to non-specific presentation of symptoms[20]. However, the literature review revealed a few neurobrucellosis cases that could be presented with cauda equina syndrome.

Menon et al.[21] reported a 57-year-old man with a year-long severe backache and bladder symptoms showing hypotonia, weakness, and absent reflexes in lower limbs. The patient's MRI indicated cauda enhancement and exudates in the conus-epiconus area. Positive cerebrospinal fluid (CSF) led to treatment with ceftriaxone, rifampicin, doxycycline, and dexamethasone, resulting in significant improvement.

Another case described by Menon et al.[21] was of a 27-year-old man with walking difficulties, bladder symptoms, and hearing loss who had spasticity, pyramidal weakness, and sensory loss up to D10. Absent plantar and abdominal reflexes with bilateral sensorineural hearing loss were noted. His MRI showed diffuse nerve root enhancement. Positive *Brucella* immunoglobulin G was detected in the serum and CSF. Treatment with antibiotics and steroids improved his condition.

The third case presented by Mahdavi et al.[22] reported a 29-year-old man with lower back pain and limb weakness for 50 days who underwent plasma exchange for suspected myelitis, albeit without improvement. Neurobrucellosis was suspected due to dairy exposure. Positive 2ME, Wright, and Coombs Wright test in the serum and CSF confirmed the diagnosis. MRI revealed cauda equina and nerve root enhancement. Electromyography suggested acute anterior horn cell disease or polyradiculopathy. Treatment included ceftriaxone, ciprofloxacin, and doxycycline. The patient was discharged with a continuation of injectable ceftriaxone, oral ciprofloxacin, and doxycycline. Improvement was observed after 1 month of the treatment.

Another interesting case was described by Yazdi et al.[23] of a 61-year-old woman with severe paraparesis and ataxia, who was diagnosed with brucellosis after presenting with fever, chills, fatigue, back pain, and limb weakness. Despite initial treatment with rifampin and doxycycline, her neurological symptoms worsened. Methylprednisolone offered temporary relief, but the symptoms relapsed. Further tests confirmed brucellosis. Brain MRI demonstrated abnormal hyperintense lesions involving bilateral superior cerebellar peduncles and intramedullary hyperintense lesions throughout the cervical and thoracic cord. Radicular enhancement was also detected in the cauda equina. Extended treatment with ceftriaxone, rifampin, doxycycline, ciprofloxacin, and prednisolone led to full recovery without any neurological damage.

Moreover, Afshar et al.[24] reported the case of a 55-year-old female with lower back pain, paraparesis, and urinary retention suggesting leukocytosis, elevated ESR, and CRP, but negative *Brucella* result. MRI revealed L4-L5 vertebral inflammation and epidural abscesses. Following laminectomy and foraminotomy, *Brucella* was cultured from the abscess. A 3-month antibiotic course with doxycycline and rifampicin resulted in a favorable outcome.

Conclusion

In the context of neurobrucellosis, cauda equina syndrome is an exceptionally rare presentation. However, when identified promptly and managed optimally, medical treatment can effectively address this condition, particularly in the absence of neurological deficits. By emphasizing early recognition and implementing appropriate therapeutic strategies, clinicians can mitigate the risk of serious complications and any unnecessary surgical interventions.

Ethics

Informed Consent: We obtained written informed consent from the patient's first-degree relatives, which included consent for publication.

