



Case report

Brucella infection presenting as infective endocarditis complicated by embolic stroke

Abdalla Fadul^{a,*}, Mohamed H. Fadul^b, Gokhan Demir^a, Mohamad Safieh^a, Ahamed Lebbe^c, Fatema Falamrz^c, Abdelaziz Mohamed^a, Nabel Hamad^d, Raza A. Akbar^a

^a Internal Medicine, Hamad Medical Corporation, Doha, Qatar

^b Faculty of Medicine, University of Khartoum, Khartoum, Sudan

^c Weill Cornell Medicine, Doha, Qatar

^d Heart Hospital, Hamad Medical Corporation, Doha, Qatar

ARTICLE INFO

Keywords:

Brucellosis
Infective endocarditis
Stroke
Cerebral infarct
Infectious diseases

ABSTRACT

Brucellosis (undulant fever) is a zoonotic infection caused by *Brucella* species. It typically presents with fever, malaise, night sweats, and arthralgia. One of its rare complications is infective endocarditis, which occurs in approximately 1.3% of patients and can be further complicated by embolic stroke. This report describes a rare occurrence of *Brucella* endocarditis presenting as an embolic stroke. A 34-year-old male presented with sudden left-sided weakness and fever. He reported headaches, fever, and generalized weakness in the preceding week. The patient worked on a farm and hence had animal contact. A neurological exam showed left-sided facial weakness, and power of 0/5 and 1/5 in the left upper and lower extremities, respectively. CT scan of the head revealed a right middle cerebral artery (MCA) territory infarct with penumbra and a right MCA occlusion. He underwent a cerebral artery thrombectomy with successful recanalization. However, he continued to have fever and high inflammatory markers. Echocardiography showed aortic valve vegetation and blood cultures grew *Brucella melitensis*. A multidisciplinary meeting was held to determine the optimal management, which included a course of rifampicin and doxycycline.

Introduction

Brucellosis, also known as undulant fever or Mediterranean fever, is a zoonotic infection caused by one of the four Gram-negative *Brucella* species [1]. It is transmitted from infected animals such as goats and sheep, either by ingestion of animal products such as milk or by contact with infected tissues and fluids [2]. Globally, approximately 500,000 cases are reported annually [3]. Once taken up by tissue phagocytes, *Brucella* disseminates systemically to infect the reticuloendothelial system and potentially other tissues [4].

Brucellosis typically presents with a spiking fever, malaise, night sweats, and arthralgia [5]. Complications from brucellosis occur in approximately 30% of infected individuals and may involve any system, including osteoarticular, genitourinary, cardiac, and others [5,6]. One of the rare complications of *Brucella* infection is endocarditis, affecting approximately 1.3% of individuals [7]. This case report describes a rare

occurrence of *Brucella* endocarditis presenting as an embolic stroke.

Case presentation

A 34-year-old man presented to the emergency department (ED) with sudden onset left-sided weakness. He awakened that morning with a headache and subjective fever. He subsequently developed weakness approximately seven hours later when he was unable to ambulate to the bathroom. He denied any visual changes, seizures, dizziness, chest pain, or shortness of breath.

One week before the onset of his symptoms, he experienced episodes of headache, subjective fever, and generalized weakness for which he did not seek medical attention. He denied recent sick contacts, nor did he report any recent travel abroad. He worked as a laborer on a farm and had some contact with animals, including sheep and camels. The patient had a 16-pack-year smoking history but had not consumed alcohol. He

Abbreviations: CT scan, Computerized Tomography Scan; ED, Emergency department; GCS, Glasgow coma scale; MCA, Middle cerebral artery; MRI, Magnetic resonance imaging; MRC, Medical Research Council.

* Correspondence to: Department of Internal Medicine, Hamad General Hospital, Hamad Medical Corporation Hamad, Hospital Street, Doha, Qatar.

E-mail address: afadul2@hamad.qa (A. Fadul).

<https://doi.org/10.1016/j.idcr.2024.e01937>

Received 16 September 2023; Received in revised form 3 March 2024; Accepted 1 April 2024

Available online 2 April 2024

2214-2509/© 2024 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

did not have any significant past medical or surgical history.

On physical examination, the patient was febrile with a temperature of 39.2 degrees Celsius. Other vital signs were stable. The patient was conscious, alert, and oriented, with a Glasgow coma score (GCS) of 15/15. Cardiovascular examination revealed a systolic murmur in the left 4th intercostal space, accompanied by a diastolic rumble. A neurological exam showed left-sided facial weakness of an upper motor neuron pattern. He also had a significantly decreased motor strength of 0/5 in his left upper extremity and 1/5 in the left lower extremity on the MRC muscle power scale.

