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Case Report: *Brucella* induced Guillain–Barré syndrome

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Abstract. Neurobrucellosis is relatively uncommon. In a prospective study of 530 patients with brucellosis, neurologic involvement was reported in only 1.7% of the patients. Unlike *Campylobacter jejuni*, the commonest infection implicated in Guillain–Barré syndrome, there are very few reports in the literature of Guillain–Barré syndrome in association with brucellosis. Out of 1,028 cases of brucellosis, polyneuritis was reported in only 2 out of 58 patients with neurological involvement.

CASE REPORT

A 54-year-old man, presented to a district hospital with a 2-week history of generalized fatigue, fever, chills, rigors, and headache. He drank raw camel milk regularly. A diagnosis of brucellosis was made on the basis of a high total *Brucella* antibody titer 1:2560 and started on intramuscular streptomycin and doxycycline. A week later, he reported numbness and muscle weakness affecting upper and lower limbs. He denied recent diarrhea or upper respiratory tract infection. Guillain–Barré syndrome (GBS) was suspected and he was started on intravenous immunoglobulin IVIG. His neurological status continued to deteriorate so he was referred to our center.

On examination, his Glasgo Coma Scale was 15 out of 15. His speech and higher mental functions were normal. There was right-sided ptosis and ophthalmoplegia together with bilateral lower motor neuron facial nerve palsy, more prominent on the right side. Muscle tone was reduced in all limbs with absent deep tendon reflexes. Muscle power was one out of five distally and three out of five proximally. Sensory functions and plantar reflexes were normal. Oral temperature, oxygen saturation, and systemic examination were all within normal limits.

Investigations included a normal chest radiograph, hemoglobin, and white blood cell count, platelets, and erythrocyte sedimentation rate. Renal and hepatic profiles were also normal. A computed tomography (CT) scan of the brain was normal, but a subsequent magnetic resonance imaging (MRI) scan showed subtle edema in the right parietal lobe with associated leptomeningeal enhancement that disappeared on follow-up MRI. Cerebrospinal fluid (CSF) analysis showed white blood cell counts of 3 cells/cubic millimeter, CSF glucose 4.4 mmol/L, and a protein of 2.61 gm./L. Cultures of blood, urine, and CSF were all negative. A repeat *Brucella* agglutinin serology was 1:20,480, mostly IgM indicating recent infection (Table 1). The CSF *Brucella* serology was negative. Serum anti-GM1 IgG antibody was normal. Electromyogram and nerve conduction studies revealed typical findings seen in association with a demyelinating type of sensorimotor polyneuropathy. The overall picture was therefore considered consistent with a diagnosis of GBS secondary to acute brucellosis.

The patient was admitted to the intensive care unit, where IVIG and antimicrobial therapy were continued. His condition gradually improved and 3 weeks later he was able to mobilize with a Zimmer frame. His ocular and facial weakness almost completely resolved. *Brucella* titer dropped to 1:160 (Table 1), and he was discharged home on oral doxycycline and rifampicin to complete a total of 3 months of treatment.

DISCUSSION

This patient's presentation was entirely compatible with a diagnosis of GBS secondary to acute brucellosis. The ascending motor weakness, absent deep tendon reflexes, and electrophysiological findings in addition to the CSF albumin-cytologic dissociation are all classical features of this syndrome, while the clearly elevated *Brucella* titer confirms the diagnosis of brucellosis. Cranial nerve palsies have been reported in 19% of patients with GBS.[1,2]

Neurobrucellosis is relatively uncommon. In a prospective study of 530 patients with brucellosis, neurologic involvement was reported in only 1.7% of the patients.[3] The nervous system involvement in brucellosis is variable. Meningitis, encephalitis, meningoencephalitis, myelitis, radiculitis, and peripheral neuritis have all been reported previously.[1] Although two chronic forms, peripheral and central are distinct, some overlap is possible.[4] Approximately two-thirds of patients with GBS have a history of antecedent infection preceding their weakness.[5] The risk of developing GBS following *Campylobacter jejuni* infection is 100 times higher than the risk in the general population.[6] However, in a 10-year review of 1,028 cases of brucellosis, polyneuritis was reported in only 2 out of 58 patients with neurological involvement.[7] Both axonal and demyelinating forms of GBS have been documented with brucellosis.[8] The earliest description of *Brucella*-related GBS in Saudi Arabia, was recorded in 1996 in a 9-year-old girl who suffered from protracted paroxysms of severe hypertension before she developed the classical signs of GBS.[9]

Molecular mimicry is an important mechanism by which infectious agents trigger an immune response leading to GBS. Anti-GM IgG antibodies are positive in 30% of GBS cases following *Campylobacte*r infection, whereas anti-GM2 IgM antibodies directed against gangeliosides are positive in 10% of GBS following cytomegalovirus infection.[10] Nervous system involvement in brucellosis might be caused by the direct effect of the intracellular organism or to an indirect effect of triggering an immunological mechanism leading to neural pathology. In an experimental animal study Watanabe and others showed the presence of GMI gangelioside-like molecules on the surface of *B. meletensis*. Cholera toxin B subunit (CTB), which binds to GMI gangeliosides, was used

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TABLE 1
Serial serology results

	06/10/2013	17/11/2013	24/12/2013
Brucella agglutinins total	1:10240	1:160	1:160
Brucella agglutinins IgG	1:320	Negative	Negative
Anti-human globulin	Negative	Negative	Negative

as a probe and found to bind to the surface of *Brucella meletensis* but not *Brucella abortus*. In addition, CTB bound to lipopolysaccharide (LPS) of *B. meletensis* and GBS-associated *C. jejuni* but with a different pattern. Sera from *B. meletensis* immunized mice has a cross-reaction with GBS-associated *C. jejuni* strain and GM1 gangelioside, but not with the non-GBS-associated ones. Furthermore, immunization with *B. melitensis,* induced the production of anti-GM1 gangeliosides antibodies that resulted in flaccid weakness and ataxia-like symptoms.[11] Cross-reactive immunological responses as a result of this molecular mimicry between *Brucella* lipooligosaccharide and GM1 gangeliosides may explain the acute axonal polyradiculopathy in *Brucella* infection.

The MRI changes with leptomeningeal enhancement and right parietal lobe changes seen in our patient may suggest a central nervous system involvement. However, simultaneous central and peripheral nervous system involvement in brucellosis has been described previously.[12] Of note, the MRI appearances in our patient normalized following *Brucella* treatment.

This case highlights that in endemic areas, acute brucellosis should be considered in patients presenting with acute paralysis consistent with GBS.

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