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Subacute Brucellosis-Induced Guillain-Barré Syndrome: Case Report

MORADI-PORDANJANI et al. Brucellosis Induced Guillain-Barré

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Abstract
Guillain-Barré syndrome (GBS) represents the most frequent cause of acute flaccid paralysis, and in two-thirds of cases, antecedent infections have been identified. Brucellosis, a zoonotic disease, rarely leads to GBS. Herein we represented two cases of subacute brucellosis associated with GBS, diagnosed through their clinical course and electromyography (EMG) and nerve conduction velocity (NCV) studies. There was a 1-month and a 5-month interval between the onset of brucellosis and GBS, respectively. The presented cases recovered after undergoing plasma exchange and intravenous immune globulin (IVIG) in addition to antibiotic therapy. Physicians should consider brucellosis as a potential etiology of GBS and pay attention to the neurological symptoms of patients with brucellosis.
Keywords Brucellosis, Guillain-Barré syndrome, Electromyography, Neurobrucellosis

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Introduction

Guillain-Barré syndrome is an immune-mediated polyradiculoneuropathy and represents the most common cause of acute flaccid paralysis worldwide. It typically presents with ascending muscle weakness and diminished deep tendon reflexes following an infection (1). *Campylobacter jejuni*, *Mycoplasma pneumoniae*, and cytomegalovirus are commonly implicated in its pathogenesis. This condition develops due to cross-reactivity or molecular mimicry between microbial antigens and peripheral nerve structures, which initiates autoantibody production (2).

Brucellosis, a zoonotic disease caused by gram-negative intracellular cocco-bacilli bacteria known as Brucella, manifests with nonspecific symptoms such as undulating fever, asthenia, or musculoskeletal pain. Worldwide, the disease spreads mainly due to direct contact with sick animals or consuming unpasteurized dairy products. In the case of human infection, the following species are involved: *Brucella melitensis, B. abortus, B. suis, and B. canis* (3, 4).

Neurological involvement in approximately 5% of cases of brucellosis is in the form of meningovascular disease, cranial nerve palsies, and myelitis, among others (4-6). GBS remains an infrequent manifestation. We herein report two cases of subacute brucellosis-induced GBS with a focus on clinical course, challenges in diagnosis, and therapeutic outcome.

Case presentation

Case 1

A 64-year-old man presented with musculoskeletal pain, fever, night sweats, weakness, and a weight loss of 6 kg over the past month. Upon admission, vital signs were within normal ranges, with blood pressure at 135/90 mmHg, pulse rate at 83 per minute, respiratory rate at 19 per minute, and a temperature of 37.4°C. The patient reported close contact with animals and consumption of unpasteurized dairy products.

Serologic tests revealed a Wright titer of 1/640 and a 2ME titer of 1/320, confirming brucellosis. Treatment with doxycycline (100 mg twice daily), rifampin (300 mg twice daily), and intravenous gentamicin (300 mg daily) was initiated.

However, three days after admission, the patient developed additional symptoms, including paresthesia in the distal extremities, nausea, vomiting, bloating, and odynophagia. Severe constipation and urinary retention ensued. Muscle strength deteriorated, with lower limb strength reduced to 3/5 and upper limbs to 4/5. Unfortunately, despite precise consultations, the patient refused to consent to lumbar puncture (LP).

Electromyography (EMG) and nerve conduction velocity (NCV) conducted on the sixth day provided evidence of distal symmetric sensorimotor mixed-type peripheral polyneuropathy and acute inflammatory demyelinating polyneuropathy (AIDP). A diagnosis of Guillain-Barré Syndrome (GBS) was established, leading to the discontinuation of gentamicin due to known neurotoxicity. The patient was subsequently transferred to the neurology department and underwent ten plasmapheresis sessions and six rehabilitation sessions over a 20-day period.

Gradual improvement was observed, with full recovery of walking ability independently. However, musculoskeletal pain and chills, suggestive of brucellosis relapse, emerged post-recovery. Outpatient treatment with doxycycline (100 mg) and rifampin (300 mg) every 12 hours was resumed. The patient was discharged 28 days after admission with normal limb strength. Two months later, there were no signs or symptoms of brucellosis or GBS during a follow-up visit. However, the decision was made to continue treatment for the next four months to prevent the relapse of brucellosis.

Case 2

A 28-year-old male shepherd complained of progressive weakness, pain, paresthesia in both upper and lower limbs, bilateral foot drop, and diminished DTRs. Brucellosis had been diagnosed five months earlier, after which the patient received doxycycline and rifampin. However, he did not comply with his medications.