The patient underwent computed tomography (CT) imaging of his brain, which revealed an acute right MCA territory infarct with penumbra and right MCA occlusion. Cerebral artery thrombectomy was performed and resulted in successful recanalization achieving grade 2b perfusion on Thrombolysis In Cerebral Infarction (TICI) scale.

However, the patient remained febrile and his inflammatory markers were elevated with a CRP level of 79 mg/dl. Routine stroke work-up included electrocardiography (ECG) and echocardiography. ECG showed sinus tachycardia and no other abnormal findings. Transthoracic echocardiogram showed a 21×5 mm mobile aortic valve vegetation with moderate aortic regurgitation with normal left ventricular ejection fraction (Fig. 1). Blood cultures grew *Brucella melitensis* and *B.abortus* and his serum antibody titers were high at 1:640. Lab results showed an elevated CRP level of 79 mg/dl, with normal WBC count, procalcitonin, and serum creatinine.

Considering these new findings, the patient was admitted with a diagnosis of *Brucella* endocarditis complicated by new aortic valve regurgitation and septic embolic stroke. He was started on an antibiotic regimen of ceftriaxone (planned for 6 weeks), gentamicin (for 4 weeks), and doxycycline and rifampicin (planned for 12 weeks). Cardiothoracic surgery was also consulted, and they initially recommended metallic aortic valve replacement after 4–6 weeks of antibiotic treatment.

During the hospital stay, the patient became drowsy and had an acute change in mental status. An emergent brain CT scan demonstrated findings suggestive of hemorrhagic transformation of the infarct. The neurosurgical team did not recommend any urgent neurosurgical intervention. Two days later, the patient again had mental status alteration, and a brain magnetic resonance imaging (MRI) confirmed multiple new acute infarcts involving the right basal ganglia and adjacent right frontal deep white matter (see Fig. 2).

The patient is currently bedridden with aphasia and poor comprehension, receiving supportive physical therapy. A multidisciplinary discussion was held to determine the best management plan for him. Because of his current neurologic status and because of the risk of further intracranial hemorrhage with valve replacement surgery, the cardiothoracic surgery team determined that non-surgical management would be in the best interest of the patient. The plan was discussed with

the co-patients including the patient's brother, and after consulting the infectious diseases team, the patient was continued on an extended course of rifampin and doxycycline for at least six months with follow-up serial echocardiography and monitoring of laboratory and clinical parameters. A few weeks later, a follow-up echocardiogram reported a vegetation size of 14×8 mm and severe aortic valve regurgitation.

Discussion

Brucellosis is endemic in South and Central Asia, the Middle East, sub-Saharan Africa, part of Central and South America, and the Mediterranean. It is relatively uncommon in the developed world. The main routes of transmission to humans include consumption of unpasteurized milk or infected animal products and inhalation of aerosolized infected particles. Skin and mucous membrane contact with infected animal material can also lead to transmission [2]. Human brucellosis is predominantly caused by the three species: *Brucella melitensis*, *B. abortus*, and *B. suis*.

The usual cardinal symptoms of brucellosis include unexplained intermittent chronic fever, malaise, lethargy, night sweats, and arthralgia. Cardiac involvement in brucellosis is rare but may be fatal. Infective endocarditis, the most common cardiac complication, is only found in 0.3–2% of the cases [7–9]. Nevertheless, it accounts for approximately 80% of the mortality in brucellosis [2]. About 75% of patients with *Brucella* endocarditis have aortic valve involvement, especially in people with pre-existing valvular damage [10,11]. Acute embolic stroke complicating *Brucella* endocarditis, as in our case, is even rarer. A similar case of a 35-year-old man presenting with acute neurological symptoms due to systemic emboli from *Brucella* endocarditis was reported in 2017 [12].

Brucella can represent a diagnostic challenge because of its protean manifestations. Serologic testing and culture of blood and body fluids are essential, with blood culture being the gold standard. Echocardiography is crucial to evaluate for cardiac involvement with infective endocarditis, valvular destruction, aneurysm or abscess formation, or heart failure [13].

