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Guillain-Barré Syndrome During Active Brucellosis

Aktif Bruselloz Sürecinde Gelişen Guillain-Barré Sendromu

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Abstract

It has been reported that approximately two thirds of patients diagnosed with Guillain-Barré syndrome (GBS) have had a prodromal illness within a four-week period preceding the onset of GBS. This prodromal illness is most commonly an upper respiratory tract illness or, secondly, gastroenteritis. However, specific infectious agents, such as mycoplasma, cytomegalovirus, Ebstein-Barr virus, vaccinia, variola, campylobacter, varicella-zoster, measles, mumps, hepatitis A and B viruses, rubella, influenza A and B viruses, coxackie and echoviruses, have also been reported to be certain or probable etiologic antecedent agents of GBS. In contrast, GBS during active brucellosis has rarely been reported. This article presents the case of a 28 year-old male patient with GBS during active brucellosis who responded fully to treatment directed to brucellosis. and it is stressed that brucellosis should be considered as a probable etiologic agent in patients with GBS who live in areas where brucellosis is endemic.

Key Words: Acute inflammatory demyelinating polyneuropathy, Brucellosis, Guillain-Barré syndrome

Özet

Guillain Barré sendromlu (GBS) olguların yaklaşık üçte ikisinde hastalığın başlangıcından önceki dört haftalık dönemde bir prodromal hastalık bulgusu olduğu bildirilmiştir. En sık karşılaşılan prodromal hastalık üst solunum yolu enfeksiyonu veya bir gastroenterittir. GBS etiyolojisinde mycoplasma, cytomegalovirus, Ebstein-Barr virus, vaccinia, variola, campylobacter, varicella-zoster, measles, mumps, hepatitis A ve B virusleri, rubella, influenza A ve B virusleri, coxackie ve echovirus gibi spesifik enfeksiyon ajanlarının kesin veya muhtemel varlığı rapor edilmiştir. Bununla birlikte, aktif bruselloz süresince GBS nadir olarak rapor edilmiştir. Bu makalede, brusella geçirmiş tedaviye tam olarak cevap veren aktif bruselloz esnasında GBS'li 28 yaşında erkek hasta sunuldu ve brusellozun endemik olduğu yerde yaşayan GBS' li hastalarda etiyolojik ajanın brusella olabileceğinin gözönünde bulundurulması vurgulandı.

Anahtar Kelimeler: Akut inflamatuar demiyelinizan polinöropati, Bruselloz, Guillain-Barré sendromu

Introduction

Guillain-Barré syndrome (GBS) is an acquired autoimmune polyradiculoneuropathy characterized by flaccid paralysis, areflexia and elevated cerebrospinal fluid protein without cellular reaction. The pathogenesis of GBS is unclear, but it is now generally accepted to result from aberrant immune responses against components of the peripheral nerve tissue [1-3]. Symptoms of GBS are preceded by an antecedent event in about two thirds of patients; the most common antecedent events are respiratory infections, which is reported in about 40% of cases within one month before the onset of the disease, and gastroenteritis, which 20% of cases experience [2-4].

Brucellosis is an infectious disease with a varied clinical presentation, and it is endemic in many parts of the world. It is transmitted to human beings mainly through direct contact with infected animals or by the ingestion of contaminated foods, especially unpasteurized milk, milk products and meat [5]. Neurobrucellosis is a rare but serious complication of brucellosis. Nervous system involvement has been reported in several locations of the nervous system, including the central and peripheral nervous systems. Brucellosis has diverse clinical picture, ranging from meningoencephalitis, myelitis, polyradiculitis, cranial nerve involvement, brain abscess and subarachnoid hemorrhage to GBS [5-10].

This article reports the case of a 28-year-old male with GBS associated with brucellosis caused by *Brucella melitensis.*

Case Report

A 28-year-old male was admitted to the infectious diseases ward with complaints of anorexia, fever, weight loss, and aches in his back and legs. From his history, it was learned that anorexia and the aches in his back and legs had been present for two months, he had lost 10 kilograms of weight during this period, and he had an occasional fever of 37-38°C.

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Examination upon admission to the ward revealed normal cardiovascular system function; his pulse rate was 68 beats/minute, and his arterial blood pressure was 120/80 mmHg. The patient had a low-grade fever of 37.8^{0}C as well as hepatosplenomegaly and lymphadenopathies. His neurological examination was normal. Test for blood count revealed leukopenia with an increased lymphocyte percentage. His erythrocyte sedimentation rate was 15 mm/hour. A Brucella agglutination test was positive in serum with a titer of 1/320. He was diagnosed to have brucellosis, and treatment was commenced with 1 g/day streptomycine intramuscularly and 200 mg/day doxocycline orally.