Footnotes

Authorship Contributions

Surgical and Medical Practices: H.M.A.R., O.M.A., A.A.E., F.M.F., Concept: H.M.A.R., O.M.A., R.M.A., Design H.M.A.R., R.M.A., F.M.F., Data Collection or Processing: H.M.A.R., R.M.A., F.M.F., Analysis or Interpretation: H.M.A.R., O.M.A., A.A.E., Literature Search: A.A.E., R.M.A., F.M.F., Writing: H.M.A.R., R.M.A., F.M.F.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Pappas G, Akritidis N, Bosilkovski M, Tsianos E. Brucellosis. N Engl J Med. 2005;352:2325-36.
2. World Health Organization. Brucellosis in humans and animals. Geneva: World Health Organization. 2006.
3. Centers for Disease Control and Prevention (CDC). Brucellosis reference guide [Internet]. Available from: https://www.cdc.gov/brucellosis/pdf/brucellosi-reference-guide.pdf
4. Greenfield RA, Drevets DA, Machado LJ, Voskuhl GW, Cornea P, Bronze MS. Bacterial pathogens as biological weapons and agents of bioterrorism. Am J Med Sci. 2002;323:299-315.
5. Pappas G, Panagopoulou P, Christou L, Akritidis N. *Brucella* as a biological weapon. Cell Mol Life Sci. 2006;63:2229-36.
6. Bosilkovski M, Dimzova M, Grozdanovski K. Natural history of brucellosis in an endemic region in different time periods. Acta Clin Croat. 2009;48:41-6.
7. Yuksek SK, Gulhan B, Parlakay AO, Tezer H. A case of childhood Brucellosis with neurological involvement and epididymo-orchitis. J Infect Dev Ctries. 2014;8:1636-8.
8. Tajdini M, Akbarloo S, Hosseini SM, Parvizi B, Baghani S, Aghamollaii V, Tafakhori A. From a simple chronic headache to neurobrucellosis: A case report. Med J Islam Repub Iran. 2014;28:12.
9. Elzein FE, Mursi M. *Brucella* induced Guillain-Barré syndrome. Am J Trop Med Hyg. 2014;91:1179-80.
10. Pappas G, Papadimitriou P, Akritidis N, Christou L, Tsianos EV. The new global map of human brucellosis. Lancet Infect Dis. 2006;6:91-9.
11. Atluri VL, Xavier MN, de Jong MF, den Hartigh AB, Tsolis RM. Interactions of the human pathogenic *Brucella* species with their hosts. Annu Rev Microbiol. 2011;65:523-41.
12. Kaya O, Avşar K, Akçam FZ. Unusual manifestations of brucellosis. Arch Med Sci. 2011;7:173-5.
13. Jayakumar RV, Al-Aska AK, Subesinghe N, Wright SG. Unusual presentation of culture positive brucellosis. Postgrad Med J. 1988;64:118-20.
14. Al-Sous MW, Bohlega S, Al-Kawi MZ, Alwatban J, McLean DR. Neurobrucellosis: clinical and neuroimaging correlation. AJNR Am J Neuroradiol. 2004;25:395-401.
15. Ceran N, Turkoglu R, Erdem I, Inan A, Engin D, Tireli H, Goktas P. Neurobrucellosis: clinical, diagnostic, therapeutic features and outcome. Unusual clinical presentations in an endemic region. Braz J Infect Dis. 2011;15:52-9.
16. Raptopoulou A, Karantanas AH, Poumboulidis K, Grollios G, Raptopoulou-Gigi M, Garyfallos A. Brucellar spondylodiscitis: non-contiguous multifocal involvement of the cervical, thoracic, and lumbar spine. Clin Imag. 2006;30:214-7.
17. Baldi PC , Giambartolomei GH. Immunopathology of *Brucella* infection. Recent Pat Antiinfect Drug Discov. 2013;8:18-26.
18. Miraglia MC, Scian R, Samartino CG, Barrionuevo P, Rodriguez AM, Ibañez AE, Coria LM, Velásquez LN, Baldi PC, Cassataro J, Delpino MV, Giambartolomei GH. *Brucella abortus* induces TNF-α-dependent astroglial MMP-9 secretion through mitogen-activated protein kinases. J Neuroinflammation. 2013;10:47.
19. García Samartino C, Delpino MV, Pott Godoy C, Di Genaro MS, Pasquevich KA, Zwerdling A, Barrionuevo P, Mathieu P, Cassataro J, Pitossi F, Giambartolomei GH. *Brucella abortus* induces the secretion of pro-inflammatory mediators from glial cells leading to astrocyte apoptosis. Am J Pathol. 2010;176:1323-38.
20. Bahemuka M, Shemena AR, Panayiotopoulos CP, al-Aska AK, Obeid T, Daif AK. Neurological syndromes of brucellosis. J Neurol Neurosurg Psychiatry. 1988;51:1017-21.
21. Menon D, Varghese N, Nagarathna S, Saini J, Netravathi M. An unusual cause for cauda equina and spastic paraparesis: two cases of brucellar arachnoiditis without spondylodiscitis or constitutional symptoms. Ann Indian Acad Neurol. 2022;25:1241-3.
22. Mahdavi FS, Abbasi Khoshsirat N, Madanipour A. Lumbosacral polyradiculitis associated with brucellosis. IDCases. 2020;23:01028.
23. Yazdi NA, Moosavi NS, Alesaeidi S, Salahshour F, Ghaemi O. Diffuse neurobrucellosis of cerebellum, brainstem, spinal cord, and cauda equina: a case report and literature review. J Radiol Case Rep. 2022;16:1-9.
24. Afshar E, Moniri R, Saeed B. Cauda equnia syndrome due to *Brucella* spondylodiscitis and epidural abscess formation: A case report. Interdiscip Neurosurg. 2019;17:42-4.