Polyradiculopathy

A rare complication of neurobrucellosis

M. Walid Al-Sous, *MD, DIS,* ***Saeed A. Bohlega,*** *FRCPC, FRCP(Ed),* ***M. Zuheir Al-Kawi,*** *MD, FACP,* ***Donald R. McLean,*** *MD, FRCPC,* ***S. Naveed Ghaus,*** *MBBS, MRCP (UK).*

ABSTRACT

Neurobrucellosis is chronic brucellosis affecting the nervous system. It may mimic many neurological diseases but it rarely presents as polyradiculopathy. Brucellar radiculopathy was diagnosed in 6 patients who presented with weakness of the lower extremities. Five patients had lumbar puncture, 4 had magnetic resonance imaging of lumbar spine and 4 had nerve conduction studies. Five patients had areflexia and weakness; one had areflexia with proprioceptive ataxia. All patients had positive Brucella serology; cerebrospinal fluid showed lymphocytic pleocytosis, elevated protein, normal-low glucose; brucella serology was positive in all specimens. Nerve conduction studies showed absent F-wave in 2 patients and polyradiculopathy with secondary motor axonopathy in 2 patients; motor conduction velocity was normal in all. Magnetic resonance imaging with gadolinium injection showed enhancement of lumbar nerve root in 3 patients, and no enhancement in one. All patients improved after treatment with antibiotics and lumbar root enhancement disappeared. Symptoms of myelopathy were unmasked after radiculopathy had resolved in one patient. In endemic areas, brucella infection should be considered in the differential diagnosis of radiculopathy. Radiculopathy is probably due to inflammation of the meninges and the intrathecal portion of the roots. The pathogenesis of myelopathy may involve demyelination as spasticity persists or worsens after radiculopathy improves.

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Brucellosis is primarily a zoonosis that affects humans as a secondary host.[1,2] The infection is acquired through contact with infected animals, drinking unpasteurized milk or milk products, or eating raw meat.[1-7] It is endemic in the Arabian Peninsula and common in countries bordering the Mediterranean Sea.[1,2,4] Bruce identified the organism from autopsy material in 1887 and in 1896 Hughes was the first person to report neurobrucellosis.[7] Involvement of the central nervous system occurs in 5-10% of cases[3-6] with a variable clinical presentation that mimics other diseases.[2] The involvement of the nerve roots, although rare, causes paralysis that can mimic other radiculopathies such as Guillain-Barré syndrome.[5,8]

Case Reports. This is a retrospective review of the records pertaining to 6 patients diagnosed with brucella radiculopathy between 1992 and 1998. The clinical presentation was weakness in the lower extremities and disturbance of gait. The diagnosis was based on serology tests for Brucella (standard agglutination test (SAT)) before and after precipitation by 2-mercapto-ethanol (2ME) in serum or cerebrospinal fluid (CSF). Functional assessment before and after treatment was carried out by neurologists in a clinical setting.

Patient One. A 38-year-old female, presented with gait disturbance, hearing loss, headache and fever. Neurological examination showed sensory ataxia, positive Romberg sign, areflexia, hypoacousia and papilledema.

Patients 2-6. Three females and 2 males aged 15-47 years, all presented with progressive lower limb weakness and areflexia. Patients 2, 3 and 5 showed mild

From the Department of Neurosciences, King Faisal Specialist Hospital and Research Centre, Riyadh, *Kingdom of Saudi Arabia*.

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Address correspondence and reprint request to: Dr. Saeed A. Bohlega, Department of Neurosciences, King Faisal Specialist Hospital and Research Centre, PO Box 3354, Riyadh 11211, *Kingdom of Saudi Arabia*. Tel. +966 (1) 464-7272 pager 9960. Fax. +966 (1) 4424761. E-mail: boholega@kfshrc.edu.sa

sensory manifestations in the form of paresthesia and distal thermoalgesic hyperesthesia. Patient 4 had sensory neural deafness with headache and tinnitus. Patient 6 developed signs of myelopathy (spasticity, hyperreflexia and Babinski sign) after resolution of radiculopathy a few months following triple antibiotic therapy. **Tables 1 and 2** describe the findings in 6 patients with neurobrucellosis and peripheral nervous system involvement.

