A case of neurobrucellosis detected during brucella treatment

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Abstract
Brucellosis is a systemic zoonotic infectious disease caused by the gram-negative Brucella bacteria that can be transmitted from infected animals to humans. Neurobrucellosis occurs when the central nervous system is directly or indirectly affected by Brucella spp. Clinical meningoencephalitis in neurobrucellosis includes meningovascular involvement, parenchymal dysfunction, peripheral neuropathy/radiculopathy, and various degrees of behavioral abnormalities. At the admission of our case, psychiatry was consulted considering psychosis due to decreased speech and agitation, there were no signs of meningeal irritation in physical examination, and no cells were seen in the first CSF examination. In the presence of unexplained neurological and psychiatric symptoms, especially in endemic areas, neurobrucellosis should be considered in the differential diagnosis, and necessary blood and CSF tests should performed.

Keywords
Meningoencephalitis, Brucellosis, Neurobrucellosis

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A case of neurobrucellosis

Introduction
Brucellosis is a systemic zoonotic infectious disease caused by the gram-negative Brucella bacteria that can be transmitted from infected animals to humans. It is the most common zoonotic disease in the world and is an important public health problem in many developing countries. Brucella can affect any organ or system, and the disease manifests in many different clinical forms. Neurobrucellosis occurs when the Central Nervous System (CNS) is directly or indirectly affected by Brucella spp. (available at: https://www.uptodate.com/contents/brucellosis-epidemiology-microbiology-clinical-manifestations-and-diagnosis?search=brucella&source=search_result&selectedTitle=1-104&usage_type=default&display_rank=1.) Neurological involvement rate can be seen in 0-25% of brucellosis cases [1]. The clinical spectrum of neurobrucellosis is very heterogeneous. Neurological manifestations in neurobrucellosis can be seen in the acute or late stages of the disease. In the clinic, it can be seen as acute/chronic meningitis, meningoencephalitis, brain abscesses, myelitis, radiculitis and/or neuritis (cranial or peripheral nerve involvement). Although the incidence of CNS involvement is not high, it may result in serious morbidity [2]. Neurobrucellosis may present with different clinical presentations and its diagnosis may be difficult. Therefore, we aimed to draw attention to this complication with our case.

Case Report
A nineteen-year-old male patient was brought to the emergency room by his relatives with complaints of sudden onset of vomiting, meaningless speech, and decreased speech, was evaluated by a psychiatrist in the emergency room and no psychiatric illness was considered. Although demyelinating and vasculitic diseases were considered in the differential diagnosis in the patient evaluated by a neurologist, consultation with an infectious diseases specialist was recommended in terms of central nervous system infection. The patient was evaluated in the emergency room, and it was learned that he had complaints of sudden onset of vomiting and impaired speech. It was learned that the patient applied to the urology outpatient clinic 8 months ago due to fever and unilateral orchitis, and that the brucella tube test was negative at that time, brucella was not considered, but the patient was diagnosed with brucellosis 5 months later, as complaints of fatigue and joint pain continued. It was learned that the patient had been using rifampicin 1x600 mg tb and doxycycline 2x100 mg tb for 3 months. It was found that the patient regularly used his drugs. From the history of the patient, it was found that he lived in the village and was engaged in animal husbandry.

On physical examination, he was conscious, partially cooperative, and disoriented. His speech was reduced, his interest in the environment was low, his attention was reduced, he had meaningless speech and aggression. There were no signs of meningeal irritation. Other system reviews were normal. There were no signs of acute bleeding or edema in the cranial tomography. Cranial diffusion magnetic resonance imaging (MRI) did not show signs of acute ischemia, and cranial MRI findings showed plaque appearances consistent with bilateral demyelinating/vasculitic lesions in the white matter (Figures 1, 2). The patient underwent lumbar puncture (LP) in the emergency. No leukocytes were seen in the cerebrospinal fluid (CSF) examination. CSF protein was 295 mg / dL (15-45), CSF glucose was 2.5 (45-80 mg / dL), concurrent blood glucose (sour blood sugar) was 111 mg / dL.

The patient was started with ceftriaxone 2x2 gr IV, vancomycin 2x1 gr IV, acyclovir 3x750 mg iv with the diagnosis of meningoencephalitis, and she was taken to the neurology intensive care unit. No features were found in the CSF Gram and ARB staining of the patient. CSF mycobacterium polymerase chain reaction (PCR) was negative, there was no growth in mycobacterial culture, Herpes simplex virus 1 and 2, human parechovirus, enterovirus, mumps and varicella zoster virus were found negative in the CSF viral meningitis panel. There was no reproduction in the CSF and blood culture. In brucella agglutination tests in CSF fluid and blood, neurobrucellosis was
considered in the patient because of positive findings in CSF with a titer of 1/640 and above and a titer of 1/320 in the blood. Treatment was continued with ceftriaxone, rifampicin, and doxycycline. The cooperation and orientation of the patient improved with the treatment. It was detected in 40 cells/mm³ in LP performed on the 21st day of treatment, it was 75% lymphocytes. CSF protein was found to be 124 mg/dL, CSF glucose 32, and concurrent blood glucose 103 mg/dL. Ceftriaxone treatment was completed within 1 month, and the patient was discharged with rifampicin and doxycycline treatment. At the end of the first month of the follow-up, the patient had no complaints, his physical examination was normal. The treatment of the patient was completed for 6 months.

Discussion
Clinical meningencephalitis in neurobrucellosis includes meningovascular involvement, parenchymal dysfunction, peripheral neuropathy/radiculopathy and various degrees of behavioral abnormalities [1]. It can be confused with chronic central nervous system infections or with migraine, convulsion, hemiplegia, temporary parkinsonism, tremor, general rigidity, psychosis and neurosis [3]. Several behavioral and neuropsychiatric diseases, sleep disorders, epilepsy, agitation and depression have been detected in patients with neurobrucellosis. The recovery of cognitive and mood disorders in brucellosis without treatment with antidepressant and/or antipsychotic distinguishes the disease from functional psychiatric diseases [4,5]. Similarly, in our case, psychiatry was consulted, considering it psychosis due to decreased speech at admission, lack of interest and attention to the environment, meaningless speech and aggression, and an increase in anxiety in the last 3 months.

It was stated that the clinical picture of neurobrucellosis can be variable, and the findings are not specific, therefore, CSF examination can be more helpful in making the diagnosis [1,4]. The diagnosis of neurobrucellosis can be made with the presence of a neurological picture that cannot be explained by another neurological disease, isolation of bacteria in the CSF or blood culture, or positivity in serological tests, abnormal CSF findings (low CSF glucose, increased CSF protein, lymphocytic pleocytosis) [3-5]. The low bacterial isolation rate in the CSF (5-30%) necessitates the use of serological diagnostic methods in most of the patients [1,4]. Similarly, in our patient, serologically positive blood and CSF were detected, but bacteria could not be isolated in the CSF and blood culture.

There are four imaging findings in the radiological diagnosis of neurobrucellosis: normal, inflammation (meningeal enhancement), white matter changes and vascular changes. In a study conducted in Turkey, 263 neurobrucellosis cases were evaluated, 54.3% had normal MRI findings, the most common changes were leptomeningeal (n = 44) and basal meningeal involvement (n = 30), white matter involvement with demyelinating lesions (n = 32), chronic cerebral ischemic changes are vascular involvement (n = 57) and brain edema (n = 40) [6].

There is no consensus on antibiotic choice, dose and duration in the treatment of neurobrucellosis. Double or triple combination therapy with doxycycline, rifampicin, trimethoprim-