

## Neurobrucellosis and steroid therapy

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### ABSTRACT

Brucellosis is a relatively frequent disease in the Mediterranean and Middle East regions. We describe a young adult male presenting with a 6-month history of fever, headache, malaise, and mental dullness. CSF studies revealed lymphocytic pleocytosis with increased protein and low glucose. Serum and CSF analysis were strongly positive for brucella. He was prescribed ceftriaxone, doxycycline, rifampin, and co-trimoxazole, but two days later he developed quadriparesia with evidence of myelitis in cervical MRI for which he has received methyl prednisolone 500mg Iv for 5 days continued with prednisolone 50mg daily. His condition was improved significantly. This case is reported because of the importance of steroid therapy in brucellosis.

**Keywords:** *Neurobrucellosis, Steroid therapy, Methyl-prednisolone.*  
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### INTRODUCTION

Brucellosis, malta, Mediterranean or undulant fever is a zoonotic disease. The array of nonspecific signs and symptoms of human brucellosis led Simpson to remark "No disease" (1).

Human brucellosis is mainly caused by 4 species belonging to the genus *Brucella*. These are *B. canis*, *B. abortus*, *B. swiss*, and *B. melitensis*, however, the most severe form of human brucellosis is caused by *B. melitensis*. Brucellosis is mainly transmitted through the consumption of raw milk or its products or consumption of raw or under-cooked liver and meat or even contact with

animal especially sheep or goats (1). Males are affected twice as frequently as females.

Brucellae are slow growing, small, non-spor-forming, immotile, non-encapsulated, aerobic, intracellular, gram-negative coccobacilli. Occasionally, they invade the central nervous system and may lead to permanent neurological deficits if left untreated. Thus, early diagnosis based on clinical manifestations and laboratory confirmation is mandatory.

### PATIENT

A 21-year old right-handed male teacher presented with a history of generalized headache during the past 3 months. He stated no other problem 6 months ago when he developed productive cough with greenish non-bloody sputum and intermittent fever without chills, loss of

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appetite, constipation, generalized malaise, fatigue, arthralgia and low back pain with accompanied mild generalized non-throbbing headache. Furthermore, he experienced apathy and was uninterested in his surrounding and preferred lying in bed, not talking to relatives and refused to work 3 months prior to his admission. He could not take care of himself and was completely bedridden during this time. His headache aggravated so that he was urged to seek medical attention. During this period, he lost his weight about 10kg and complained of night sweating. However, he did not complain of blurred vision, diplopia, vomiting, seizure, and articular swelling. He could remember a history of contact with cattle (goat) and ingestion of non-pasteurized milk. Other members of his family were in good health.

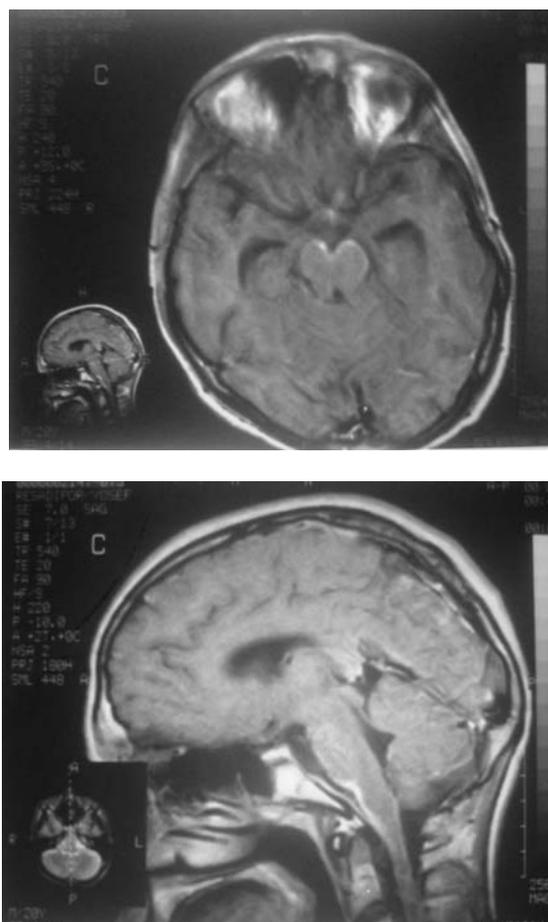
On physical examination, the patient appeared cachectic, ill and apathetic with generalized muscle wasting. He was blinking infrequently (10/min) and was not answering questions correctly. He was febrile (38°), but his blood pressure and pulse and respiratory rates were within normal range. He weighted 40 kg. Cardiac, pulmonary and abdominal examination revealed nothing significant.

