

Extensive cranial, spinal and abdominal involvement in brucellosis: a case with review of the literature

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DOI: 10.18621/eurj.378485

ABSTRACT

Brucellosis is still an endemic disease in certain parts of world. It's clinical and radiological features are crucial for an accurate diagnosis. Although systemic disease in brucellosis shows common typical features, it's also very important to know the uncommon features of multisystemic involvement. Herein we present a case of brucellosis with unique imaging features of extensive cranial, spinal, abdominal involvement in a middle aged woman.

Keywords: *Brucella*, spine, multisystemic, magnetic resonance imaging

Received: January 13, 2018; Accepted: May 2, 2018; Published Online: May 28, 2018

Brucellosis is a multisystemic, granulomatous infection involving several organs or systems of the body. It's mainly seen in endemic areas of the world and transmitted from animals to humans via unpasteurized milk and milk products or direct occupational contact [1]. Systemic dissemination can cause the disease to become recurrent and chronic if it progresses after resolution of acute phase. Osteoarticular system is found to be the most common site of involvement followed by central nervous, genitourinary systems, liver and skin [2]. Although central nervous system involvement is not very common it causes important sequela. Here we present a case of brucellosis with extensive spinal, cranial and abdominal involvement.

CASE PRESENTATION

A 48-year-old woman admitted to our hospital

with fatigue, abnormal gait, weakness in legs, vertigo and hearing loss complaints. Medical history examination revealed that her symptoms were progressive over the last 18 months. She told that she had worked in a farm with responsibility of animal care. Her general condition was good; she exhibited full consciousness, orientation and cooperation. Neurological examination showed features compatible with pyramidal and sensorineural system involvement. ENT examination also confirmed bilateral sensorineural hearing loss. Laboratory tests, including liver and renal functions, urine and blood biochemical analysis were all within normal limits except mild elevation of serum cholesterol.

MRI examination of brain and spinal cord were performed to evaluate a possible central nervous system pathology. Cranial magnetic resonance imaging (MRI) showed T2-hyperintense cortical nodular lesions with mild perilesional vasogenic edema at the right frontal lobe (Figure 1). Lesions



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e-ISSN: 2149-3189

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Figure 1. Signs of early cerebritis and meningitis in cranial MRI. Enhancing cortical nodular lesions in the right frontal lobe (arrow) with peripheral vasogenic edema (open arrow) can be seen clearly on sagittal post-contrast T1W (a) and FLAIR (b) images. Diffuse meningeal enhancement extending to the spinal cord (short arrows) is also noticed on sagittal post-contrast T1W image (c).

were diffusely enhancing after iv. gadolinium (Gd) injection. There was also diffuse prominent pachymeningeal contrast enhancement extending to the cervical spinal region that is compatible with meningitis (Figure 1). Posterior fossa imaging demonstrated that cisternal parts of bilateral trigeminal, abducens, facial and vestibulocochlear nerves were also thickened and showed diffuse enhancement through their course (Figure 2). Retrospective evaluation of the cranial MRI, which was performed 10 months ago, appeared to be normal besides persistent and stable slight ventriculomegaly.

Spinal MRI examination covering cervical, thoracic and lumbar regions also demonstrated diffuse meningeal enhancement (Figure 3). A longitudinally extending extramedullary soft tissue mass slightly compressing the spinal cord was noticed at the levels

of Th6-7 vertebrae (Figure 3). This lesion showed hypointensity on T2W images and showed diffuse homogenous enhancement. There were also diffuse, poorly delineated increased signal on T2W images effecting the cross section of the spinal cord at the levels of Th1 to Th4 and Th11 to L2 vertebrae. The spinal cord was edematous and showed patchy enhancement after iv. Gd injection at the levels of Th1 to Th4 vertebrae (Figure 3). Findings were thought to be compatible with spinal meningitis, multilevel spinal cord myelitis and extramedullary granuloma. Vertebral column and intervertebral disks did show any specific pathology besides mild degenerative changes.

