Case Report / *Olgu Sunumu*

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Neurobrusellosis: Two Case Reports

Nörobruselloz: İki Klinik Vaka

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Abstract

Brucellosis is one of the most common zoonotic diseases caused by Brucella bacteria and is characterized with nonspecific findings such as corrugated fever, sweating, myalgia, joint pain, loss of appetite, nausea, vomiting, fatigue, weakness, weight loss, headache, and dizziness. The involvement of the nervous system is rare. We aimed to present two cases of paraplegia due to radiculitis and loss of upper extremity strength due to cervical abscess after infection caused by Brucella. In the etiology of fever of unknown origin in areas where Brucella is endemic, brucellosis is a disease that must be considered in the differential diagnosis. If early diagnosis and appropriate treatment are not given, it can leave serious neurological sequelae. Recognition and treatment by physicians in endemic areas is of critical importance.

Keywords: Neurobrucellosise, paraplagia

Öz

Bruselloz, Brucella bakterilerinin neden olduğu en yaygın zoonotik hastalıklardan biridir ve dalgalı ateş, terleme, kas ağrısı, eklem ağrısı, iştahsızlık, bulantı, kusma, yorgunluk, halsizlik, kilo kaybı, baş ağrısı ve baş dönmesi gibi spesifik olmayan bulgularla karakterizedir. Sinir sisteminin tutulumu nadirdir. Brucella'nın neden olduğu enfeksiyon sonrası radikülite bağlı parapleji ve servikal apseye bağlı üst ekstremite kuvvet kaybı olan iki olguyu sunuyoruz. Brucella'nın endemik olduğu bölgelerde nedeni bilinmeyen ateş etiyolojisinde bruselloz ayırıcı tanıda düşünülmesi gereken bir hastalıktır. Erken tanı ve uygun tedavi yapılmazsa ciddi nörolojik sekeller bırakabilir. Endemik bölgelerde hekimler tarafından tanınması ve tedavisi kritik öneme sahiptir.

Anahtar Kelimeler: Nörobruselloz, parapleji

Introduction

Brucellosis is one of the most common zoonotic diseases caused by Brucella species. *Brucella melitensis, Brucella abortus, Brucella suis, Brucella canis* are the four species that cause human brucellosis. The most common strain reservoir is *B. melitensis*, which is sheep and goats. Concurrently, *B. melitensis* is the most invasive and pathogenic strain. Transmission usually occurs through the consumption of contaminated raw milk and dairy products. Brucellosis can be transmitted less frequently by contact with infected animals and by inhalation. The diagnosis of brucellosis is made with clinical findings, isolation of the *B. melitensis* in blood culture, and serological tests (1-4).

Although brucellosis most commonly affects the musculoskeletal system, it can affect all systems such as cardiovascular, gastrointestinal, central nervous, genitourinary and pulmonary systems and may present with atypical clinical pictures. Neurobrucellosis is a complication of systemic brucellosis infection and the incidence of neurobrucellosis is reported to be between 2-10% (3,5,6). Neurobrucellosis occurs by direct

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spread of bacteria to the CNS or by autoimmune mechanisms due to toxins (1,3,4,6). Clinical manifestations of neurobrucellosis include meningitis, meningoencephalitis, brain abscess, intradural and epidural abscess, granuloma, myelitis-radiculoneuritis. Although rare, hearing and vision loss may occur due to meningovascular complications, multifocal white matter disease, arachnoiditis, polyradiculopathy, mononeuropathy, cerebellitis, radiculitis, cranial nerve involvement (1-3).

The purpose of this report is to offer cases presenting with two less common clinical forms of neurobrucellosis, such as radiculitis and epidural abscess.

Case Report

Case 1

A 15-year-old female patient presented with intermittent fever, malaise, widespread muscle pain and weight loss for three months. Patient complained of progressive weakness in both lower extremities and avoid from squatting, climbing and descending stairs for the last one month. In addition, she had intermittent headache, nausea and vomiting. The patient, whose complaints of urinary and fecal incontinence were added, was referred to our hospital. The patient lived in a rural area and their livelihoods were farming and husbandry. His brother had been treated for brucellosis six months ago. The patient's admission vital signs were normal. On physical examination, respiratory system and cardiovascular system were normal and hepatosplenomegaly was present. On neurological examination, the patient was conscious, oriented and cooperative. The patient's meningeal irritation signs were negative. Cerebellar system examination was normal. In the manual muscle strength examination, it was normal in both upper extremities; proximal muscle strength was 2-3/5 and distal muscle strength was 0/5 in both lower extremities. Bilateral lower extremity deep tendon reflexes could not be obtained. In addition, there was hypoesthesia in L1-S1 dermatomes in both lower extremities. Bilateral sacroiliac joint compression test, FABER (Flexion Abduction External Rotation), FADER (Flexion Adduction External Rotation) and Mennel test were positive.

