

Acquired progressive spastic paraparesis due to neurobrucellosis : a case report

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Abstract

A 39-year-old man with a 4-month history of transient pins and needles sensations occurring below the waist while walking and difficulty walking presented to our outpatient clinic. He had an approximate 1-year history of bilateral hearing loss, the etiology of which was unknown. His symptoms had been progressive, and there was no significant family history. He demonstrated a spastic gait and required assistance for walking. Deep tendon reflexes were hypertonic ; a sensation deficit was defined as originating from the 12th thoracic vertebra. Babinski's sign was positive bilaterally. Sphincter abnormalities were seen in the patient's bladder and bowel functions. Cerebral and spinal magnetic resonance images with contrast media were unremarkable. An analysis of the patient's cerebrospinal fluid was consistent with neurobrucellosis. Owing to spastic paraparesis and hearing loss, the diagnosis of neurobrucellosis was made. Combined antimicrobial therapy was started and continued 6 months. His neurologic condition improved, and he was able to walk without help after 3 months' treatment.

Our case illustrates that acquired progressive spastic paraparesis may occur during the course of neurobrucellosis. Neurobrucellosis should be borne in mind when patients present with spastic paraparesis.

Key words : Neurobrucellosis ; progressive spastic paraparesis.

Introduction

The high incidence of human brucellosis in developing countries has been attributed to the lack of hygienic milk processing and inadequate eradication of the infection from carrier animals (1). In adults with systemic brucellosis, neurobrucellosis has a reported incidence of between 5% and 25% (2-8). Neurobrucellosis also manifests in several locations of the nervous system, including the central nervous system (CNS) and the peripheral nervous system (8, 9). Meningitis ; diffuse and localized encephalitis ; myelitis ; polyradiculoneuritis ; and involvement of the second, seventh, and eighth cranial nerves have all been reported (10,

11). The outcome is favorable if treatment is started early and continued for an adequate period (6-8, 12, 13, 14). Here, we report the case of a rare complication of neurobrucellosis with acquired progressive spastic paraparesis.

Case report

A 39-year-old man with a 4-month history of transient pins and needles sensations occurring below the waist while walking and difficulty walking presented to our outpatient clinic. He described sacral hypoesthesia and severe gait imbalance. He also stated that he had an approximate 1-year history of bilateral hearing loss, the etiology of which was unknown. His symptoms had been progressive, and there was no significant family history.

He was working in a primary school as a teacher and he came from a moderate socioeconomic status group. He had admitted to eating cheese made from unpasteurized goat's milk. During a neurologic examination, he demonstrated a spastic gait and required assistance for walking, deep tendon reflex hyperactivity in the lower extremities, positive Babinski's sign, loss of proprioceptive sensation, and positive Romberg's sign. He showed sensory deficit below the level of the 12th thoracic vertebra, and retention-type sphincter dysfunction was seen in the bladder and bowel. Results of nerve conduction velocity studies of the motor and sensory nerves and an electromyography of the upper and lower extremities were within normal limits. Somatosensory evoked potential studies showed normal responses in the upper extremities, but late and deformed responses were present in the lower extremities. Cerebral and spinal magnetic resonance (MR) images with contrast media were unremarkable. The protein content in the cerebrospinal fluid (CSF) was 106 mg/dL (normal range, 15-45 mg/dL) ; the glucose content of the CSF was 26 mg/dL, while the simultaneous blood glucose concentration was 106 mg/dL. Microscopic examination of the CSF displayed 100 leucocytes per cubic milliliter with a predominance of lym-