Chest X-ray, thoracic and abdominal CT imaging were performed to rule out any possible primary malignancies and metastatic processes. While X-ray and thorax CT images were unremarkable, abdominal CT

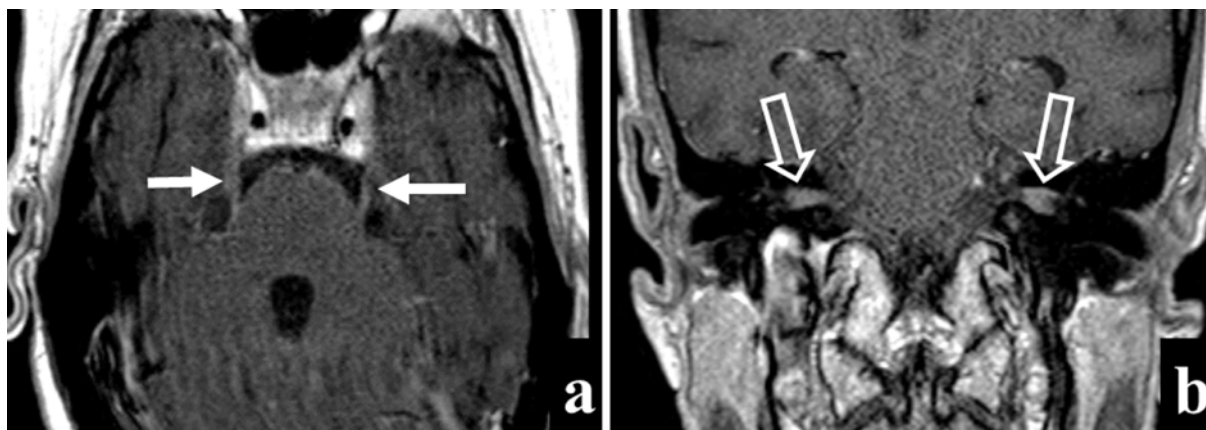


Figure 2. Demonstration of cranial nerve involvement in posterior fossa MR images. Diffuse enhancement of bilateral trigeminal (a, arrows), facial and vestibulocochlear (b, open arrows) nerves can be seen in post-contrast coronal (a) and axial (b) T1W images.



Figure 3. Spinal meningitis, transverse myelitis and extramedullary granuloma formation in MR images. Post-contrast sagittal T1W images of servical (a) and thoracic (b) regions show diffuse meningeal enhancement enshasing the whole spinal cord (arrows). Spinal cord is edematous and shows increased signal at the levels of Th1 to Th4 (c) and Th11 to L2 vertebrae (d) in sagittal T2W images (open arrows). There’s also contrast enhancement in spinal cord itself at the upper thoracic region (a, short arrow). Extramedullary soft tissue that’s causing compression of spinal cord at the levels of Th6-7 vertebrae, shows low signal on T2W images (d, dotted arrow) and enhances diffusely after injection of contrast medium (b, dotted arrow).

images showed lobulated, thick, crescent shaped hypodense lesions located at the subcapsular regions of both liver and spleen (Figure 4). Ultrasonographic evaluation confirmed subcapsular collections as hypoechogenic, lobulated collections which have internal septations (Figure 4). Abdominal MRI

examination demonstrated that these lesions also have diffuse hypointense signal on both T1W and T2W images (Figure 4). There were no diffusion restriction and contrast enhancement found in these collections.

Evaluation of these images with clinical findings pointed out a possible granulomatous infection.



Figure 4. Hepatosplenic subcapsular collections in abdominal ultrasound, CT and MRI images. Hypodense collections located at the subcapsular regions of liver (a) and spleen (b) can be seen in coronally reformatted post-contrast CT images (arrows). Ultrasound image also shows hypoechogenic subcapsular hepatic collection (c, open arrow). Axial T2W MRI image (d) demonstrates diffuse hypointense signal in these collections (short arrows). It’s importantly noted that neither calcifications (CT and ultrasound images) nor enhancement after injection of contrast medium (CT and MR images) was seen in these collections.

