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Case Report

Cerebral infarct due to meningovascular neurobrucellosis: a case report

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ABSTRACT

Brucellosis is a common and multisystemic zoonotic infectious disease. Central nervous system involvement is rarely seen in brucellosis, with an incidence of 0.5–25%. The aim of this report is to underline the importance of brucellosis, which is an endemic infection in our country, during the diagnostic evaluation of stroke.

1. Introduction

Brucellosis is a common infectious disease. Humans can become infected by direct contact with an infected animal, the consumption of dairy products, and/or inhalation of infectious particles. It is a systemic zoonotic disease that can persist for years if not treated, and can cause various complications depending on the organs affected.[1,2] Although it has been completely eradicated in industrialized countries, brucellosis is an important public health problem in developing countries such as Turkey.[3]

A rare but important complication of Brucella infection is neurobrucellosis, which can be seen at all stages of the disease. Neurobrucellosis can present with acute or chronic meningoencephalitis, myelitis, radiculitis, cranial nerve involvement, brain abscess, subarachnoid bleeding, and neuropsychiatric symptoms.[3–5]

Central nervous system (CNS) involvement is either due to the direct effect of the bacterium via cytokines or endotoxins on peripheral nerves, spinal cord, meninges, and brain or vascular involvement. Transient cerebral ischemic attacks can be seen secondary to the vascular–perivascular inflammatory reaction or vascular spasm. Large vessel involvement is rare in neurobrucellosis.[2,6,7] In this report, we present a case of stroke due to neurobrucellosis. Our aim is to underline the importance of neurobrucellosis in the differential diagnosis of stroke in areas where brucellosis is endemic, such as our country.

2. Case report

A 28-year-old male patient was hospitalized in the Physical Medicine and Rehabilitation Department, with a diagnosis of stroke for rehabilitation. The patient had first presented to a different university hospital with symptoms of sudden speech disorder, blurred consciousness, and weakness of the left half of the body. Magnetic resonance imaging (MRI) and cerebral angiography testing performed at that hospital had revealed a frontoparieto-temporal infarct in the right cortical area supplied by the middle cerebral artery (MCA) and a prominent stenotic segment distal to the right MCA. A stent was placed into the right middle cerebral artery. Although the patient regained consciousness after this treatment, he was referred to our clinics for rehabilitation, as his left hemiparesis had persisted.

During evaluation of the patient at our clinics, we learned that the patient consumed unpasteurized milk. The patient's medical history revealed that he had also presented to a health center with symptoms such as depressive mood and fatigue, and had been diagnosed with depression and given medical treatment for this disorder. However, no resolution of the depression was observed following this treatment. His family history did not include any significant characteristics. A physical examination was performed and his vital findings were recorded: blood pressure 130/80 mmHg, heart rate 78/min, body temperature 37.2 °C. The patient was still in a markedly depressive mood. Physical examination of other systems, including the musculoskeletal system, revealed no abnormal findings. Neurological examination of the patient showed that he was conscious, oriented, and cooperative. However, his speech was dysarthric. He had left facial paralysis,

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hemiparesis, and hypoesthesia on the left side of his body. His deep tendon reflexes were brisk. He had pathological reflexes and Achilles clonus. There was spasticity of the left lower extremity, which was more prominent in the gastrocnemius–soleus complex. He had a good sitting balance and could stand up with support. His total functional independence measure (FIM) was recorded as 85. The FIM measures independent performance in self-care, sphincter control, transfers, locomotion, communication, and social cognition. The possible total score ranges from 18 (lowest level of independence) to 126 (highest level).

