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Case Report / Olgu Sunumu

Psychotic Attacks Due to Toxic Neurobrucellosis in Two Adolescent Patients

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ABSTRACT

Psychotic attacks due to toxic neurobrucellosis in two adolescent patients

Brucellosis is a multisystem disease which can present with a broad spectrum of clinical manifestations and complications and affect the central nervous system directly or indirectly. Immunopathologic mechanisms like T-cell mediated cytotoxicity and microglia activation are suggested to play a role in neurobrucellosis. The diagnosis of toxic neurobrucellosis is confirmed by isolation of Brucella organism from blood cultures and/or positive Coombs Wright test and the Standard agglutination test (SAT) in serum when there are no cerebrospinal fluid (CSF) findings. The magnetic resonance imaging (MRI) of brain in patients with neurobrusellosis may show different findings mimicking such neurological diseases as inflammation, white matter changes and vascular involvements and other infectious and inflammatory conditions. Different clinical manifestations of neurobrucellosis have been described including meningitis, meningoencephalitis, myelitis, and psychiatric disorders. It has been indicated in case studies that neurobrucellosis may lead to psychotic disorders. In this study, we present two adolescents who presented with psychotic symptoms due to toxic neurobrucellosis.

Key words: Adolescent patient, psychotic episode, toxic neurobrucellosis

ÖZET

Toksik nörobruselloza bağlı iki ergen hastada görülen psikotik atak

Birçok organı etkileyebilen ve çeşitli klinik tablolarla seyredebilen Bruselloz enfeksiyonu santral sinir sistemini direkt ya da indirekt yollarla etkileyebilir. Sitotoksik T hücre aracılı ve mikroglia aktivasyonu gibi bazı immünopatolojik mekanizmalar nörobrusellozda rol oynayabilir. Toksik nörobruselloz tanısı herhangi bir beyin omirilik sıvısı (BOS) bulgusu olmamasına rağmen kan kültüründe etkenin üretilmesi veya serolojik olarak pozitif bulunması ile doğrulanır. Nörobrusellozun manyetik rezonans görüntülemesinde inflamasyon, beyaz cevher değişiklikleri ve damar tutulumları gibi nörolojik hastalıkları, diğer enfeksiyöz ve enflamatuvar durumları taklit eden değişik bulgular görülebilir. Nörobrusellozda menenjit, meningoensefalit, myelit ve psikiyatrik bozukluklar şeklinde farklı klinik tablolar tanımlanmıştır. Vaka çalışmalarında nörobrusellozun psikotik tablolara yol açabileceği bildirilmiştir. Bu çalışmada toksik nörobruselloza bağlı iki ergen hastada görülen psikotik ataklar sunulmuştur.

Anahtar kelimeler: Ergen hasta, psikotik nöbet, toksik nörobruselloz

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INTRODUCTION

Brucellosis is an infectious disease which may be transmitted to humans through skin contact with such bodily fluids as urine, faeces, saliva, and blood from such infected animals as sheep, pigs, dogs, and camels, or as a result of consuming meats or particularly such fresh and insufficiently pasteurized dairy products as milk and cheese of such animals, may affect many organs and mimic symptoms of many diseases since it

can present with many different clinical manifestations and complications including especially fever, night sweats, headache and painful joints, and therefore may result in delayed diagnosis (1-3). Insofar as causative agents of the disease populate and reproduce within mononuclear phagocytic system cells, the disease may affect many systems including especially reticuloendothelial system, musculoskeletal system, gastrointestinal system, cardiopulmonary system, genitourinary system and central nervous system (4-6).

Just as brucella may affect central nervous system through direct invasion thereof, which is called neurobrucellosis, it may also affect it by means oftoxins (7). It may present with meningitis, meningoencephalitis, meningovascular complications, white matter disease or various psychiatric symptoms (2,8,9). It has been reported that neurobrucellosis may mimic insidious psychiatric diseases and present with psychotic manifestations and complications (2,6,9). It is generally diagnosed by clinical properties, production of bacteria in cerebrospinal fluid (CSF), demonstrating antibody titre thereof and CSF findings (domination of lymphocytes;decreased glucose level and increased protein level) (2,6). A culture positivity of less than 25% of patients and the fact that patients with negative CSF serology have also been reported suggest that it may be difficult to diagnose in some patients (3,10,11). In this article are presented psychotic manifestations and complications of two adolescent cases resulting from toxic neurobrucellosis with brucella serology positive in blood, but negative in CSF.