The analysis of cerebrospinal fluid (CSF) indicated a non-inflammatory pattern, characterized by a glucose level of 62 mg/dL, no detectable white blood cells (WBC), elevated protein at 127 mg/dL, lactate dehydrogenase (LDH) at 14, and red blood cells (RBC) at 20. EMG-NCV indicated acute motor-axonal polyneuropathy, a subtype of GBS associated with a worse prognosis.

He was treated with intravenous immunoglobulin 30 grams daily for five days. At discharge, outpatient physiotherapy was continued along with supportive care. At four weeks of follow-up, the only residual symptom was mild claudication (Table 1).

Table1: Summary of patient characteristics, clinical manifestations, and interventions.

Case	Sex/age	Signs and symptoms	Limb Strength	GBS Subtype	Lab data	Treatment
1	64-year-old male	Weakness, constipation, pricking, sensation, gastroparesis, urinary retention, dysphagia-diminished DTR	Lower=2/5 Upper=3/5	AIDP	WBC:16,200; Lymphocytes:67.8%; Uric acid:6.1; CRP:9; ESR:15	10 sessions of plasmapheresis
2	28-year-old male	Weakness, foot drop, diminished DTR	Lower: 3/5; Upper: 4/5	AMAN	WBC:5,200; Lymphocytes:58.3%; Uric acid:5.7; CRP:8; ESR:21	IVIG 30g/day for 5 days

AIDP: Acute inflammatory demyelinating polyneuropathy, AMAN: Acute motor axonal neuropathy, DTR: Deep tendon reflexes, WBC: white blood cell, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, IVIG: Intravenous immunoglobulin

Discussion

Brucellosis remains as a significant threat to both health and economies, particularly in developing countries. Delayed diagnosis and inadequate treatment may lead to chronic, persistent illness, accompanied by notable complications, including central nervous system(CNS) and cardiovascular involvement (7). Brucellosis presents with various neurological manifestations, such as meningoencephalitis, cranial nerve (CN) involvement, diffuse CNS involvement, and polyradiculoneuropathy, Additionally, in rare cases, it serves as the antecedent pathology for GBS (8).

For both cases described, blood and urine cultures and stool examinations were negative for other infections. Patients did not report respiratory or gastrointestinal symptoms upon admission. Although testing for *Campylobacter jejuni* or *Mycoplasma pneumoniae* (via PCR) would have provided more definitive evidence, such tests were unfortunately unavailable. Thus, evidence is circumstantial. Both cases were compatible with previous reports showing GBS occurring either concomitantly to or after brucellosis infection.

Alanazi et al, reported and reviewed 19 brucellosis induced GBS that mostly occurred in male patients. Reports show that the severity of this complication could even lead to death that implies its diagnosis and appropriate treatment important. Although in our presented case GBS was occurred in setting of subacute brucellosis, reports show that GBS could be the initial presentation of this infectious disease (3). *Varol* et al, reported a 5-year-old boy with GBS and Brucellosis. 2gr/kg of IVIG was ineffective and the treatment changed to plasmapheresis; after five sessions of plasmapheresis DTR and limbs strength returned to normal (9). Reported cases discussed different therapeutic approaches for dealing with this neurological complication, like IVIG administration and plasma exchange, which need more evidence to identify the efficacy of each one; Still, it should be noted that physicians should consider treating underlying infectious diseases besides other rehabilitation approaches (3, 4, 10).

Although comprehensive and complete information regarding the pathogenesis of GBS has not yet been obtained, in two-thirds of cases, there is an infectious disease before developing GBS, which is usually a respiratory infection or gastroenteritis (11). GBS, the most common cause of acute flaccid paralysis, occurs at any age and has different variants; some of which occur in the form of axonal involvement and some in the form of nerve demyelination. Also combination of both axonal damage and nerve demyelination may happen (12). Structural similarity of bacterium antigens causes an autoimmune reaction against nerve autoantigens. Molecular mimicry is a crucial mechanism through which infectious agents trigger an immune response, leading to GBS (13). In an animal study, the ganglioside-like molecules expressed on the outer membrane of *Brucella* stimulated autoantibodies against myelin gangliosides, causing acute paralysis and GBS signs (8). It is supposed that molecular mimicry between *brucella* and myelin gangliosides triggers a cross-reactive immunological response and leads to GBS (14).