The patient's laboratory data were: white blood cell counts 3.500/mm^3, neutrophils 46%, hemoglobin 8.1 g/dL, platelets 100.000/mm^3, erythrocyte sedimentation rate (ESR) 26 mm/h and C-reactive protein (CRP) 32 mg/L, aspartate aminotransferase (AST) 77 U/L, alanine aminotransferase (ALT) 68 U/L. Complete urinalysis was normal. Rose Bengal positive and Brucella tube agglutination test in serum was 1/640 positive. Lumbar puncture was performed. Cerebrospinal fluid (CSF) analysis revealed 210/mm^3 cells with 80% lymphosmonocytic cell dominance, protein and glucose contents were 141 mg/L (upper limit 40 mg/dL) and 33 mg/dL (simultaneous blood glucose= 102 mg/dL), CSF Brucella tube agglutination test= 1/320 (+) was positive. With CSF findings, patient was diagnosed with neurobrucellosis. The patient was started on ceftriaxone (100 mg/kg/day, two doses), doxycycline (2.2 mg/kg/dose, two doses), and rifampicin (20 mg/kg/day, two doses) due to the diagnosis of neurobrucellosis. While there was no growth in the patient's CSF culture, *B. melitensis* grew in the blood culture. Spinal and brain magnetic resonance imaging (MRI); "Contrast uptake was detected in phylum fibers around the conus and in perineural soft tissues in the neural foramen". It was found to be compatible with radiculitis (Figure 1). Also, electromyography (EMG); "Significant anterior root/forehorn damage was detected in bilateral L5-S1". Fundus examination was normal. The patient was diagnosed with neurobrucellosis and radiculitis. In addition, due to radicular root involvement, methylprednisolone 1 mg/kg/day was administered intravenously (IV) for five days. A 45-session physical therapy and rehabilitation program was planned for the patient. Neurophysiological exercises, passive-active-assisted range of motion exercises, isometric and isotonic strengthening exercises, balance-coordination exercises, ambulation training were applied. Functional electrical stimulation (FES) was applied to both ankle dorsiflexor muscles and extensor halluxis longus muscle. At the end of the physical therapy and rehabilitation process, the muscle strength of the proximal muscles in the lower extremities was 5/5, and the muscle strength of the distal muscles was 4-5/5. The patient, who was mobilized without support and independently, was discharged with recommendations to complete the ceftriaxone treatment for four weeks and the doxycycline and rifampicin treatment for three months.

Figure 1. Contrast uptake was detected in phylum fibers around the conus and in perineural soft tissues in the neural foramen.

Case 2

An eleven-year-old female patient was admitted to our outpatient clinic with complaints of fever, weakness, fatigue, night sweats and neck pain that had persisted for a month. It was learned that the patient's complaints gradually increased and pain and numbness in the right arm were added to his complaints, especially in the last 10 days. When anamnesis was deepened, it was learned that he had a history of consuming fresh cheese from raw milk and that his father had been treated for brucellosis one year ago. The patient's admission vital signs were normal. On physical examination, respiratory, cardiovascular and gastrointestinal systems were normal. On her neurological examination, he was conscious, oriented and cooperative. There was nuchal rigidity. There was tension and spasm in paracervical muscles, and the cervical joint range of motion was almost completely limited in all directions, more prominently on the right. While there was no loss of muscle strength in bilateral lower extremities and left upper extremities, the right upper extremity abduction was limited and the muscle strength was 3/5. There were no biceps reflex in the right arm.

In the laboratory examination of the case, routine hemogram and biochemistry results were normal except for CRP= 25 mg/L (upper limit= 5). PA chest X-ray was normal. The Rose Bengal and Brucella tube agglutination test was 1/640 positive. *B. melitensis* grew in the blood culture of the patient. The patient was diagnosed with brucellosis. Ceftriaxone (100 mg/kg/day, two doses), doxycycline (2.2 mg/kg/dose, two doses) and rifampicin (20 mg/kg/day, two doses) was started upon hospitalization. Spinal and brain MRI taken due to neck stiffness and fever; "The axial dimensions are 23 x 9 mm, craniocaudal extension 48 mm, localized in the anterior epidural area, T2A heterogeneous hyperintense, cutaneous contrast enhancement was detected, extending from the level of C2 intervertebral disc to the level of the lower end plateau of the C6 vertebra corpus, and the appearance was evaluated in favor of epidural abscess". The described lesion obliterates the anterior subarachnody distance and it is observed that it compresses the spinal cord more prominently on the right side, most prominently at the level of C4-5 vertebrae (Figure 2). Epidural abscess drainage was performed. There was no growth in the abscess culture. The patient, whose antibiotic treatment was continued, was included in a 15-session physical therapy and rehabilitation program due to the limited range of motion of the neck joint. Warm hot pack/TENS, passive-assisted range of motion and isometric strengthening exercises and coldpack were applied to the paraspinal muscles after rehabilitation. At the end of physical therapy and rehabilitation, cervical joint range of motion was complete in all directions. The patient was discharged with recommendations to complete his medical treatment in three months.