phocytes. Cytologic CSF analysis showed ependymal cells and cytolytic polymorphonuclear leucocytes and lymphocytes, which is consistent with chronic infections. Results of staining with Rose Bengal were positive, as they were for a Wright agglutination test (with or without Coombs' serum – the standard tube agglutination test) at a dilution of 1/5120 for brucella in serum. Results of a CSF brucella agglutination test at a dilution of 1/64 also were positive. Results of all laboratory analyses, including erythrocyte sedimentation rate, complete blood count, fasting blood sugar, rheumatoid factor, serum complement levels, antinuclear antibody, tuberculin skin test, and urine analysis were normal. The results of other tests for infection with human immunodeficiency virus, hepatitis C virus, venereal disease, salmonella, toxoplasmosis, *Borrelia burgdorferi*, herpes simplex virus, and cytomegalovirus were all negative in serum. The results of other CSF examinations such as cultures for tuberculosis and viral markers were all negative. The patient was diagnosed as having neurobrucellosis. The organism was not isolated in serum or a CSF culture. Treatment was initiated with ceftriaxone (2 g IV, q 12 h), and rifampicin (600 mg/day PO) and doxycycline (100 mg PO, q 12 h) in the first month. Following discharge, the patient continued triple antimicrobial regimen with trimetoprim/sulphamethoxazole (160/800 mg PO, q 12 h), doxycycline (100 mg PO, q 12 h) and rifampicin (600 mg/day PO) until the end of the sixth month. He was hospitalized for 1 month and then seen regularly each month at the outpatient clinic. His neurologic symptoms have improved, and after 3 months, he gained the ability to walk without help. Lumbar puncture was repeated at the end of the sixth month, at which time an examination of the CSF revealed a protein level of 46 mg/dL and a glucose level of 35 mg/dL (simultaneous serum glucose was 102 mg/dL). No cells were present in the CSF, but results of a brucella agglutination test were above the normal range (at a dilution of 1/8).

Discussion

Brucellosis is a zoonotic disease that is endemic in many parts of the world including coastal areas of the Mediterranean Sea including Turkey, the Middle East, and Central and South America. According to statistics, in 2003, there were 14,572 cases in Turkey and the incidence of brucellosis was 2/100 000 (15). The microorganism is transmitted to human beings mainly through direct contact with infected animals or ingestion of contaminated foods, especially raw milk and its derivatives (11). Brucellosis can affect all age groups, but people living close to animals such as shepherds, veterinarians, butchers, and abattoirs are at high risk. Nervous system involvement in

brucellosis, termed *neurobrucellosis*, is rare in adults. The estimated incidence of neurobrucellosis in adults with systemic brucellosis varies between 5% and 25% (5-6, 13, 16-19). This wide variation in incidence may be due to delays in diagnosis and negative results for agglutination tests for the disease in patients with localized infections. Neurobrucellosis appears with a lower frequency in children : 0.8% of children affected with systemic brucellosis manifest neurobrucellosis (20).

Brucella enters the CNS through the blood. The organism may act directly or indirectly through its endotoxins (6). Then, latent or clinical meningitis occurs ; after that, microorganisms may eventually invade neighboring structures (20). The spinal cord or nerve root may be involved secondarily owing to spondylitis, vasculitis, or arachnoiditis (4). Clinical manifestations of neurobrucellosis vary widely. The clinical categories of neurobrucellosis are meningoencephalitis, meningovascular involvement, peripheral neuropathy/radiculopathy, and various degrees of behavioral abnormalities (21). The most frequent clinical presentation of neurobrucellosis is meningitis occurring in about 50% of the cases (6) and usually presents in an acute or chronic form (22, 23). Subarachnoid hemorrhage, intracerebral hemorrhage, subthalamic hemorrhage, and cerebral venous thrombosis have been reported as meningovascular complications of neurobrucellosis (24).

Neurologic manifestations in neurobrucellosis may occur early or late in the course of the disease or months after recovery from acute infection. Early manifestations appear during the course of the septicemia or shortly after septicemia ends, while later manifestations, which are more frequent, may last months or years after having occurred during the septicemic period ; many times these later manifestations are subclinical (22). Abramsky has reported 4 patients in whom acute neurologic conditions were the first presentation of brucellar disease (25).

