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Subacute Brucellosis-induced Guillain-Barré Syndrome: a Case Report

Subakut Bruselloz ile ilişkili Guillain-Barré Sendromu: Vaka Bildirimi

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Abstract

Guillain-Barré syndrome (GBS) is the most frequent cause of acute flaccid paralysis, and in two-thirds of the patients, antecedent infections have been identified. Brucellosis, a zoonotic disease, rarely leads to GBS. Herein, we present two patients with subacute brucellosis-induced GBS that were diagnosed on the basis of their clinical course and electromyography and nerve conduction velocity study results. There was a 1-month and 5-month interval between the onset of brucellosis and GBS in the two patients. The patients recovered after undergoing plasma exchange, intravenous immunoglobulin administration, and antibiotic therapy. Our findings indicate that physicians should consider brucellosis as a potential etiology of GBS and closely monitor the neurological symptoms of patients with brucellosis.

Keywords: Brucellosis, Guillain-Barré syndrome, electromyography, neurobrucellosis

Öz

Guillain-Barré sendromu (GBS), akut flask felcin en sık görülen nedenidir ve vakaların üçte ikisinde, öncül enfeksiyonlar tanımlanmıştır. Zoonotik bir hastalık olan bruselloz, nadiren GBS'ye yol açar. Burada, klinik seyirleri ve elektromiyografi ve sinir iletim hızı çalışmaları ile teşhis edilen GBS ile ilişkili iki subakut bruselloz vakasını bildiriyoruz. Bruselloz tanısı şikayetler başladıktan 1 ay sonra kondu ve GBS tanısı bruselloz tanısı konduktan 5 ay sonra kondu. Sunulan vakalar, antibiyotik tedavisine ek olarak plazma değişimi ve intravenöz immün globulin uygulandıktan sonra iyileşti. Hekimler brusellozu GBS'nin olası bir etiyolojisi olarak düşünmeli ve brusellozlu hastaların nörolojik semptomlarına dikkat etmelidir.

Anahtar Kelimeler: Bruselloz, Guillain-Barré sendromu, elektromiyografi, nörobruselloz

Introduction

Guillain-Barré syndrome (GBS) is an immune-mediated polyradiculoneuropathy and 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].

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

In approximately 5% of cases of brucellosis, neurological involvement can be observed in the form of meningovascular disease, cranial nerve (CN) palsies, myelitis, and others^[4-6]. However, GBS remains an infrequent manifestation. Thus, herein, we have reported two cases of subacute brucellosis-induced GBS and focused on the clinical course, challenges in diagnosis, and therapeutic outcome of the condition.

Case Report

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. At the time of admission, the patient's vital signs were within the normal ranges (blood pressure, 135/90 mmHg; pulse rate, 83 beats/minute; respiratory rate, 19 breaths/minute; and temperature, 37.4 °C). The patient reported a close contact with animals and consumption of unpasteurized dairy products.

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

Three days after admission, the patient developed additional symptoms, including paresthesia in the distal extremities, nausea, vomiting, bloating, and odynophagia. Subsequently, severe constipation and urinary retention ensued. Furthermore, muscle strength deteriorated (lower limb power, 3/5 and upper limb power, 4/5). Despite precise consultations, the patient refused to consent to lumbar puncture. Electromyography (EMG) and nerve conduction velocity (NCV), which were conducted on the sixth day, provided evidence of distal symmetric sensorimotor mixed-type peripheral polyneuropathy and acute inflammatory demyelinating polyneuropathy. A diagnosis of GBS was established, and gentamicin was discontinued due to its known neurotoxicity. The patient was subsequently transferred to the neurology department. He underwent ten plasmapheresis sessions and six rehabilitation sessions over a 20-day period.

The patient gradually improved, with full recovery of his ability to walk independently. However, he subsequently developed musculoskeletal pain and chills, which was suggestive of a

brucellosis relapse. Outpatient treatment with doxycycline (100 mg) and rifampin (300 mg) every 12 h was administered. 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 the follow-up visit. However, treatment was continued for the next 4 months to prevent the relapse of brucellosis.

Case 2

A 28-year-old male shepherd complained of progressive weakness, pain, and paresthesia in both the upper and lower limbs. Examination revealed bilateral foot drop and diminished deep tendon reflexes (DTRs). The patients had been diagnosed with brucellosis 5 months earlier. Although, the patient had been prescribed doxycycline and rifampin, he was not compliant with his medications.

Analysis of the cerebrospinal fluid (CSF) revealed a non-inflammatory picture (glucose level, 62 mg/dL; white blood cell count, not detected; protein level, 127 mg/dL; lactate dehydrogenase, 14; and red blood cell count, 20). EMG-NCV results indicated acute motor axonal polyneuropathy, a subtype of GBS associated with a poor prognosis.