As the patient was young, the etiology of stroke was evaluated in detail by laboratory testing. Routine blood count, biochemistry, erythrocyte sedimentation rate, vitamin B12 and folic acid levels, urinary tests, coagulation profile, hematological tests for hypercoagulability, and immunologic markers were within the normal ranges. C-reactive protein was 26.2 mg/l. Duplex ultrasound of the carotid arteries, cranial computerized tomography (CT), chest radiography, and echocardiography were all normal. The Brucella standard tube agglutination test (Wright test) was negative. As the blood culture result was positive for *Brucella melitensis*, a lumbar puncture was performed. Cerebrospinal fluid (CSF) albumin was increased at 43 mg/dl, CSF IgG increased at 15 mg/dl, and oligoclonal IgG was seen on CSF immune fixation electrophoresis. CSF glucose was decreased at 26 mg/dl and CSF total protein was increased at 76.8 mg/dl. PCR for *Mycobacterium tuberculosis* and CSF cultures for other bacteria were negative. A CSF culture was positive for *Brucella melitensis*. As Brucella was positive in both blood and CSF cultures, the patient was diagnosed with neurobrucellosis. Cranial MRI showed that there were hemorrhagic infarcts in the frontoparietal cortical–subcortical areas supplied by the right MCA (Figure 1). Angiography was normal. As well as continuing with his routine rehabilitation program, the patient also received triple antibiotic treatment consisting of trimethoprim–sulfamethoxazole 160/800 mg three times a day, rifampin 900 mg/day, and doxycycline 200 mg/day. CSF analysis was repeated in the sixth month of therapy. There was no abnormality on CSF examination. After a year of follow-up, significant improvements in the paresis of the left lower and upper extremities were recorded. There was no significant change in the level of spasticity. The patient was mobilized with one walking stick. His FIM score increased to 109. The most significant improvement was observed in the depressive mood of the patient seen during the first evaluation.

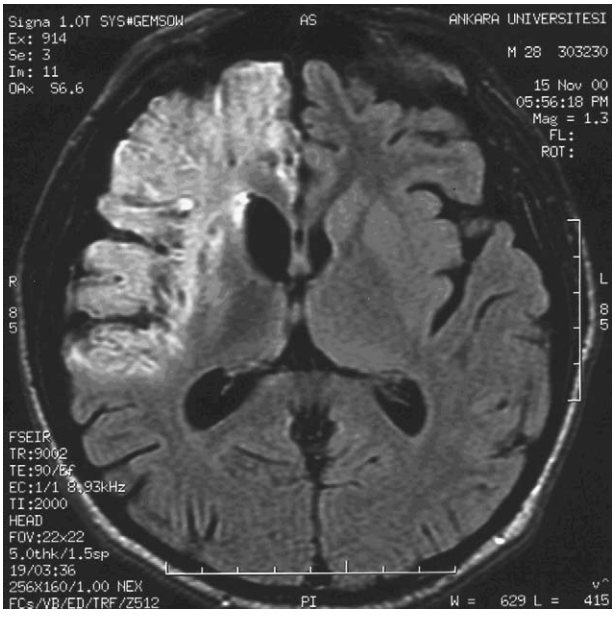

Figure 1. Magnetic resonance image of the brain: focal brain involvement of brucellosis.

3. Discussion

Brucellosis is a zoonotic infectious disease with a low mortality and high morbidity. It is endemic, especially in the east and southeast regions of our country, and it can be seen with different clinical presentations and a variety of complications.[8] Neurobrucellosis can mimic many central and peripheral nervous diseases, including transient ischemic and hemorrhagic stroke. CNS involvement, which has an incidence of 0.5–25%, can be the only finding, and clinical findings can emerge during the late phases of the disease.[9] The clinical presentation of neurological involvement can be diverse, including meningitis, meningoencephalitis, radiculitis, cranial nerve involvement, meningomyelitis, sensorial and motor abnormalities, cerebellar ataxia, brain or spinal abscess, stroke, intracranial hypertension, polyradiculoneuritis, transverse myelitis, and subarachnoid bleeding. Neurological findings can present during the active phase of the disease or can emerge later.[2,9,10]