Lumbar puncture was performed to clarify imaging findings. Macroscopic examination of cerebrospinal fluid (CSF) showed decreased viscosity with dark-yellow color change. Laboratory examination showed prominent elevation of protein (4405 mg/dL), elevated leucocytes (109/mm³), normal chlorine (109 mEq/L) and normal glucose (62 mg/dL) with concurrent blood glucose also in normal limits (101 mg/dL). Acid-fast bacilli stain and PCR for mycobacterium turned out to be negative and together with non-specific thorax imaging findings, neurotuberculosis and neurosarcoidosis were excluded from differential diagnosis list. Test for *Treponema pallidum* from CSF was also found to be negative. Since the patient had a job history with direct animal contact in a farm and moreover she has been living in an endemic region, laboratory tests for Brucellosis were performed. Rose-Bengal and tube agglutination tests within blood serum and CSF were positive (1/80 and 1/640 in titers, respectively). Although blood cultures did not yield growth for any bacteria, diagnosis of brucellosis was made considering the relatively low sensitivity of cultures for *Brucella* spp. [1]. Patient was then treated with combination of ceftriaxone, rifampicin and doxycycline. Symptoms of fatigue, muscle weakness and hearing loss were found to be partially relieved at control examinations after hospital discharge. Follow-up abdominal ultrasonography and MRI examination performed at 3th month did not show any change in hepatosplenic subcapsular collections.

DISCUSSION

Hereby we presented a case of brucellosis with extensive, progressive multisystemic involvement. Central nervous system involvement of brucellosis is rare; reported incidences vary between 0.5%-25% in different studies [2-4]. Most common manifestations of neurobrucellosis are meningitis, meningoencephalitis, cerebritis, brain abscess, leukoencephalopathy, demyelinating or vascular diseases [3, 4]. Among those, meningitis and meningoencephalitis are seen in approximately half of the cases [3]. Pseudotumor cerebri together with optic neuritis may cause papilledema. Vestibulocochlear nerve is the most commonly affected nerve causing hearing loss. MRI with contrast is the method of

imaging to evaluate neurobrucellosis. Kizilkilic and Calli [3] indicated that the course of cerebral parenchymal infection in neurobrucellosis resembles to those seen in chronic brain abscesses starting from early cerebritis to well demarcated rim enhancing abscess formation. At the presented case, brain MRI showed diffuse pachymeningeal thickening and enhancement together with nodular, diffusely enhancing, T2 hyperintense lesions located at the right frontal cortex. Findings were determined to be recently developed since the former MRI scan was normal. Together with the findings compatible with meningitis and spinal infection, these cortical lesions appeared to be the components of "early cerebritis" phase of parenchymal infection resembling tuberculomas of neurotuberculosis. Lack of diffusion restriction and peripheral enhancement ruled out classical abscess formations that may be seen in later phases of progressing infectious course. Posterior fossa imaging delicately showed involvement of 8th and other cranial nerves which may be only partially seen in routine cranial MRI examinations. Presence of widespread cranial nerve involvement although the patient had symptoms of only vestibulocochlear nerves, emphasizes the benefits of posterior fossa imaging in this group of patients.

Osteoarticular system, including the spinal column is the most common site of focal disease seen in 25%-65% of Brucellosis cases [2, 5]. Disruption of blood brain barrier results in meningitis and also spondylitis. Involvement of spinal cord itself is a very rare entity [5]. Spinal granulomas are also rare complications more commonly seen in tuberculosis and may develop from myelitis. Our case have imaging findings compatible with spinal meningitis, granuloma and multilevel spinal cord lesions compatible with longitudinally extensive transverse myelitis without primary focus of spondylodiscitis. We believe that this might be the first case of brucellosis in the English literature with simultaneous, multilevel, long segment transverse myelitis without spondylitic origin. Only Kirshnan *et al.* [4] presented a case of brucellosis with recurrent episodes of transverse myelitis under controlled treatment. Besides our patient had symptoms over approximately for 1.5 years without any treatment; lack of previous spinal imaging raises doubts about the time of initiation and the synchronicity of spinal cord lesions. We thought that