Aygol et al. (2010) reported a 28-year-old man with brucellosis receiving streptomycin with doxycycline as the treatment regimen. Developing progressive paresis led to changing treatment to oral trimethoprim–sulfamethoxazole (TMP-SMZ) and rifampin for better CNS penetration. after three months the patient was admitted to intensive care unit with respiratory distress, loss of DTR and flaccid tetraparesis. EMG-NCV and CSF analysis revealed GBS. therefore, 0.4 gr/kg/day IVIG was administered five consecutive days. He was discharged a month later with the ability to walk independently (15). Early diagnosis of GBS could prevent long-term hospitalization and probable complications. Physicians should pay attention to GBS in Brucellosis patients, especially in endemic areas.

Conclusion

Considering these two cases and similar cases reported globally, it becomes imperative to contemplate brucellosis as a potential etiological factor for GBS in endemic areas. Conducting pertinent bacteriological and serological tests, followed by EMG-NCV, is crucial in such scenarios. The presented cases recovered after undergoing plasma exchange, IVIG, and antibiotic therapy, showing the importance of appropriate treatment for the prognostic outcome. The diverse range of presentations and economic ramifications underscores the significance of research and efforts toward preventing and treating brucellosis.

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

Declarations

Ethics approval and consent to participate. All actions done in this study involving human participants in concordance with the ethical standards of the institutional and/or national research committee at which the

studies were conducted and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Consent for publication. Informed documented written consent was obtained from the patients.

Competing interests. The authors declare no competing of interests for this work.

References

1. Shahrizaila N, Lehmann HC, Kuwabara S. Guillain-Barré syndrome. Lancet (London, England). 2021;397(10280):1214-28.
2. Babamahmoodi F, Babamahmoodi A. Brucellosis, presenting with guillain-barré syndrome. Journal of global infectious diseases. 2011;3(4):390-2.
3. Alanazi A, Al Najjar S, Madkhali J, Al Malik Y, Al-Khalaf A, Alharbi A. Acute Brucellosis with a Guillain-Barre Syndrome-Like Presentation: A Case Report and Literature Review. Infectious disease reports. 2021;13(1):1-10.
4. Doya LJ, Haidar I, Sakkour S. The association between acute brucellosis with a Guillain–Barré syndrome-like presentation: a case report. J Med Case Reports. 2023;17(1):25.
5. Ozer G, Kutlu G, Inan LE. A rare clinical presentation of neurobrucellosis paraparesis: a report of two cases. 2018.
6. Soares CN, Angelim AIM, Brandão CO, Santos RQ, Mehta R, Silva M. Neurobrucellosis: the great mimicker. Rev Soc Bras Med Trop. 2022;55:e05672021.
7. Bagheri Nejad R, Krecek RC, Khalaf OH, Hailat N, Arenas-Gamboa AMJPNTD. Brucellosis in the Middle East: Current situation and a pathway forward. 2020;14(5):e0008071.
8. Watanabe K, Kim S, Nishiguchi M, Suzuki H, Watarai M. Brucella melitensis infection associated with Guillain-Barré syndrome through molecular mimicry of host structures. FEMS immunology and medical microbiology. 2005;45(2):121-7.
9. Varol F, Yusuf Can Y, Sahin E, Sahin SB, Akyuz G, Aydin A, et al. Successful treatment with therapeutic plasmapheresis of a pediatric patient with Guillain-Barré syndrome associated with neurobrucellosis. Journal of Clinical Apheresis. 2022;37(5):522-6.
10. Li Q, Liu J, Jiang W, Jiang L, Lu M, Xiao L, et al. A case of brucellosis-induced Guillain–Barre syndrome. BMC Infect Dis. 2022;22(1):72.
11. Montalvo R, García Y, Navincopa M, Ticona E, Chávez G, Moore DA. [Guillain Barré syndrome in association with Brucellosis]. Revista peruana de medicina experimental y salud publica. 2010;27(2):292-5.
12. Ansari B, Basiri K, Asghar A. Epidemiology and Clinical Features of Guillain-Barre Syndrome in Isfahan, Iran.
13. Yuki N. Infectious origins of, and molecular mimicry in, Guillain-Barré and Fisher syndromes. The Lancet Infectious diseases. 2001;1(1):29-37.
14. Elzein FE, Mursi M. Case Report: Brucella induced Guillain–Barré syndrome. The American journal of tropical medicine and hygiene. 2014;91(6):1179.
15. Aygul R, Deniz O, Guzelcik M, Kotan D. Guillain-Barré syndrome during active Brucellosis. The Eurasian journal of medicine. 2010;42(3):157.