CASE 1

A is a 15-year-old student living in a village within the municipal boundaries of Van Province. Such complaints as talking nonsense, hallucinations, laughing to oneself, detrimental behaviour towards people, insomnia and lack of appetite were reported to have started a month before the patient's application to the psychiatry outpatient service. He was reported to have started showing such behaviour as burning his clothes with a lighter, aimlessly carrying around the dry woods stacked in front of the house, not allowing other family members to speak, reluctance to stay in the same place as other family members, breaking plates and bending forks while eating, beating his siblings, and restlessness and continuous movement. He said that he heard voices threatening him and saying "We will kill your elder brother; we will kill your father", saw his father and uncle as ghostly figures around him and was followed by strangers who had guns in their hands to kill him. He was reported to have been quiet, intended and mediocre student with few friends, respectful to his elders and performing tasks he was given in his premorbidity. In his physical examination, it was revealed that he had pain and sensitivity in his left hip joint aggravating upon movement and causing a limp in his walk. He had no drug use history. There was a history of diagnosis and treatment of brucellosis in family members; but no psychosis, schizophrenia or any other psychiatric disease history was present in his family history. It is indicated in his medical history that he consulted a doctor about two months earlier due to a pain in his left thigh and hip area and was initiated on a treatment upon diagnosis of brucellosis. Results of mental state examination of the patient hospitalized in psychiatry clinic with preliminary diagnoses of acute psychotic attacks and psychotic disorder are as follows: he had a reduced level of self-care; he was indifferent to consultation and his surroundings; it was difficult to communicate with and elicit goal-oriented answers from him; he had a reduced level of attention; had visual and auditory hallucinations in perception, and poor content of thought and persecutory delusions. He showed restricted affect, psychomotor restlessness and aggression in behaviour, and had lack of insight, reduced amount of sleep and appetite.

In laboratory analyses, white blood cell count was 7700/mm^3 (polimorphonuclear leukocytes 54.5%); haemoglobin count was 15.5g/dL and thrombocyte count was 303000/mm^3. Results of liver, kidney and thyroid function tests as well as B12, folic acid and Electroencephalopathy (EEG) were reported to be within the normal range. Brucella tube agglutination test Wright was positive in the titre of 1/60. Protein level was 0.8 mg/dL glucose level 53 mg/dL and no cells were

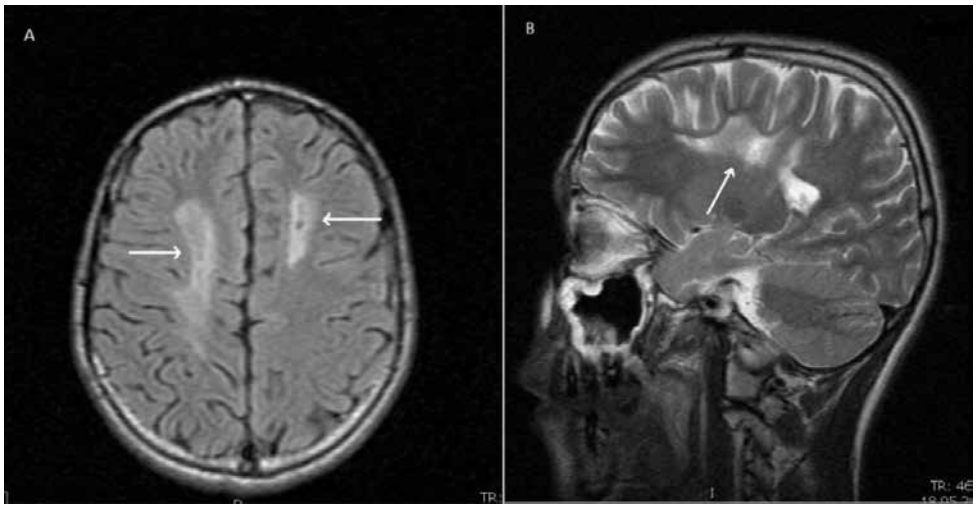

Figure 1: Cranial MR shows leukoencephalopathic changes on axial flair (A) and sagittal T2-weighted (B) series in peri-supraventricular white matter in both hemispheres.

detected in the analysis of CSF taken by lumbar puncture (LP). Wright tube agglutination test, CSF Brucella IgM and IgG were reported as negative (-) in CSF. Brucellosis treatment was initiated again. Leukoencephalytic changes in peri-supraventricular white matter were monitored in both cerebral hemispheres through Magnetic Resonance Imaging (MR) (Figure 1). Milimetric focal edema in inferior acetabular skeleton and signal changes which may be compatible there with were detected in magnetic resonance (MR) imaging of the hip.

