

A rare presentation of brucellosis: polyradiculopathy and peripheral neuritis

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Aim: To present 8 patients with polyradiculopathy or polyradiculoneuritis caused by brucellosis. Polyradiculopathy or polyradiculoneuritis are occasional neurological involvements of brucellosis.

Materials and methods: The diagnosis was made with clinical, serological and/or cerebrospinal fluid, and electromyographic examinations.

Results: All of the patients except one improved quickly after specific antimicrobial treatment. Furthermore, electrophysiological examinations revealed normal findings in 6 patients.

Conclusion: This clinical form of brucellosis is mostly reversible if it is diagnosed earlier and treated effectively.

Key words: Brucellosis, neurobrucellosis, polyradiculopathy, peripheral neuritis

Brusellozun ender görülen tutulum şekli: poliradikülopati ve periferel nevrıt

Amaç: Poliradikülopati veya poliradikülonevrit brusellozun nadir görülen nörolojik tutulum şekilleridir. Bu yazıda, bruselloza bağlı poliradikülopati veya poliradikülonevritli sekiz olgu sunulmuştur.

Yöntem ve gereç: Hastalığın tanısı klinik, serolojik ve/veya beyin omurilik sıvısı ve elektromiyografik incelemelerle konulmuştur.

Bulgular: Bir hasta dışında tüm olgular spesifik antimikrobiyal tedaviyle iyileşmiştir. Altı hastada elektrofizyolojik bulgular da normale dönmüştür.

Sonuç: Brusellozun bu klinik formu erken tanı konulup tedavi edilirse çoğunlukla geri dönüşlüdür.

Anahtar sözcükler: Bruselloz, nörobruselloz, poliradikülopati, periferel nevrıt

Introduction

Human brucellosis is a zoonosis caused by a gram-negative bacillus. Neurological complications of brucellosis occur in less than 5% of infected patients (1-4). Neurobrucellosis may develop at the onset of the illness, during convalescence, or months to years after recovery from the acute infection. Neurological involvements include acute, subacute, or chronic meningitis; meningoencephalitis; myelitis; peripheral neuritis; polyradiculopathy; cranial nerve palsies; and subarachnoid hemorrhage (2,5). The purpose of this report was to document our experience of 8 cases presenting polyradiculopathy or polyradiculoneuritis caused by brucellosis.

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Materials and Methods

At the Department of Infectious Diseases and Clinical Microbiology of Ankara Training and Research Hospital, Turkey, 8 patients with neurobrucellosis presenting with polyradiculopathy or polyradiculoneuritis were diagnosed between January 2004 and July 2007.

The diagnosis of brucellosis was suspected based on clinical and epidemiological features and was confirmed by microbiological and serological tests in serum. Because the patients had neurological signs and symptoms, magnetic resonance imaging scans, nerve conduction studies and electromyography (EMG), and/or lumbar puncture were done. The technique for nerve conduction studies was that described by Oh (6). Our tests included sensory and motor involvement in 1 median, 1 ulnar, 1 peroneal, 1 posterior tibial, and 1 sural nerve, and F waves in the median, ulnar, peroneal, and posterior tibial nerves. The needle EMG was done for at least 2 distal muscles in 1 extremity and at least 4 paraspinal muscles. The electrophysiological studies were performed in the first evaluation for all of the patients except 1 and repeated 3-6 months following the end of the treatment. In case 4, the control EMG could not be performed because the patient did not come to the control appointment. All of the patients were investigated for paraproteinemia, endocrinopathy, vitamin B12 and folate deficiencies, connective tissue disorder, infections other than brucellosis, alcohol abuse, and hepatic and renal failure. The polyradiculopathy or peripheral neuritis due to brucellosis was diagnosed by EMG and/or demonstration of antibodies of *Brucella* spp. in the cerebrospinal fluid (CSF) at any titer in the presence of any abnormality of the CSF when no other causes were found.

Results

All of the patients had a history of stock farming and/or consumption of raw milk products. The mean age was 41.6 ± 15.8 years (range: 26-71 years). Details of the clinical presentation and treatment

protocols of the patients are summarized in Table 1. All of the patients had polyradiculopathy in their EMG studies. Peripheral neuritis, especially in the lower extremities, was detected in cases 1, 7, and 8, in addition to polyradiculopathy. CSF findings could not be assessed in cases 4 and 5, due to the patients' rejection of the lumbar puncture. The findings of CSF and EMG are shown in Table 2.

Magnetic resonance imaging scans, which were performed due to the patients' symptoms, were normal in cases 1, 2, 6, 7, and 8. However, in the others, spondylodiscitis was detected (in cases 3, 4, and 5, respectively, at the C3-C4 vertebrae, T11-T12 vertebrae, and L4-S1 vertebrae).