In patient one, computerized tomography (CT) scan of brain results were normal, brucella titers were positive in serum and CSF, lumbar puncture showed predominantly lymphocytic pleocytosis (372), high protein (1280 mg/ml, N=450 mg/ml) and low glucose (1.1 mmol/l). Nerve conduction study and magnetic resonance imaging (MRI) were not carried out.

Patients 2-6 all had positive titers for brucella in serum and CSF, and all CSF samples showed lymphocytic pleocytosis (32-220), high protein (1600-6673 mg/l) and normal or low glucose. Only patient 4 refused lumbar puncture. Nerve conduction studies were carried out in 4 patients and these showed normal motor and sensory conduction velocity; 2 showed absent F-wave. Needle electromyography showed active denervation potential with polyphasic motor unit potentials in 4 patients. Four patients had MRI of the lumbar spine with gadolinium injection and enhancement of nerve roots was seen in 3 patients (**Figures 1 & 2**).

Recovery or improvement was seen following treatment with triple antimicrobials: co-trimoxazole, rifampin and doxycycline. Duration of treatment ranged from 3-8 months; improvement was associated with resolution of lumbar nerve root enhancement and normal CSF studies. Signs of myelopathy (spasticity, hyperreflexia and extensor-plantar response) appeared after resolution of polyradiculopathy in one patient, with no sensory level and normal MRI of spine.

Discussion. Brucellosis is an endemic infection caused by gram negative microorganisms. Involvement of the nervous system occurs in 5-10% of cases of systemic brucellosis.[3-7] Due to the variety and multiplicity of symptoms it frequently mimics other

Table 1 - Peripheral nervous system involvement in 6 patients with neurobrucellosis.

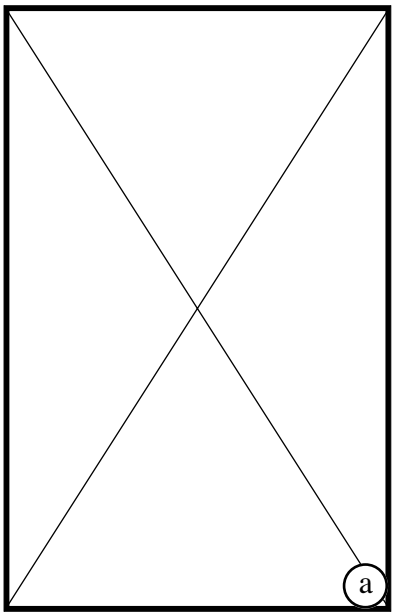
Age/sex	Weakness	Reflexes	Sensory	Other	General
38/F	none	absent	sensory ataxia, Romberg+	Papilledema, sensory neural deafness	fever, headache
15/F	mild	absent lower limbs	decreased sensation distally, lower limbs	absent	fever, myalgia, low back pain
20/F	moderate	absent lower limbs	decreased sensation distally, lower limbs	absent	fever, myalgia, low back pain
47/F	moderate	absent	absent	sensory neural deafness	headache, tinnitus
17/M	severe	absent	paresthesia lower limbs	absent	fever
33/M	severe	absent	absent	myelopathy after radiculopathy resolved	-

+ positive; - negative

Table 2 - Summary of investigations.

