Brucellosis, Presenting with Guillain-Barré Syndrome

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ABSTRACT

Brucellosis is an infectious disease caused by gram-negative bacteria of the genus *Brucella*. Involvement of the gastrointestinal, hepatobilliary, and skeletal systems has been reported frequently in the literature. Involvement of the nervous system is relatively uncommon and has been reported in only 3%–25% of cases of generalized brucellosis. Guillain-Barré syndrome is a prototypical postinfectious autoimmune disease. We report a case of Guillain-Barré syndrome in a 26-year-old woman as an uncommon presentation of neurobrucellosis.

Key words: Brucellosis, Guillain-Barré syndrome, Neurobrucellosis

INTRODUCTION

Brucellosis is endemic in many countries throughout the world, including Iran, and continues to be an important public health problem.[1] Brucellosis is a zoonotic infection of domesticated and wild animals caused by organisms of the genus *Brucella*. Humans contract the disease through ingestion of infected animal food products, direct contact with infected animals, or inhalation of infectious aerosols either by accident or as a result of biological warfare.

Guillain-Barré syndrome (GBS) is an acute inflammatory polyneuropathy that is most commonly characterized by rapidly progressive, ascending, symmetric weakness and areflexia.[2] Since the marked decline in poliomyelitis incidence, GBS has become the most common cause of acute flaccid paralysis in the world. In two-thirds of the cases, the development of GBS is preceded by an acute infection, typically of the gastrointestinal or respiratory systems. Infectious agents related to GBS include *Cytomegalovirus, Epstein-Barr virus, Campylobacter jejuni, Mycoplasma pneumoniae, and Hemophilus influenzae*.[3] Although its pathogenesis is not clear, molecular mimicry seems to be responsible for GBS development after infection, through the synthesis of autoantibodies against myelin gangliosides.[4]

Uncommonly, brucellosis can present as neurobrucellosis, which can affect any part of the central or peripheral nervous system. Clinical syndromes are ultimately diverse, and the clinical picture may be confused by the coexistence of two or more syndromes in the same patient. The most common neurologic manifestation is a subacute or chronic meningoencephalitis. Acute toxic manifestations (e.g., headache, neck pain, backache, insomnia, depression, and muscle weakness) are seen during the acute phase of infection.[5]

Brucella-induced GBS has only been rarely reported.

We report a case of a 26-year-old woman who was admitted with a variety of symptoms, including gradual weakening of the muscles and stuttering.

CASE REPORT

A 26-year-old woman was referred to our hospital because of fever, headache, night sweats, decreased ability to walk, stuttering, and speech impairment. The patient was from a small village in the northern part of Iran. The patient's symptoms had begun 17 days before hospitalization, and she had been admitted and diagnosed with brucellosis at a local city hospital. She had received doxycycline (100 mg bid), co-trimoxazole (960 mg tid), and streptomycin (1 g daily)

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without any improvement. After 5 days, the patient left the hospital at her own written request.

Three days later the patient came to our facility and was admitted to the infectious diseases ward with a preliminary diagnosis of neurobrucellosis. This diagnosis was considered because brucellosis is endemic in Iran, and in every patient with fever and neurological problems neurobrucellosis must be considered in the differential diagnosis.

Serological tests confirmed our initial impression. The patient's past medical history was not significant. Her family history revealed that her husband had been diagnosed with brucellosis in the previous year but had recovered with treatment. The patient was a housewife (i.e., she did not have immediate contact with contaminated animals) but reported consumption of unpasteurized dairy products. She complained of generalized headache but no vomiting or any gastrointestinal problem.

On admission, she was alert and afebrile. She could not stand up but could sit without support. The deep tendon reflexes (DTRs) were absent in all extremities. Muscle strength was 4/5 in the upper extremities and 3/5 in the lower extremities. Proprioception in the lower extremities was impaired, but she did not have any sensory problems. The physical examination of the chest was unremarkable and chest X-ray was unremarkable. The spleen was palpable 2 cm below costal margin but the rest of the abdominal physical examination was normal. Abdominal sonography showed mild splenomegaly without evidence of space-occupying lesions. She could not speak clearly because of her newly developed stuttering.

A cerebrospinal fluid (CSF) examination revealed a raised protein level of 111 mg/dl (normal value: 15–45 mg/dl) and glucose level of 72 mg/dl (normal value: 50–80 mg/dl); the corresponding blood glucose was 80 mg/dl (normal value: 60–100 mg/dl). Microscopy revealed 128 red blood cells (RBC) per cubic millimeter (normal values: 0 cells/mm^3) but no white blood cells (WBC). CSF culture did not yield any bacterial growth. Nerve-conduction studies were suggestive of demyelinating polyneuropathy. Serum IgG and IgM antibodies to *Campylobacter jejuni* were negative, and serum anti-GM1 IgG antibody was positive. The complete blood cell count showed WBC count of 12200/mm^3 (normal value: 4000–10000/mm^3), with 72% polymorphonuclear granulocytes and 24% lymphocytes. The platelet count was 332 × 10^9/L (normal value: 140–450 × 10^9/L). Coombs Wright titration was 1/640 (normal value: 1/320), 2-mercaptoethanol titer was 1/320 (normal value: ≥1/40). Our region is an endemic area for brucellosis and therefore the diagnosis of brucellosis is based on a standard tube agglutination titer (SAT) >1/160 and detection of 2-mercaptoethanol *brucella* agglutination in a titer of ≥1/40. The erythrocyte sedimentation rate was 17 mm in 1 hour (normal value: (age + 10)/2=18 mm in 1 hour), and the rheumatoid factor was positive.