On the eighth day after his admission, he developed paraparesis, and this weakness progressed into tetraparesis during the following week. Failure of treatment may have been due to the intracellular nature of the infection and the inability of agents, such as streptomycin and tetracycline, to reach the brain in therapeutic concentrations. Streptomycine was withdrawn, and doxycycline was replaced by oral trimethoprim–sulfamethoxazole (TMP-SMZ) because of the low cerebrospinal fluid (CSF) levels achieved by tetracyclines. TMP-SMZ and rifampin are effective against brucellosis. Both drugs have good central nervous system penetration and may act synergistically. Consequently, the patient was treated with rifampin (600 mg/day) and TMP-SMZ (640-3200 mg/day) for 3 months. Brain and cervicothoracal MRI examinations were normal. Neurologic assessment revealed flaccid tetraparesis, loss of deep tendon reflexes, and respiratory distress. There were no pathologic reflexes. Upon his transfer to the neurological intensive care unit, the development of facial diplegia was also observed. As respiratory distress progressed, the patient was provided synchronized respiratory support in the intensive care unit.

At lumbar puncture, the CSF pressure was 150 mm H_20. Microscopic examination of the CSF revealed 13 lymphocytes/mm^3, and the biochemical examination of the CSF revealed a protein level of 237 mg/dl and a glucose level of 48 mg/dl. CSF and serum *Cytomegalovirus, Herpes simplex* and *Herpes zoster* viruses titers were negative. Electrophysiological examination of the patient revealed prolonged distal latencies, slowing of conduction velocities, loss of F-responses, temporal dispersion and conduction blocks. These findings are compatible with acute inflammatory demyelinating polyradiculoneuropathy. *Brucella* was cultured from the patient's bone marrow. The patient's diagnosis was confirmed as GBS caused by Brucella infection. The patient was subsequently started on intravenous immunoglobulin for 5 days at a dose of 0.4 g/kg/day intravenously and discharged from the intensive care unit 2 weeks later. When discharged from the hospital a month later, the patient had facial diplegia, areflexia and a mild loss of strength in the lower extremities. The patient was able to walk unaided. In the control examination 3 months later, he had normal neurological findings aside from mild facial diplegia and areflexia.

Discussion

Brucellosis is a multi-system disease that presents with a number of different clinical manifestations. The symptoms frequently dominate one organ system, with skeletal, gastrointestinal and hematological complications being the most common. Though infrequent, cardiac and neurological involvements are more serious. Central or peripheral nervous involvement is observed in approximately 2-7% of patients with brucellosis [5-7]. GBS is believed to be a syndrome with autoimmune origins [1-4]. Viral, mycoplasmal or bacterial infections are reported to be present in two thirds of cases before the clinical onset of GBS. The most common precedent infections are of the upper respiratory or gastrointestinal tracts [1-4]. *Campylobacter jejuni*, an enteric pathogen, is the most appropriate example for the direct relationship between GBS and the preceding infections. The pathogen is frequently seen before GBS, and it is present in 30% of the cases, even without infection [1-4]. Some serotypes have a common lipopolisaccharide antigen with the ganglioside epitopes of the peripheral nerves. The relationship between GBS and *Campylobacter jejuni* infections increases the likelihood of the "cross reaction" or "molecular similarity" theories, which suggest that the immune reaction toward the microorganism also develops toward a neural antigen [1]. Among the other infections preceding GBS are *Cytomegalovirus, Ebstein-Barr* virus*, Herpex simplex, Hepatitis* viruses*,* HIV*, Rubella,* measles*,* chicken pox*,* mumps*, Influenza* viruses*,* enteroviruses*, Shigella* and *Clostridium* species [1-4]. GBS rarely develops following *Brucella* infections. The development of GBS during active brucellosis is restricted to a few cases, according to the literature [9, 10]. It is unknown how this variety of immune reactions can cause complement fixation and perivenous neural inflammation. The role of the host sensitivity in the development of GBS is another unknown given that GBS develops in only a few of the cases infected with the same agent [1].

This case highlights the fact that the probability of brucellosis as an etiologic agent should be considered in patients with GBS who live in areas where brucellosis is endemic.

Conflict of interest statement: The authors declare that they have no conflict of interest to the publication of this article.

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