On Folstein's minimal state examination, he could correctly state the time only, but respond other questions uninterestedly. He spoke with frequent pause and hesitations and was uttered in single words or short phrases and his speech was monotone.

His pupils were equal and reactive and fundoscopic examination was normal. Extraocular movements were full with bidirectional horizontal nystagmus especially to the left side. Facial sensation and movement were normal. The remaining cranial nerve functions were preserved and the strength of the extremities was normal. The plantar response was flexor; however, there were no primitive reflexes. There was fine tremor especially at the right side with minimal cog-wheel rigidity in both upper extremities. Cerebellar tests

were impaired at the left side. He had neck stiffness and positive Kernings and Brudzinski signs. He walked slowly with shuffling and small shallow steps with mild flexed posture and decreased both arm swing.

The same day, brain MRI with and without contrast was performed and showed pial enhancement along the anterior surface of the brainstem (figure 1). Then, a lumbar puncture was carried out and the fluid was xanthochromic, not under tension and the analysis was as follow: total protein 840mg/dl, sugar 40mg/dl (simultaneous blood sugar 145mg/dl) and WBC count 715/mm<sup>3</sup> (12% polymorphonuclear and 88% lymphocyte), RBC count 50/mm<sup>3</sup> while routine gram and acid-fast staining were negative.



**Figure 1.** A T1- weighted scan of brain with gadolinium showing pial enhancement along the anterior surface of the brainstem



## DISCUSSION

Brucellosis is still a frequent disease in the Mediterranean and Middle East regions. Physicians should remember that it may first present with neurological manifestations (2). Although depression and mental inattention are common complaints in brucellosis, direct invasion of central nervous system occurs in less than 5% of cases (1,3,4). Indeed, neurological manifestations may appear during the active phase of disease.

Neurobrucellosis has a confusing picture that may affect any part of the central and peripheral nervous system. According to clinical and radiographic findings, it seems that our patient developed transverse myelitis as a complication of neurobrucellosis. Meningitis can be the presenting manifestation or it may occur later (5). Prior investigators have reported neurobrucellosis to be presented with acute or chronic meningitis, encephalitis, brain abscess, subdural empyema, spinal epidural abscess, cord compression, myelitis, radiculopathy (usually lumbosacral), myelopathy, demyelinating syndrome, multifocal white matter disease, meningovascular syndrome (transient ischemic attack or stroke), intracerebral hemorrhage from mycotic aneurysm, hydrocephalus, papilloedema and intracranial hypertension, optic neuritis, diabetes insipidus, cranial nerve palsy (6<sup>th</sup>, 7<sup>th</sup> and 8<sup>th</sup> nerve), psychosis, parkinsonism, peripheral neuropathy, Guillain-Barre syndrome and myositis, epileptic seizure and aggressive mood (1-12). Generally, CNS infection can have a chronic course characterized by fatigue, low grade fever, extrapyramidal signs, and cataplexy (13). Unfortunately, neurobrucellosis could be toughly differentiated from other causes of meningitis (1). CSF analysis of patients with neurobrucellosis may reveal a lymphocytic pleocytosis, elevated protein content and low to normal glucose level (1,2,5). Gram stains are usually negative and culture may reveal positive in less than one quarter of the cases (1). Finally, the diagnosis is confirmed by finding

specific antibodies in the serum and CSF as well as response to specific therapy (1,5). The most frequently used test is standard tube agglutination test (STA). Most cases of active infection show titers higher than 1/160 (1). On the other hand, coomb's test may be the only positive serological study (14). Prozone phenomenon due to the presence of blocking antibodies may cause false negative reactions in ST. When agglutination tests are equivocal, the brucella ELISA study can be helpful (1). Furthermore, MRI may present cerebral atrophy, signs of chronic meningitis, multiple infarcts or hydrocephalus (13).

Neurobrucellosis is treated with a three-drug regimen including doxycycline, an aminoglycoside and rifampin for at least 12 weeks; however, children aged less than 8 years are treated with co-trimoxazole in combination with an aminoglycoside and rifampin. Although steroids are not a constant part in treatment of brucellosis and adding steroids in neurobrucellosis has not been proved to be consistently beneficial (15), adjunctive corticosteroid therapy has been used for concurrent vasculitis or demyelinating disease (5).

In summary, brucellosis should be kept in mind in the differential diagnosis of nearly all neurological disease in endemic area and in every patient presenting with features of chronic lymphocytic meningitis. A high index of suspicion for brucellosis is particularly true if the patient has a high risk occupational background or consumes non-pasteurized milk or raw meat and administering steroid as an adjunctive therapy for neurobrucellosis should be considered before developing major complications.

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