thick exudate in CSF together with meningeal thickening may have caused focal obstructions in flow resulting in adhesions and loculations. Pooling of CSF in these areas precipitated focal inflammatory processes and resulted in granuloma and myelitis at multiple segments. Low viscosity and very high pleocytosis in CSF also supports this theory.

Reticuloendothelial system is almost always affected in systemic brucellosis. Hepatic and splenic involvement in brucellosis is not rare and reported with varying incidences ranging from 2% to 60% in different series [2, 6]. Presentation may change from mild granulomatous hepatitis to acute/subacute abscesses in both liver and spleen. Cases with hepatitis are generally underdiagnosed because of insidious course. Elevation of liver enzymes may be a clue but not all cases with elevated liver enzymes are can be evaluated as liver involvement of brucellosis. Hepatomegaly, splenomegaly, cholecystitis, pancreatitis, colitis, peritonitis and lymphadenopathy may also be seen [2]. Colmenero *et al.* [6] described rare cases of chronic hepatosplenic abscesses in brucellosis. They identified intraparenchymal and subcapsularly located, hypodense and peripherally enhancing abscess formations in CT examinations that were histopathologically verified. All of the cases presented large central calcifications. Spontaneous splenic rupture (SSR) is also another rare entity that occurs due to several etiological factors. Renzulli *et al.* [7] categorized the etiological factors of SSRs in their systematic review as follows; malignities, infectious disorders, inflammatory disorders, drug-related disorders, mechanical disorders. Dülger *et al.* [8] presented an extremely rare case of atraumatic SSR due to *Brucella* itself. The infectious processes cause some precipitating factors making the spleen more susceptible to hemorrhage and rupture: congestion and dilatation in the sinusoids, capillary thrombosis and focal necrosis in the splenic pulps. At the presented case, subcapsular lesions in both liver and spleen did not enhance in CT and MRI examinations unfavoring expected abscess formations due to brucellosis. Furthermore, lesions were diffusely hypointense on both T1W and T2W images. Granuloma formations also can cause focal hypointense signal changes in MRI due to coarse calcifications. Since CT imaging did not show any sign of calcification, laboratory examinations did not show abnormalities in liver

enzymes and thrombocyte counts, patient did not have a symptom of upper quadrant pain and did not have a history of trauma, follow-up examinations did not show any resolution; these lesions were thought to be either chronic subcapsular hematomas resulting spontaneously from brucellosis or chronic non-calcified granulomatous collections. Liver and spleen sizes were normal and there was no sign of intraabdominal bleeding on CT scan to suspect spontaneous splenic or hepatic rupture at this stage. Any further histopathological confirmation could not be made since the patient did not confirm fine needle aspiration procedure.

CONCLUSION

Brucellosis is an endemic disease in certain parts of the world. Recognition of the disease and its diverse complications is crucial for a timed treatment to avoid sequela, especially in cases of neurobrucellosis. It's much easier to diagnose brucellosis in a patient with lumbar spondylodiscitis but absence of it should not remove the suspicion of systemic or focal forms of the disease. Differentiation from other granulomatous diseases, vasculitic syndromes, malignancies is also important and can be challenging. Above mentioned spontaneous hepatosplenic subcapsular collections, multilevel transverse myelitis and spinal granulomas are unusual components of the disease that should be kept in mind in evaluation of brucellosis patients.

Authorship declaration

All authors listed meet the authorship criteria according to the latest guidelines of the International Committee of Medical Journal Editors, and all authors are in agreement with the manuscript.

Informed consent

Written informed consent was obtained from the patients for publication of this case report and any accompanying images.

Conflict of interest

The authors declared that there are no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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