Brief Report

Brucellar Psychosis

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Abstract
Brucellosis is the most common worldwide zoonotic infection of which psychosis is a rare feature of this disease. Brucellar psychosis should be considered in a patient with unexplained, nonspecific psychological complaints. Its timely diagnosis relies on special attention to the epidemiologic profile of the patient for a possible exposure to the brucella species. This article has presented three cases of brucellar psychosis initially misdiagnosed because the risk factors which made them at risk for the disease were ignored.

Keywords: Brucella, neurobrucellosis, psychosis

Case report

Case A: Acute psychosis

An 18-year-old girl referred to the Emergency Unit of the Department of Infectious Diseases at Imam Reza University Hospital, Mashhad, Iran with high-grade fever and a presumed sepsis syndrome. The patient had an acute psychosis which manifested as a personality disorder that resulted in admission to a psychiatric center two days prior. The patient thought she was a dog. She scratched herself, squatted on the bed like an animal, and howled through the windows. She grabbed at the empty space around her and attacked, attempting to bite anyone within her vicinity. On admission she had an axillary temperature of 38.7°C, pulse rate of 90/min, respiratory rate of 29/min and blood pressure of 100/60 mmHg. The patient was an illiterate girl of 38.7°C, pulse rate of 90/min, respiratory rate of 29/min and blood pressure of 100/60 mmHg. The patient was an illiterate girl who, for most of her life in a village located 130 km from Mashhad. Upon examination, she had no remarkable findings. Her hematological and biochemical parameters were within normal limits. She received intravenous ceftriaxone (1 g, bid) pending culture results of the blood samples. A lumbar puncture was performed but the cerebrospinal fluid (CSF) analysis was normal. On the third day of admission, while her mental status remained unchanged, both the serum and CSF serological assays for acute brucellosis gave significant positive results, as well as the blood culture which isolated Brucella abortus a few days later (Table 1). She was treated with intramuscular streptomycin (1 g, qd), oral rifampin (600 mg, qd) and doxycycline (100 mg, bid) without any anti-psychotic therapy, with dramatic improvement after about ten days. The oral drugs were continued for five months, when her CSF-Wright test had a negative result. She was followed for several months thereafter, only to be assured that there was no problem with her mental status.

Case B: Recurrent acute psychosis

The patient was a 60-year-old peasant man without any significant past psychiatric history. He was admitted to the Department of Infectious Diseases at Imam Reza University Hospital, Mashhad, Iran because of a gradual onset of fever accompanied by headache, nausea and vomiting and progressive confusional state which started about one week before admission. Upon examination, he had an oral temperature of 38.4°C, pulse rate of 98/min and respiratory rate of 18/min. He had no neck stiffness, no abnormal heart sounds, and no skin lesions, however scattered coarse crackles were heard over his right lower lung. He was conscious but disoriented with visual and auditory hallucinations of seeing imaginary people and hearing voices without external stimuli. His mental impairment persisted even though the patient was afebrile, and a lumbar puncture was performed to evaluate for encephalitis. CSF analysis (Table 1) revealed a lymphocytic pleocytosis and he was treated with intravenous ceftriaxone (1 g, bid), ampicillin (1 g, qid) and gentamicin (80 mg, tid) for a possible diagnosis of viral encephalitis with superimposed aspiration pneumonia. He was discharged from the hospital with some improvement after two weeks. A number of weeks later, he was readmitted because of relapsed mental illness that presented again as bizarre behavior and a variety of hallucinations. This time, serologic markers of brucellosis in his serum and CSF confirmed the diagnosis of neurobrucellosis (Table 1). He was treated with trimethoprim-sulfamethoxazole (2 DS tablets/bid) and rifampin (600 mg, bid) for six months with no evidence of mental disturbance at the end of therapy.

Case C: Acute psychosis

A 24-year-old man was referred to Imam Reza University Hospital, Mashhad, Iran with a possible diagnosis of rabies encephalitis. The young man, a rancher who resided in a village near the city had been bitten by a stray dog a few days prior to the onset of his mental disturbance. According to his father, one night the patient returned from the grassland uneasy and restless. He was febrile and stated irrelevant things about himself and others. The patient saw imaginary people and he laughed, cried, bawled, bit himself and insulted others. He had a type of hydrophobia. The...
patient became irritated, withdrew and began to whimper when offered something to drink. There was no evidence of any photophobia, aerophobia, or sialorrhea. However, he was extremely agitated and fidgety. Concerning the possible diagnosis of rabies encephalitis, rabies serum and antirabies were started and the patient also received rabies human immunoglobulin. His CSF analysis was normal, but serologic markers of the patient confirmed acute brucellosis with central nervous system (CNS) involvement (Table 1). Doxycycline (100 mg, bid), rifampin (600 mg, qd) and trimethoprim-sulfamethoxazole (2 DS tablets, bid) were prescribed and the patient was discharged from the hospital with a normal mental status.