Our patient's presentation involved a sudden onset of left-sided weakness and fever, prompting a thorough neurological examination and imaging studies. Identification of a right MCA territory infarct with penumbra has reinforced the need for prompt investigation for the cause, considering the patient's young age and absence of other risk factors. For this reason, endocarditis should be considered in patients with stroke and a clinical history suggestive of systemic infection to establish an early diagnosis and appropriate medical or surgical management [14,15].

While the occurrence of *Brucella* endocarditis complicated by embolic stroke is fairly uncommon, it is undoubtedly true that initiation

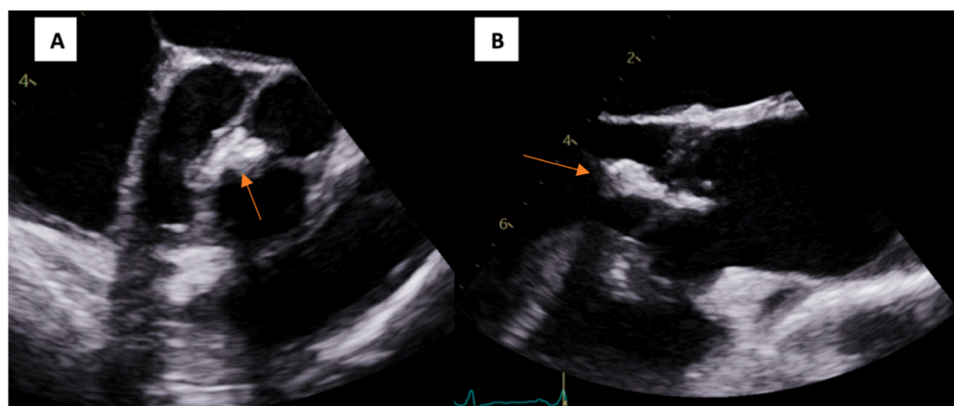


Fig. 1. Trans-esophageal echocardiogram showing a large, protruding, mobile vegetation attached to the aortic valve measuring 21×5 mm (arrows). A short-axis view (A) and a three-chamber view (B) of the aortic valve are shown.