Immune-mediated demyelination has been proposed to explain certain chronic forms of neurobrucellosis (26). Pathologically, dysmyelination of the nervous system, meningovascular pictures, cerebral and intra-medullary abscesses (27), and cerebral venous thromboses have been described (24).

In a report from India about the spectrum of neurobrucellosis, 12 of 92 patients with systemic brucellosis had neurobrucellosis, and only 2 had spastic paraparesis due to myelitis (10). All of these patients presented with fever, severe headache, altered consciousness, and arthralgia, all of which are prominent in brucellosis. In a report by Kochar, 2 patients had spastic weakness in the lower extremities and extensor plantar responses ; their CT myelography findings were both reported as normal. These 2 patients were diagnosed as having

neurobrucellosis ; they were cured quickly with no neurologic sequelae using combined antibiotics (10). In earlier reports, authors have observed that myelitis due to neurobrucellosis recovers completely, while some authors claim this not to be the case (28, 29). In our patient, the prominent clinical picture also was rare progressive spastic paraparesis.

Owing to brucellar meningitis, deafness, which is rapid in most instances, was observed (3, 12, 30). Gouider has reported involvement of the acoustic nerve in 7 of 8 patients with neurobrucellosis (23). In series of neurobrucellosis, sensorineural-type hearing loss was prevalent in 90% of the patients (31) ; however, peripheral brucellosis did not appear to be associated with hearing loss (32). Our patient had sensorineural-type hearing loss of an unknown etiology initially, but after the diagnosis, we considered it due to neurobrucellosis.

Common findings of neurobrucellosis in the CSF are low titers of glucose, high levels of protein, and lymphocytic pleocytosis. Although a positive culture of CSF is essential for diagnosis, low titers of Wright agglutination tests in the serum and CSF do not exclude the diagnosis. Two thirds of patients have low titers of agglutination tests in the CSF with negative culture results (24). If the clinical appearance is suggestive of neurobrucellosis, the diagnosis can be made. Because blocking antibodies may cause negative results of agglutination, higher titers can be obtained "with a Coombs' agglutination test" (1, 3, 10, 33, 34). Considering the foregoing, brucella agglutination tests should be repeated with Coombs' serum in patients with suspected history. Some postinfectious cases may have clinical signs incompatible with decreasing titers. Krishnan and associates reported a case of recurrent transverse myelitis following neurobrucellosis with progressive decline of CSF brucella antibody titers suggesting a postinfectious, rather than an infectious, etiology (35).

There are no specific guidelines regarding the antibiotic regimens and duration of treatment for neurobrucellosis. The duration of treatment varies from 8 weeks to 2 years depending upon the individual. Drugs such as doxycycline, rifampicin and trimethoprim-sulfamethoxazole have been found to be effective owing to their good CNS penetrations and synergistic actions (4, 14). Tetracycline and streptomycin are good for systemic brucellosis, although their CNS penetration is poor (4, 14, 24).

We believe that our patient experienced hearing loss due to neurobrucellosis early in the disease course. He also had transverse myelopathy characterized by progressive spastic paraparesis, sphincter abnormality, sensory deficit at the 12th thoracic level, pathological reflexes, and posterior column dysfunction of 4 months' duration. CSF findings revealed meningitis. Chronic meningomyelitis was diagnosed by the clinical picture and CSF findings.

The definitive diagnosis of neurobrucellosis was based on the existence of positive results on a brucella agglutination test in the CSF and blood, although there was no abnormality on neuroradiologic investigation. Ours is a rare presentation of brucellosis with both meningeal and spinal cord involvement in addition to hearing loss, which responded to long-term treatment with a partial recovery.

In summary, neurobrucellosis, a rare entity, should be borne in mind, particularly when patients present with acquired progressive spastic paraparesis. The neurologic findings are reversible with present antimicrobial therapy. However, in endemic areas, the disease should be ruled out in all patients who develop unexplained neurologic symptoms.

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