Brucella titers				CSF			NCS EMG	MRI lumbar spine
Serum		CSF		Glucose	Protein	Cells		
SAT	2ME	SAT	2ME	mmol/L	mg/L	WBC		
1280	640	640	640	↓1.15	↑1280	↑372	not carried out	not carried out
20480	20480	1280	640	normal	↑1600	↑61	normal CV, radiculopathy, 2° motor axonopathy	not carried out
5120	2560	1280	640	normal	↑1797	↑32	normal CV, absent F-wave	enhanced lumbar roots
1280	640	refused	refused	refused	refused	refused	not carried out	normal
1280	640	160	160	↓2.4	↑2308	↑65	normal CV, radiculopathy, 2° motor axonopathy	enhanced lumbar roots
2560	2560	1280	640	↓3	↑6673	↑220	normal CV, absent F-wave	enhanced lumbar roots

SAT - standard agglutination test; 2ME - 2-mercapto-ethanol; CSF - cerebrospinal fluid; WBC - white blood cells; NCS - nerve conduction study; EMG - electromyogram; CV - conduction velocity; MRI - magnetic resonance image



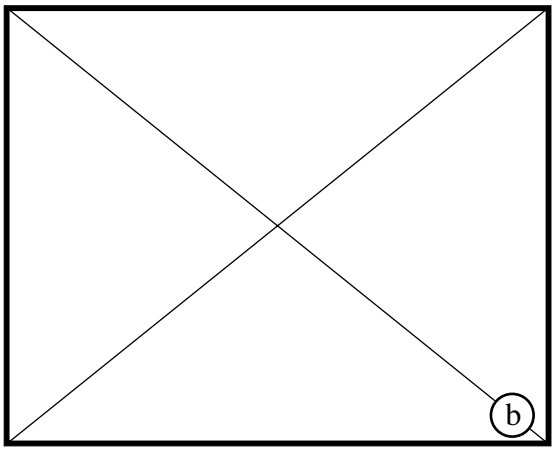
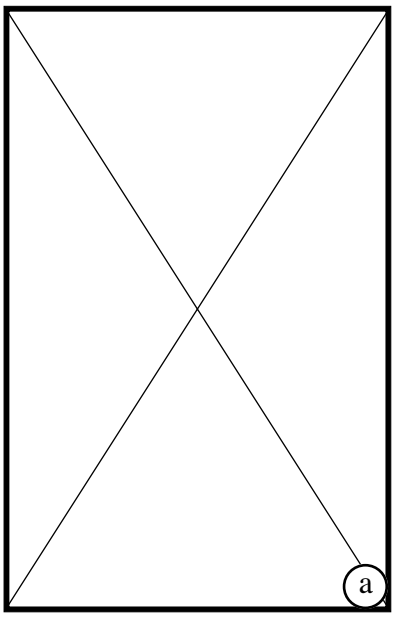


Figure 1 - Normal T1-weighted magnetic resonance images of lumbar spine of patient 3 **a)** sagittal and **b)** axial.



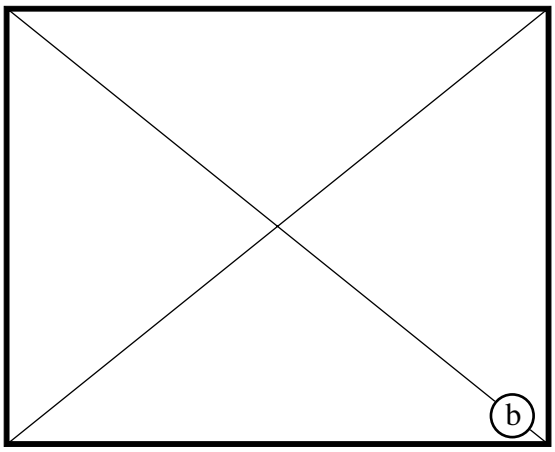


Figure 2 - T1-weighted magnetic resonance images of lumbar spine of patient 3 after gadolinium injection, showing enhancement of the cauda equina components (arrow head) **a)** sagittal and **b)** axial.

disease entities.[2,8] The clinical presentation of brucellosis can be categorized as acute or chronic.[4] Acute meningoencephalitis, a well-recognized mode of presentation of neurobrucellosis, is probably due to the effect of the organism or its products on the meninges and brain.[2-4] Chronic meningitis has been described with involvement of cranial nerves VI, VII and VIII, polyradiculitis or myeloradiculitis.[1-8] Chronic polyradiculitis in neurobrucellosis usually takes the form of predominantly motor involvement affecting lower limbs more than upper limbs,[3,4,6-8] but sensory neuropathy is possible.[5,8,9] Only one of our patients had sensory ataxia with areflexia, and 5 had motor radiculopathy with neurophysiological evidence of denervation and re-innervation.