Neurological complications such as depression, amnesia, mood changes, agitation, manic or paranoid behaviors can be seen in these patients.[11] In countries where brucellosis is endemic, such as Turkey, neurobrucellosis must be kept in mind in the differential diagnosis of patients with neurological deficits and neuropsychiatric symptoms, and these patients should be evaluated for neurobrucellosis in order to make an early diagnosis and treatment. The diagnosis of neurobrucellosis is based on CSF findings, such as normal or low glucose levels, increase in lymphocyte count and protein levels, and positivity of Brucella antibody titer. Bacteria can be isolated in half of the CSF cultures, thus, culture negativity is not essential for elimination of neurobrucellosis. Moreover, CSF antibody may also not be positive. Furthermore, the blood agglutination test and blood cultures may also be negative.[7,10,12] This case presented for medical care with stroke and findings of depression. The patient was young and he did not have any risk factors for stroke. He had a normal complete blood count and biochemistry tests. Although the blood Brucella agglutination test was negative, the bacterium was isolated from blood culture. Moreover, CSF findings were in accordance with neurobrucellosis. As CSF culture was positive for brucellosis, the final diagnosis of neurobrucellosis was made. The CSF findings are similar to tuberculous meningitis and can be misleading in the diagnosis, especially in regions where tuberculosis is common. Thus, we evaluated our patient for tuberculosis; however there were no findings suggesting tuberculosis.

The pathogenesis of ischemic stroke in Brucella infection is not clear. Preclinical research with Brucella endotoxin on laboratory animals has shown that vascular and perivascular inflammatory reactions can develop in the endothelial wall. Encephalopathy in brucellosis is nearly always seen secondary to vascular involvement. Moreover, autoantibodies and immune complex production, which causes neural involvement, has been reported.[2,7,13]

Stroke can develop secondary to mycotic aneurysm rupture in neurobrucellosis. A case who developed neurobrucellosis secondary to subarachnoid bleeding due to a basilar artery mycotic aneurysm rupture has been reported.[6]

Although the imaging methods are important for the diagnosis of neurobrucellosis, the test results must be in accordance with the patient's clinical condition in order to have diagnostic value. A focal cortical cerebral lesion with nodular enhancement and surrounding edema, increase in perivascular vascularization and generalized inflammation of the white matter can be seen on CT and MRI.[9,14] The MRI of our patient showed hemorrhagic infarct areas

supplied by the MCA on the right hemisphere. Although this image is not specific for neurobrucellosis, it explains the stroke in our patient.

In order to prevent complications and relapse in brucellosis, appropriate combination treatment for a sufficient period of time is necessary. Doxycycline, streptomycin, rifampin, and trimethoprim–sulfamethoxazole are recommended for its treatment. As the bacterium is located intracellularly, a double or triple combination regimen is especially important. Furthermore, combinations including third-generation cephalosporins, ampicillin, imipenem, or fluoroquinolone have also been investigated. The duration of treatment for neurobrucellosis is 6 months, however, this duration may be changed based on clinical and laboratory findings.[15,16] This case also received a combination treatment. Motor, sensory, or mental alterations are rarely persistent in patients after treatment and these sequelae, particularly neuropsychiatric symptoms, generally regress. In accordance, we also observed significant improvement in the neuropsychiatric symptoms of our patient.

Stroke can be related to many different etiologies, and neurobrucellosis must be kept in mind especially in young patients. Although CNS involvement in Brucella infection is rare, it is more common in regions such as Turkey, where brucellosis is endemic. A delay in diagnosis can significantly increase mortality and morbidity. In some cases, the disease can cause neuropsychiatric symptoms such as depression, mood changes, delirium, and hallucination, without significant neurological deficits. As neurobrucellosis can clinically present with such symptoms, patients must be evaluated with caution. In conclusion, as our country is one of the regions where brucellosis is common, Brucella and its complications must be kept in mind in the differential diagnosis of neuropsychiatric symptoms and findings.

Conflict of interest: No conflict of interest to declare.

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