Patient was initiated on olanzapin treatment with a dose of 10mg/day as from his first hospitalization and the dose was gradually increased up to 20mg/day. In the follow-up visits of the patient a significant decline was noted in complaints and such complaints as insomnia, lack of appetite, auditory and visual hallucinations, delusions, agitation and disorganized behaviour were eliminated. However, such complaints as dullness, reduced speech and reluctance were monitored to persist in his 6-month follow-up.

CASE 2

B is a 14-year-old female applying for treatment from Patnos district of Province of Ağrı. She dropped out of school in the 6th grade and is the second of eight siblings, and does not work. The patient, not having applied for psychiatric help so far, was brought to our psychiatry outpatient service by her relatives with complaints of such behaviour as talking nonsense, talking to herself, insomnia, nervousness, hearing voices calling her name, leaving home, breaking things, punching people around her, attempting at setting the house on fire, tearing her clothes off, seeing non-existent things such as a man in white, two girls and two dogs and saying that she was talking with them and an increase in movements and amount of speech.There was nothing special in her medical history. In her family history, no members of her family had psychosis, schizophrenia and any other psychiatric disorder. She was reported to have been a mediocre student and an extraverted adolescent often quarrelling with her family in her premorbidity. She had no history of drug use and was not taking any medication. In her mental state examination; she showed her age and had restricted eye contact, reduced level of self-care, her clothing was below expectations for her socio-cultural level; had little interest in the consultation; was conscious, had partly impaired orientation to place and time, full orientation to person, distractibility, difficulty in focusing, distractible attention, immediate and recent memory functions were impaired, had simple visual and

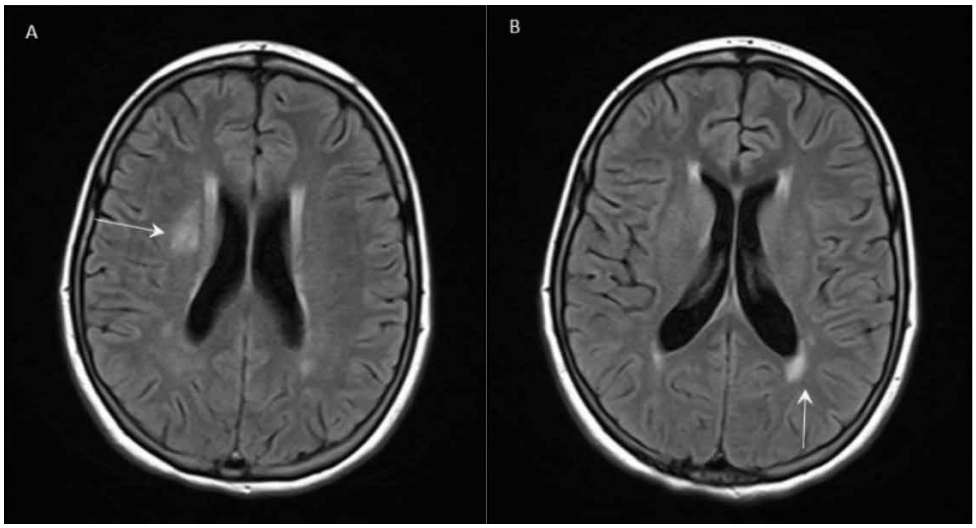

Figure 2: Cranial MR shows increased white matter signals on axial flair (A) at the level of corona radiate on the right hand side and axial flair (B) in the vicinity of lateral ventricle atrium on the left hand side.