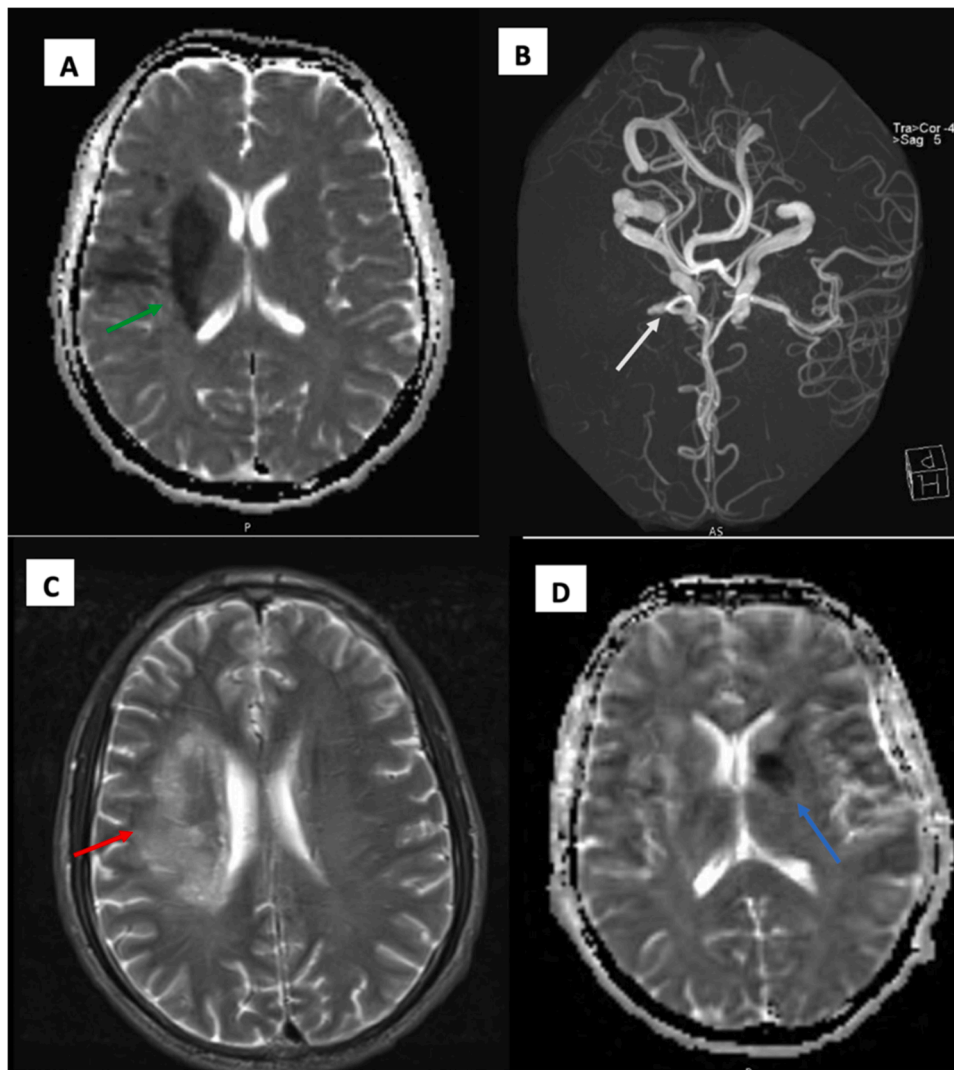


Fig. 2. MRI/MRA head showing diffusion restricting acute infarction involving the right basal ganglia and adjacent right frontal deep white matter (A). MRA shows an occluded right middle cerebral artery immediately after its origin (B). Two weeks later T2 enhanced MRI showing subacute/chronic right MCA territory infarction (C) with a new left-sided basal ganglial infarction shown on MRI Diffusion-weighted image (D).

of antibiotic therapy is vital for preventing stroke in endocarditis patients. Nevertheless, embolization is most likely to occur within the first days after antibiotic initiation [16]. Furthermore, patients with infective endocarditis treated with antiplatelet therapy do not show a reduction in embolization risk [17]. Conversely, antiplatelets would be contraindicated in the setting of a recent ischemic stroke since they increase the risk of mycotic aneurysm-induced fresh hemorrhage and hemorrhagic transformation of infarcts [17].

Few studies have suggested that native or prosthetic valve IE can be successfully treated with antibiotics alone. In this case, doxycycline and aminoglycosides were combined with rifampin. The recommended antibiotic regimen consists of doxycycline and rifampin for at least 12 weeks and an aminoglycoside (streptomycin or gentamicin) for the first month. If the patient undergoes valve replacement or repair surgery, a six-week course of triple antibiotics should be given preoperatively in addition to at least 1–3 months postoperatively [18]. Since the patient was not a candidate for surgery, he was continued on antibiotics and monitored with serial follow-up investigations as described above.

Conclusion

Brucellosis is a zoonotic infection with protean manifestations, and,

therefore, requires a high index of suspicion, especially in patients presenting with stroke and fever of unknown origin who have a known history of exposure to animals. Brucella endocarditis is a rare complication of Brucella infection and has a high mortality rate. This case report highlights the importance of early consideration of Brucella infection in the differential diagnosis in a patient with compatible clinical symptoms and epidemiological risk factors. Early diagnosis and treatment may prevent complications such as endocarditis and subsequent stroke. A multidisciplinary team approach is essential to optimally manage such patients due to the multisystem involvement and potential complications of this disease.

Ethical approval

This case report complies with the Declaration of Helsinki and has been approved by the Ethics Committee of Hamad Medical Corporation. This study protocol was reviewed and approved by the Medical Research Center in Hamad Medical Corporation, approval number (MRC-04-23-576).

Funding

Open access agreement is provided by Qatar National Library.

Consent

Written informed consent was obtained from the patient for the publication of this case report and any accompanying images.

CRedit authorship contribution statement

Ahamed Lebbe: Conceptualization, Data curation, Resources, Writing – original draft. **Mohamad Safieh:** Conceptualization, Data curation, Resources, Writing – original draft. **Gokhan Demir:** Conceptualization, Data curation, Resources, Writing – original draft, Visualization. **Mohamed H. Fadul:** Conceptualization, Data curation, Methodology, Writing – original draft, Visualization. **Abdalla Fadul:** Conceptualization, Data curation, Investigation, Methodology, Writing – original draft. **Raza A. Akbar:** Conceptualization, Project administration, Supervision, Writing – review & editing. **Nabiel Hamad:** Software, Writing – review & editing. **Abdelaziz Mohamed:** Data curation, Resources, Supervision, Writing – review & editing. **Fatema Falamrz:** Conceptualization, Data curation, Resources, Writing – original draft, Visualization.

Declaration of Competing Interest

The authors have no conflicts of interest to declare.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

- [1] Alton GG, Jones LM, Pietz DE. *Laboratory techniques in brucellosis*. Monograph series, 55. World Health Organization; 1975. p. 1–163.