Clinical improvement was achieved in all of the patients except in case 7. Treatment was continued until clinical, electrophysiological, radiological, and CSF findings improved. In cases 2 and 5, the EMG study was normal at month 3 of the treatment. In cases 1, 3, 6, and 8, the EMG study was normal; nerve conduction studies were also normal for cases 1 and 8 at month 6 of the treatment. In case 7, electrophysiological findings had not improved at month 6 of the treatment. Moreover, after rehabilitation, only minimal clinical improvement was observed and the patient's electrophysiological findings had not changed. In cases 3-5, spondylodiscitis healed with only medical treatment and the control MRI findings were normal at the end of the treatment.

Discussion

Polyradiculopathy or polyradiculoneuritis is one of the rare presentations of brucellosis. Brucellosis can affect the nervous system because of the direct effect of bacilli, cytokines, or endotoxins on peripheral nerves, spinal cord, meninges, and the brain (7-9). It is postulated that the pathologies of this involvement might differ, being a direct infection in the acute form and an immune-related, possibly demyelinating process in the chronic forms. We do not know how the bacteria cause the peripheral nerve dysfunction or why it is reversible (8-10). Previous case studies have implicated inflammation of the proximal nerve

Table 1. Clinical signs and symptoms and treatment protocols of 8 patients.

Case	Age/sex	Complaints	Physical findings	Treatment protocol (duration)
1	56/F	Fever, sweating, myalgia, progressive weakness of lower extremities, and difficulty in walking (3 months)	Paraparesis (2/5), hypoactive DTR, and pain-touch sensation loss in the right lower extremity below the knee	CRO* + RIF + DOX (9 months)
2	26/M	Vertigo, dizziness, vomiting, progressive weakness of all extremities, and difficulty in walking (4 months)	Absence of DTR, ataxic walking, positive Romberg test, and decreased vibration senses of lower extremities	CRO* + RIF + DOX (3 months)
3	43/M	Fever, sweating, headache, and pain in shoulders and neck (1 month)	Fever, restricted mobility of the neck, hepatomegaly, and absence of DTR	CRO* + RIF + DOX (6 months)
4	71/M	Fever, sweating, lumbar pain, and numbness in right lower extremity (5 months)	Weakness, hyperesthesia, and loss of DTR in right lower extremity	RIF + DOX (3 months)
5	46/M	Fever, sweating, myalgia, lumbar pain, and difficulty in walking (6 weeks)	Hypoesthesia in right lower extremity and hypoactive DTR in lower extremities	RIF + DOX (3 months)
6	30/M	Fatigue, weakness of all extremities, and difficulty in walking (4 months)	Absence of DTR and paraparesis (4/5)	RIF + DOX (9 months)
7	35/M	Progressive weakness, pain in lower extremities, difficulty in walking, and arthralgia (3 months)	Paraparesis (4/5) and loss of DTR	CRO* + RIF + DOX (9 months)
8	26/M	Lumbar pain and difficulty in walking (4 months)	Ataxia, right ankle dorsiflexion deficiency (4/5), and absence of DTR	RIF + DOX (6 months)

CRO: ceftriaxone, RIF: rifampin, DOX: doxycycline, DTR: deep tendon reflexes

*First month of the treatment.

Table 2. The findings of CSF and EMG for 8 patients.

Case	SAT titer	Blood				CSF			EMG	
		Culture	WBC/mm ³	Protein (mg/dL)	CSF/blood glucose (mg/dL)	SAT titer	Culture	SAT titer	Culture	SAT titer
1	1/160	Negative	810	327	5/98	1/64	Negative	1/64	Negative	Peripheral neuritis and L2-5, S1 polyradiculopathy
2	1/1280	Negative	350	484	31/102	1/64	Negative	1/64	Negative	L2-5 polyradiculopathy
3	1/640	<i>B. melitensis</i>	30	135	44/127	1/16	Negative	1/16	Negative	L3-5, S1 polyradiculopathy
4	1/1280	<i>B. melitensis</i>	-	-	-	-	-	-	-	T12, L1-3 polyradiculopathy
5	1/640	<i>B. melitensis</i>	-	-	-	-	-	-	-	L2-5 polyradiculopathy
6	1/160	Negative	90	254	16/90	1/128	Negative	1/128	Negative	L1-5 polyradiculopathy
7	1/2560	Negative	280	420	6/98	1/16	Negative	1/16	Negative	Peripheral neuritis and T11-12, L1-5 polyradiculopathy
8	1/320	Negative	10	319	20/85	1/80	Negative	1/80	Negative	Peripheral neuritis and L3-S1 polyradiculopathy

SAT: serum agglutination test

roots as one cause, but this would not explain the mild nerve dysfunction in systemic patients (9). The effect of brucellosis on the spinal cord may occur because of the compression of abscesses or granuloma (2,7). In the MEDLINE database, there are some cases or case studies with polyradiculopathy, polyradiculoneuritis, or peripheral neuropathy due to the *Brucella* microorganism (4,8-22). These cases are reported in a series of neurobrucellosis patients, whereas, in this report, we wanted to evaluate only polyradiculopathy or polyradiculoneuritis, which are rare involvements of brucellosis.