auditory hallucinations, no insight into the hallucinations, disordered associations in thought process and train of thought and perseverations. As for her content of thought, she had such grandiose persecutions and reference hallucinations such as that she was the God and a prophet and married with children, and her mother was not her real mother; some of her relatives were demons and their neighbours spread rumours about her. Her affect was restricted, variable and inappropriate. Mood: indifferent on the whole, dysphoric and delirious from time to time. She experienced increased psychomotor activity and had occasional aggressions in terms of behaviour. She has a reduced amount of sleep and a normal appetite. She was hospitalized in psychiatry clinic with preliminary diagnoses of psychotic attacks and organic psychotic disorder. Treatment was initiated on quetiapine 200mg and risperidone 2mg/day and doses were increased up to 400mg/day and 6mg/day respectively. As for organic aetiology, increased white matter signals were recorded and monitored at the level of right corona radiata and in the vicinity of left lateral ventricle atrium in Brain MR (Figure 2). Lumbar puncture (LP) was applied to the patient, whose results were assessed by an adult neurologist since there were no child neurologists at the clinic, which revealed nothing special. In her CSF analysis, protein level was 49mg/dL, glucose 35mg/dL (simultaneous blood glucose 80mg/dL) and white blood cell count 20/m^3. Wright agglutination tests yielded negative results in CSF and serum. In her clinical follow-up visit, she was consulted to the department of infectious diseases since she had fever at sub-febrile levels, and a blood culture sample collected at the time of her fever was sent there too. Brucella reproduced in the blood culture. It was found out that she stayed at her uncle's in village as a guest for a few days shortly before her received medical history and eaten cheese in the meantime. She was initiated on doxycycline and trimethoprim/sulfametoxazole treatment with diagnosis of brucellosis at doses of 200mg/day and 800/160mg/day respectively. We had difficulty in bringing the patient's psychiatric symptoms under control in the follow-up visits so far; her visual and auditory hallucinations persisted; her agitated behaviour in the first days of her hospitalization in the psychiatry service were eliminated; her disorganized behaviour such as taking her clothes off in public was recurring from time to time. She was talking to herself, speaking of genies and demons, and stating that she saw soldiers. Her psychomotor restlessness persisted. In the third month of her hospitalization in the psychiatry clinic, an evident improvement was noted

in the state of the patient thanks to treatment of brucellosis initiated later in the course of her stay, and quetiapine treatment was discontinued with gradual reduction of the dose. The patient was discharged from the hospital on risperidone 3mg/day, and in her follow-up visits, it was observed that laughs which may be considered awkward persisted; she managed her self-care with her elder sister's warning; however, she did not return to her premorbid functionality.

DISCUSSION

Neuropsychiatric complications of brucellosis can be caused either by its acute toxic effect or in the case that infection factor deposits directly in the central nervous system. Classical neurobrucellosis can be diagnosed by production of infection factor, detection of antibodies or increased protein levels and decreased glucose levels due to domination of lymphocytes; in toxic neurobrucellosis, on the other hand, for all that CSF findings are normal brucella can be identified as culture or serologically in the blood (7). Furthermore, the fact that the clinical picture cannot be explained by other medical conditions and a previous history of brucellosis may pave the way for diagnosis of neurobrucellosis (9). Contrary to the fact that CSF findings were negative, a recent diagnosis of brucellosis, detection of antibodies in the blood and presence of joint findings indicating systemic involvement in addition to brain imaging findings for the first case, and fresh cheese consumption history, inexplicable brain MR findings and fever and identification of the infection factor in the blood culture for the second case reinforce the fact that psychotic pictures accompanied by present atypical symptoms in patients from rural areas arise out of neurobrucellosis.

It has been stated in previous studies that radiological imaging may assist in diagnosis of neurobrucellosis, that various findings have been detected from almost half of the cases, that various findings such as inflammation, vascular and white matter changes, demyelinating appearance and leukoencephalopathy-like extensive involvement of the white matter may be observed, and that findings and symptoms may be reversible in some cases, however, in others, although clinical and CSF symptoms may revert to normal with adequate treatment, no improvement has been recorded with regard to white matter changes in MR follow-ups (1,2,8,10-12). Detection of leukoencephalopathic areas in our first case and demyelinating-like focuses in our second case confirm neurobrucellosis diagnosis in line with the literature.

Although cause of changes detected in neurobrucellosis via brain imaging are not known precisely, it is suggested that it may be associated with immonopathologic processes and linked to cytotoxic T cell response stated to play a key role in immune response of brucella together with autoimmune and excessive microglia activation despite its benefits on the whole (1,10,11). These authors have stated that infection may trigger immune mechanisms leading to demyelination, changes they observed in neurobrucellosis patients in their histopathological autopsy studies resembled demyelinating lesions in multiple sclerosis and it may be confused with this disease. These data suggest that white matter involvement may be an immune-mediated reaction in central nervous system to brucellosis infection. Persistence of residual symptoms in follow-up visits of the two cases demonstrates that the bacteria may give rise to longer and chronic processes due to toxic effect since bacteria can trigger immune mechanisms (9). These cases have shown that the diagnosis of neurobrucellosis may be difficult and it can be confused with other various diseases due to variability of laboratory results. Neurobrucellosis must be kept in mind in cases of multiple demyelinating lesions in the brain even if anti-Brucella antibodies have not been detected in CSF especially in endemic areas.

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