The patient was treated with intravenous immunoglobulin (IVIg; 30 g daily) for 5 days. After discharge, outpatient physiotherapy was continued along with supportive care. After 4 weeks, the only residual symptom during the follow-up visit was mild claudication (Table 1).

Discussion

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

In both cases described in this report, the blood and urine cultures and stool examination yielded negative results for other infections. Furthermore, the patients did not report respiratory or gastrointestinal symptoms upon admission. Although testing for *Campylobacter jejuni* or *Mycoplasma pneumoniae* (via polymerase chain reaction) would have provided more definitive evidence, such tests were unavailable. Thus, the evidence is circumstantial. Both of our cases were comparable to those previously reported in which GBS developed either concomitantly with or after brucellosis infection.

Table 1. Characteristics and clinical manifestations of our patients and the interventions performed

Case	Sex/Age	Signs and symptoms	Limb strength	GBS subtype	Lab data	Treatment
1	Male/64 years	Weakness, constipation, pricking, sensation, gastroparesis, urinary retention dysphagia-diminished DTR	Lower: 2/5 Upper: 3/5	AIDP	WBC (cells/ μ L) count: 16,200; Lymphocyte: 67.8%; Uric acid (mg/dL): 6.1; CRP (mg/dL): 9; ESR (mm/hr): 15	10 sessions of plasmapheresis
2	Male/28 years	Weakness, foot drop, diminished DTR	Lower: 3/5 Upper: 4/5	AMAN	WBC (cells/ μ L) count: 5,200; Lymphocytes: 58.3%; Uric acid (mg/dL): 5.7; CRP (mg/dL): 8; ESR (mm/hr): 21	IVIG: 30 g/day for 5 days

GBS: Guillain-Barré syndrome, 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

Alanazi et al.^[3] reported and reviewed 19 cases of brucellosis-induced GBS that mostly occurred in male patients. They found that the severity of this complication could even lead to death, which implies that its diagnosis and appropriate treatment are important. Although GBS occurred in the setting of subacute brucellosis in our patient, reports demonstrate that GBS could be the initial presentation of this infectious disease. Varol et al.^[9] reported the case of a 5-year-old boy with GBS and brucellosis. Because IVIG (2 g/kg of body weight) was ineffective in the child, plasmapheresis was initiated. After five sessions of plasmapheresis, DTR and strength of the limbs returned to normal^[9]. Different therapeutic approaches, including IVIG administration and plasma exchange, have been discussed in the reported cases for dealing with GBS. However, more evidence regarding the efficacy of each approach is required. Nonetheless, physicians should consider treating the underlying infectious diseases in addition to providing rehabilitation^[3,4,10].

Although comprehensive and complete information regarding the pathogenesis of GBS is lacking, an infectious disease, usually a respiratory infection or gastroenteritis, is present before the development of GBS in two-thirds of the patients^[11]. GBS, the most common cause of acute flaccid paralysis, can occur at any age and has different variants, including those with axonal involvement and nerve demyelination. Furthermore, a combination of both axonal damage and nerve demyelination may occur^[12]. The structural similarity of the bacterium antigens causes an autoimmune reaction against the nerve autoantigens. Molecular mimicry is a crucial mechanism via 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 the production of autoantibodies against the myelin gangliosides, causing acute paralysis and GBS signs^[6]. It has been hypothesized that

molecular mimicry between *Brucella* and myelin gangliosides may trigger the cross-reactive immunological response that leads to GBS^[14].

Aygul et al.^[15] reported the case of a 28-year-old man with brucellosis who was treated with streptomycin and doxycycline. The development of progressive paresis led to a change in treatment to oral trimethoprim-sulfamethoxazole and rifampin for better CNS penetration. After 3 months, the patient was admitted to the intensive care unit with respiratory distress, loss of DTR, and flaccid tetraparesis. EMG-NCV and CSF analysis confirmed the diagnosis of GBS. Therefore, IVIG (0.4 g/kg/day) was administered for 5 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. Thus, physicians should pay attention to GBS in patients with brucellosis, especially in endemic areas.

Conclusion

Considering our two patients and similar cases reported globally, it is imperative to consider 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, demonstrating the importance of appropriate treatment for a good outcome. The diverse range of presentations and economic ramifications highlights the significance of research and efforts toward preventing and treating brucellosis.

Ethics

Informed Consent: In this case report, informed consent has been taken from the patient, and there is not any specific data in the manuscript identifying the patient.

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Footnotes

Authorship Contributions

Concept: M.M-P., A.M-G., Design: M.M-P., A.M-G., Data Collection or Processing: M.M-P., Analysis or Interpretation: M.M-P., Literature Search: M.M-P., A.M-G., S.M-P., F.R., Writing: M.M-P., A.M-G., S.M-P., F.R.

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