Chronic brucellar meningitis may be due to persistence of intracellular organisms or an immune mechanism leading to demyelination.[4,7] The peripheral nerve lesions probably occur within the intrathecal portion of the peripheral nerve system, causing radiculopathy.[6] This was supported by the fact that 3 out of 4 of our patients had nerve root enhancement on MRI spine after gadolinium enhancement with complete resolution of the enhancement after successful treatment.

The diagnosis of polyradiculopathy, due to brucellosis, requires a high index of suspicion in the endemic area, abnormal CSF with increased protein and lymphocytic pleocytosis, positive brucella agglutination tests in blood and CSF, and a favorable clinical response to antibiotic therapy.

Rare cases of neurobrucellosis with albumino-cytological dissociation have been described, as well as negative results of agglutination tests.[9-11] In these cases, neurobrucellosis was confirmed by enzyme linked immunosorbent assay or positive CSF culture.

Combination therapy of 3 antibiotics with good CNS penetration is recommended for at least 3 months.[2,3,5,7] The duration of treatment is determined by clinical recovery or stability, normalization of CSF cell count and decreased CSF protein; serological tests remain positive for a long time after treatment, therefore they are of little value in determining the end point of treatment.[2,3,5,7,8]

In our patients, the duration of triple therapy ranged from 3 to 8 months with significant to complete recovery and normalization of CSF cell count in all patients.

References

1. Madkour MM, Abdelrahman E, Mohamed E, Samad TMA, Kudwah AJN. Brucellosis in Saudi Arabia. ***Saudi Med J*** 1985; 6: 324-332.
2. Al-Kawi MZ. Brucellosis. In: Mohr JP, Gautier JC, editors. Guide to clinical neurology. New York (NY): Churchill Livingstone Publishers; 1995. p. 677-690.
3. Bashir R, Al-Kawi MZ, Harder EJ, Jinkins J. Nervous system brucellosis: diagnosis and treatment. ***Neurology*** 1985; 35: 1576-1581.
4. Shakir RA, Al-Din ASN, Araj GF, Lulu AR, Mousa AR, Saadah S. Clinical categories of neurobrucellosis: a report of 19 cases. ***Brain*** 1987; 110: 213-223.
5. Al-Deeb SM, Yaqub BA, Sharif HS, Phadke SG. Neurobrucellosis: clinical characteristics, diagnosis and outcome. ***Neurology*** 1989; 39: 490-501.
6. McLean DR, Russell N, Khan MY. Neurobrucellosis: clinical and therapeutic features. ***Clin Infect Dis*** 1992; 15: 582-590.
7. Akdeni ZH, Irmak KH, Anlar O, Demiroz AP. Central nervous system brucellosis: presentation, diagnosis and treatment. ***J Infect*** 1998; 36: 297-301.
8. Bahemuka M, Shemena AR, Panayiotopoulos CP, Al-Aska AK, Obeid T, Daif AK. Neurological syndromes of brucellosis. ***J Neurol Neurosurg Psychiatry*** 1988; 51: 1017-1021.
9. Oliveri RL, Matera G, Foca A, Zappia M, Aguglia V, Quathone A. Polyradiculopathy with cerebrospinal fluid albuminocytological dissociation due to neurobrucellosis. ***Clin Infect Dis*** 1996; 23: 833-834.
10. Pedro-Pos A, Fox M, Codina A, Rey C. Les neurobrucelloses (étude de 41 cas). ***Cahiers Médecine*** 1972; 13: 855-862.
11. Araj GF. Enzyme-linked immunosorbent assay, not agglutination, is the best test of choice for the diagnosis of brucellosis. ***Clin Infect Dis*** 1997; 25: 942.