The patient was imaged with brain MRI, which did not show any remarkable findings. With a diagnosis of brucellosis, she was given a course of antibiotic therapy (doxycycline 100 mg bid, rifampin 900 mg/day, and gentamicin 80 mg tid). During hospitalization she received intensive care unit (ICU) care and intravenous immunoglobulin (20 g/day for 5 days). After 15 days she was discharged and advised to continue oral antibiotics for 2 months. On discharge, she was able to walk with support. In a follow-up visit 4 weeks after discharge, the stuttering had disappeared and she was able to walk normally without aid.

DISCUSSION

This case demonstrates the development of postinfectious autoimmune polyneuropathy that may rarely occur with brucellosis. The patient's ascending, symmetric, weakness; absence of DTRs; as well as the history and physical examination findings were compatible with a diagnosis of GBS. The electrodiagnostic findings and the albuminocytologic dissociation in the CSF supported this diagnosis.

Nervous system involvement in brucellosis can be categorized into central and peripheral. The former is usually acute and presents as meningoencephalitis, whereas the latter may either be acute or chronic. Involvement of the peripheral nervous system often presents as polyradiculopathy and less commonly as cauda equina–like syndromes and peripheral mononeuritis. The infection may trigger an immune system–mediated demyelination (GBS).[6]

There have been a few case reports of GBS associated with brucellosis in the literature. One of these reported a case of a 14-year-old girl with GBS-associated *Brucella melitensis* infection[7] and a case of 9-year-old girl who suffered from protracted paroxysms of severe hypertension before she developed the classical signs of GBS. Significant *Brucella* antibody titers were found in the serum of both girls and complete recovery was observed after appropriate

therapy.[8] Garcia *et al.* reported three patients with GBS during active brucellosis, one consistent with the axonal form and the other two with the demyelinating form of the disease.[9]

Zadeh *et al.* described a 28-year-old Iranian man who presented with acute paralysis, areflexia, and ataxia-like GBS, whose serology confirmed brucellosis.[6] Another case was also reported from Iran: a 9-year-old boy admitted with GBS and a history of previously treated brucellosis.[10]

Molecular mimicry is an important mechanism by which infectious agents may trigger an immune response against autoantigens. Gangliosides are composed of glycosphingolipids, with one or more sialic acids linked to the carbohydrate moieties. Anti-GM1 IgG antibody is positive in about 30% of GBS cases occurring after *C jejuni* infection. Anti-GM2 IgM antibody is positive in 10% of GBS cases occurring after cytomegalovirus infection.[10,11,12]

CONCLUSION

This case suggests that brucellosis should be considered a precursor of GBS in brucellosis-endemic areas. Serological tests for brucellosis should be performed in cases of patients presenting with acute paralysis and GBS-like signs and symptoms in such areas.

REFERENCES

1. Hasanjani Roushan MR, Mohrez M, Smailnejad Gangi SM, Soleimani Amiri MJ, Hajiahmadi M. Epidemiological features and clinical manifestations in 469 adultpatients with brucellosis in Babol, Northern Iran. Epidemiol Infect 2004;132:1109-14.
2. Jacobs BC, Rothbarth PH, van der Meche FG, Herbrink P, Schmitz PI, de klerk MA, *et al.* The spectrum of antecedent infections in Giullain-Barre syndrome: A case control study. Neurology 1998;51:1110-5.
3. Hughes RA, Hadden RD, Gregson NA, Smith KJ. Pathogenesis of Giullain-Barre syndrome. J Neuroimmunol 1999;100:74-97.
4. Izadi S. Neurobrucellosis. Shiraz E-Medical Journal 2001;2(2-6).
5. Namiduru M, Karaoglan I, Yilmaz M. Giullain-Barré syndrome associated with acute neurobrucellosis. Int J Clin Pract 2003;57:919-20.
6. SharafoddinZadeh N, Keyhani Fard M. A Case of Neurobrucellosis Mimicking Guillain-Barre syndrome. J Isfahan Med School 2007;25:111-115.
7. Al-Eissa YA, Al-Herbish AS. Severe hypertension: An unusual presentation of Giullain-Barré syndrome in a child with brucellosis. Eur J Pediatr 1996;155:53-5.
8. García T, Sánchez JC, Maestre JF, Guisado F, Vilches RM, Morales B. Brucellosis and acute inflammatory polyradiculoneuropathy. Neurologia 1989;4:145-7.
9. Shakir RA, Al-Din AS, Araj GF, Lulu AR, Mousa AR, Saadah MA. Clinical categories of neurobrucellosis. A report on 19 cases. Brain 1987;110:213-23.
10. Yuki N. Infectious origins and molecular mimicry in Giullain-Barré and Fisher syndromes. Lancet Infect Dis 2001;1:29-37.
11. Barzegar M, Shoaran M. Giullain Barre syndrome associated with Brucellosis. Pak J Med Sci 2009;25:329-31.
12. Watanabe K, Kim S, Nishiguchi M, Suzuki H, Watarai M. *Brucella melitensis* infection associated with Giullain-Barré syndrome through molecular mimicry of host structures. FEMS Immunol Med Microbiol 2005;45:121-7.

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