- [2] Pappas G, Akritidis N, Bosilkovski M, Tsianos E. Brucellosis. *N Engl J Med* 2005; 352(22):2325–36. (<https://doi-org.wcmq.idm.oclc.org/10.1056/NEJMra050570>).
- [3] Centers for Disease Control (CDC) Brucellosis Reference Guide 2017. (<https://www.cdc.gov/brucellosis/pdf/brucellosis-reference-guide.pdf>) [Accessed on May 23, 2019].
- [4] Smith Laurie D, Ficht Thomas A. Pathogenesis of Brucella. *Crit Rev Microbiol* 1990; 17(3):209–30. <https://doi.org/10.3109/10408419009105726>.
- [5] Seleem MN, Boyle SM, Sriranganathan N. Brucellosis: a re-emerging zoonosis. *Vet Microbiol* 2010;140(3-4):392–8. (<https://doi-org.wcmq.idm.oclc.org/10.1016/j.vetmic.2009.06.021>).
- [6] Bosilkovski M, Krteva L, Dimzova M, Vidinic I, Sopova Z, Spasovska K. Human brucellosis in Macedonia - 10 years of clinical experience in endemic region. *Croat Med J* 2010;51(4):327–36. <https://doi-org.wcmq.idm.oclc.org/10.3325/cmj.2010.51.327>.
- [7] Narimisa N, Razavi S, Khoshbayan A, Masjedian Jazi F. Prevalence of *Brucella* endocarditis: a systematic review and meta-analysis. *Health Sci Rep* 2023;6(5): e1301. <https://doi.org/10.1002/hsr2.1301>.
- [8] Ferreira P, Gama P, Correia J, et al. *Brucella* endocarditis: case report and literature review. *Rev Port Cardiol* 2008;27:1309–15.
- [9] Lee SA, Kim KH, Shin HS, Lee HS, Choi HM, Kim HK. Successful medical treatment of prosthetic mitral valve endocarditis caused by *Brucella abortus*. *Korean Circ J* 2014;44:441–3. <https://doi.org/10.4070/kcj.2014.44.6.441>.
- [10] Reguera J, Alarcon A, Miralles F, Pachon J, Juarez C, Colmenero J. *Brucella* endocarditis: clinical, diagnostic, and therapeutic approach. *Eur J Clin Microbiol Infect Dis* 2003;22:647–50. <https://doi.org/10.1007/s10096-003-1026-z>.
- [11] O'Meara JB, Eykyn S, Jenkins BS, Braimbridge MV, Phillips I. *Brucella melitensis* endocarditis: successful treatment of an infected prosthetic mitral valve. *Thorax* 1974;29:377–81. <https://doi.org/10.1136/thx.29.3.377>.
- [12] Pendela SV, Agrawal N, Mathew T, Vidyasagar S, Kudravalli P. An uncommon presentation of *Brucella* endocarditis masquerading as neurobrucellosis. *OD10-OD11 J Clin Diagn Res JCDR* 2017;11(2). <https://doi.org/10.7860/JCDR/2017/22979.9273>.
- [13] Al Dahouk S, Nöckler K. Implications of laboratory diagnosis on brucellosis therapy. *Expert Rev Anti Infect Ther* 2011;9:833–45. <https://doi.org/10.1586/eri.11.55>.
- [14] Young EJ. An overview of human brucellosis. *Clin Infect Dis* 1995;21:283–9. quiz, 290.
- [15] Jacobs F, Abramowicz P, Vereerstraeten P, LeClerc JL, Zech F, Thys JP. *Brucella* endocarditis: the role of combined medical and surgical treatment. *Rev Infect Dis* 1990;12:740–4.
- [16] Vilacosta I, Graupner C, San Román JA, Sarriá C, Ronderos R, Fernández C, et al. Risk of embolization after institution of antibiotic therapy for infective endocarditis. *J Am Coll Cardiol* 2002;39(9):1489–95. [https://doi.org/10.1016/s0735-1097\(02\)01790-4](https://doi.org/10.1016/s0735-1097(02)01790-4).
- [17] Patel J, Patel I, Desai D, Desai S, Pandya H. Acute ischemic stroke as a presenting feature of brucellosis: a case report. *Ann Indian Acad Neurol* 2021;24(5):821.
- [18] Raza MA, Ejaz K, Kazmierski D. *Brucella* endocarditis of the native mitral valve treated with antibiotics. *Cureus* 2020;12:5.