Figure 2. Epidural abscess.

Discussion

Brucellosis is still an important public health problem all over the world, especially in the Mediterranean region, the Balkans, the Middle East, and Central and South America. Half a million new cases are identified each year and cause serious socioeconomic burden in developing countries. While the incidence in the world varies between 0.03-160 per 100.000, it is 23 per 100.000 people in Türkiye (1,5,6).

Neurological complications of brucellosis are rare but an important clinical entity. Central nervous system involvement is usually in the form of meningoencephalitis, but it is seen in atypical involvements. In our cases, it is a rarer form of radiculitis and epidural abscess of neurobrucellosis.

Diagnosis of neurobrucellosis, isolation of bacteria from CSF, *Brucella* spp. at any level in CSF. It is diagnosed by detecting the presence of antibodies or abnormal CSF findings. The isolation rate of bacteria in CSF is low, and culture growth may occur in less than 20% of patients. When CSF findings in neurobrucellosis are examined, pleocytosis with lymphocyte predominance, low glucose level and increase in protein level are expected (7-9). However, in some cases, cells will not be seen in CSF, and protein and glucose levels may be found to be normal (10,11). Our first case in whom lumbar puncture could be performed was diagnosed as neurobrucellosis with CSF findings and tube agglutination positivity with Brucella Coombs in CSF. Lumbar puncture could not be performed in our 2nd case because of focal neurological deficit and a diagnosis of epidural abscess in the C2-C6 range. *B. melitensis* could not be isolated in the epidural abscess culture, but *B. melitensis* growth in the blood culture of our case, the history of eating fresh cheese and the parents' treatment for brucellosis, the patient was evaluated as neurobrucellosis.

The reason for walking difficulty in our first case was because Brucella affected the spinal cord. Myelitis and myeloradiculopathy may be due to direct spread of the bacteria, as well as compression of adjacent lesions may cause spinal cord lesion. Shakir et al. reported cases with hypotonia, tendon areflexia and paraparesis in the neurobrucellosis series he published. EMG detected axonal degeneration in one of these cases and demyelinating radiculopathy in the others (12). In the EMG performed in our patient who had bilateral lower extremity hypoesthesia, tendon areflexia and motor deficit, significant anterior root/anterior horn damage was detected bilaterally in L5-S1. However, no lesion was found to explain these findings in the cranial MRI taken to rule out possible parasagittal lesions. Contrast enhancement in the perineural soft tissues in the phylum fibers around the conus and in the neural foramen in the examination findings and examinations explains the occurrence of radiculopathy due to Brucella.

In the presence of epidural abscess, infections should be considered in the foreground. The abscess requires drainage for both diagnosis and administration of appropriate treatment. Although epidural abscess due to brucellosis is rare, it can cause myelomalacia by compressing the spinal cord. In our case, an abscess that limited the range of motion of the neck joint in all directions and caused significant spinal cord compression was drained (13,14).

In the treatment of neurobrucellosis, antibiotic combinations with bactericidal effect that can pass into the CSF are recommended in order to have *Brucella* spp. localized intracellularly and to prevent the risk of relapse development. Therefore, ceftriaxone rifampicin, doxycycline/trimethoprim-sulfamethoxazole are used in the treatment of neurobrucellosis. The duration of neurobrucellosis treatment is 3-12 months with control lumbar puncture and imaging methods (1,3,13). Although there is no consensus on the use of steroids, it is recommended to be used in severe forms of the disease.

Brucellosis may present with atypical clinical pictures and difficulties may be experienced in diagnosis and treatment since it mimics many diseases. Our cases are radiculitis and epidural abscess, which is a rarer form of neurobrucellosis. As a result, the recognition and treatment of neurobrucellosis by physicians in endemic regions is of critical importance. Serious neurological sequelae can be prevented with early diagnosis and appropriate treatment.

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