It is generally accepted that the organisms gain access to the central nervous system (CNS) via the blood stream, and the predisposition to CNS brucellosis by spondylitis is well known. Mousa et al. (23) reported that 14 of 22 (64%) patients with brucellar spondylitis had some form of neurological complications and 6 of them had radiculopathy. That 3 of our patients had spondylodiscitis also justifies this pathogenic mechanism. However, extradural abscess or granuloma was not detected in our patients.

Pain, numbness and progressive weakness of the extremities, and difficulty in walking were the symptoms of polyradiculopathy or neuritis exhibited by our patients. Unfortunately, the duration of the complaints until diagnosis was long (from 6 weeks to 5 months). The causes of delay were postponing a visit to the doctor and not considering the disease in the differential diagnosis or misdiagnosis. Unfortunately, a delay in the diagnosis and treatment of the disease may deteriorate the prognosis.

The CSF findings of neurobrucellosis are positive antibody titers to *Brucella* spp., low titers of glucose, high levels of protein, and lymphocytic pleocytosis (4,14). Isolation of the *Brucella* microorganism from the CSF or blood is possible in 15%-70% of patients (14,18,24). In our patients for whom lumbar puncture was performed (cases 1-3, 6, and 7), the CSF findings were compatible with neurobrucellosis but the cultures were negative. Only in cases 3, 4, and 5 were the blood cultures positive for *Brucella*. Moreover, normalization of the CSF findings with specific antimicrobial therapy verified the diagnosis.

Nerve conduction studies and EMG confirmed polyradiculopathy in cases 2-6 and polyradiculopathy together with peripheral neuritis in cases 1, 7, and 8. Cases 1, 7, and 8 had prolonged F waves and distal latencies, and decreased nerve conduction velocities and amplitude in the peroneal and posterior tibial nerve. The compound nerve action potential of sural nerves was absent in case 1, while there was only a decrease in velocities and amplitude in cases 7 and 8. Those patients had prolonged F waves and denervation potentials in the paraspinal muscles and muscles innervated by the lumbar root. Cases 2-6 had normal conduction velocities, except for the prolongation of the F waves of the lower extremities; however, denervation potentials were present in paraspinal muscles innervated by lumbar root. Involvement in the polyradicular form is usually purely motor (10,11,14); however, it was reported by Kochar et al. that mild sensorial changes can present (7). In cases 1, 2, 4, and 5, neurological examinations revealed sensorial changes. Clinical and electrophysiological complete recovery was detected in all patients, except for in case 7. Good clinical response may be related to the acute or subacute presentation of our patients. The neurological changes are usually reversible after initiation of antimicrobial therapy, although minor sequela is reported to be frequent (2-4,10,12,15,18), but in case 7, only minimal clinical and no electrophysiological improvement was observed, despite the treatment of brucellosis and rehabilitation program. In our patients, rifampin plus doxycycline and/or ceftriaxone were used for 3-9 months. Previous reports show little consistency in antibiotic regimens for neurobrucellosis. Rifampin, trimethoprim-sulfamethoxazole (TMP-SXT), and doxycycline have good CSF penetration. The combinations most commonly used are tetracycline or doxycycline with streptomycin or rifampin or TMP-SXT (2,4,10,25). Ceftriaxone also achieves high concentrations in CSF. Moreover, in several studies from Turkey, in vitro sensitivity tests showed that ceftriaxone has enough activity to affect *Brucella* spp. (26,27). Furthermore, some cases with neurobrucellosis in which ceftriaxone

was used for the treatment were reported, and so it was used here to treat cases 1-3 and 7 (5,11,19,28). There is no consensus about the ideal duration of the treatment for neurobrucellosis. It is suggested to continue the therapy until the patient recovers or remains clinically stable, the CSF glucose returns to normal, protein and antibody titers begin to decrease, and cell count becomes normal or there are few cells (2,15).

We did not use corticosteroids, and almost of the patients improved with only the use of antimicrobial therapy. The beneficial effects of corticosteroids on

localized brucellosis have been reported; however, there is no proof to support their use (1,4,10,15).

The diagnosis of polyradiculopathy or polyradiculoneuritis due to brucellosis was made with clinical findings, CSF, and serological and electromyographic examinations in our patients. This clinical form is almost reversible when diagnosed early and treated effectively. In patients living in endemic regions, considering brucellosis as a cause of polyradiculoneuritis in the differential diagnosis may lead to early diagnosis and treatment.

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