**Discussion**

Neurobrucellosis was initially reported by Hughes in 1896. Acute or chronic meningitis is the most frequent nervous system complication. CNS infection can have a chronic course that is characterized by fatigue, low-grade fever, extrapyramidal signs, and cataplexy or the dementia syndrome with attentional and memory deficits. Psychiatric changes in neurobrucellosis are rare. There are few reports of brucellar psychosis in the literature. Analysis of CSF in brucellar meningitis reveals a lymphocytic pleocytosis, elevated protein, and normal or low glucose concentrations. Nevertheless, a normal CSF does not rule out CNS involvement, as in cases A and C. The psychiatric manifestations that have been previously reported are: depression, amnesia, agitation, nightmares, personality disorders, euphoria, nervousness, loss of perception, disturbance of spontaneous and voluntary attention, disturbances in the process of thinking with poverty of content, hallucination, delirium, convulsion, dysarthria, psychosis, and night ravings.

Gram stains and cultures of CSF are often negative; therefore, the diagnosis depends on the presence of specific antibodies or real-time polymerase chain reaction. Most serological studies for the diagnosis of brucellosis are based upon antibody detection and include serum agglutination (standard tube agglutination), complement fixation, rose Bengal agglutination, antibrucella Coombs, and enzyme-linked immunosorbent assay (ELISA). While some experts suggest that ELISA (IgG, IgM and IgA profiles) is the test of choice in the diagnosis of patients with brucellosis, particularly those with chronic or CNS infection, others express concern that ELISA assays suffer from poor sensitivity and specificity when compared with agglutination tests. Osoba et al. have reported the sensitivity of IgM ≥ 1/200 as 77% and IgG ≥ 1/1600 as 41.5% among non-bacteremic patients with brucellosis. Our cases B and C had low serum IgM titers (and low IgG titer for case B), while their agglutination titers were significantly high (Table 1). In fact, detection of neurobrucellosis is based on the existence of a neurological picture not explained by any other neurological disease, as evidenced by systemic brucellar infection and the presence of inflammatory alteration in the CSF.

All three of our cases were misdiagnosed initially despite the strong epidemiologic profile of residing in brucellosis-prevalent rural areas. Initially, no medical professional expressed concern about the possibility of neurobrucellosis. Case A, the sheep herder, was admitted to a psychiatric center even though she had high a grade fever which had been attributed to a superimposed infection. The first presentation of case B was diagnosed a plausible viral encephalitis, but no diagnostic tests for brucellosis were performed. Although the mental status of patients with neurobrucellosis may wax and wane, the partial improvement noted in case B before his second admission was probably due to the administration of ceftriaxone for a presumed bacterial infection. The initial diagnosis of case C, the rancher, was rabies encephalitis, however the interval between the dog bite and onset of symptoms was too short. Two of our three cases (cases A and C) had normal CSF, and in one (case C) the CSF agglutination test was also negative. Neurobrucellosis requires special attention. Most authorities recommend two or three drugs which cross the blood-brain CSF barrier, such as doxycycline, rifampin, and trimethoprim-sulfamethoxazole. The duration of therapy is generally prolonged, varying from 1 to 19 months. Antimicrobials are usually continued until the CSF analysis returns to normal. All three of our cases have responded well to specific antimicrobial therapy without the need for adjunctive anti-psychotic drugs.

These cases demonstrate that brucellar infection can present in various clinical forms. Therefore regarding the growing numbers of immigrants in the developed world, the undulant course of the disease and its marked tendency to relapse, medical professionals should consider a diagnosis of brucellosis in patients who experience unexplainable signs and symptoms that include neurological and psychiatric problems when there is a history of a possible exposure to the brucella species, even in countries where the disease is not endemic.

**References**


**Table 1. Patients’ laboratory data.**

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<tr>
<th></th>
<th>Wright (serum)</th>
<th>2 M E - Wright (serum)</th>
<th>Wright (CSF)</th>
<th>IgM-Elisa (serum)</th>
<th>Ig G - ELISA (serum)</th>
<th>WBCCSF</th>
<th>Glucose CSF</th>
<th>Protein CSF</th>
<th>Blood culture</th>
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<td>1/2560</td>
<td>1/80</td>
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<td>---</td>
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<td>Neg</td>
<td>76 mg/dL</td>
<td>35 mg/dL</td>
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<td>Case B</td>
<td></td>
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<tr>
<td>First</td>
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<td>---</td>
<td>---</td>
<td>150 μL</td>
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<td>Neg</td>
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