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Case report

Brucellosis causing subacute motor polyradiculopathy and the pathological correlation of pseudomyopathic electromyography: A case report

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ABSTRACT

Introduction: Brucellosis is a rare cause of polyradiculopathy. We aim to present a case of subacute motor polyradiculopathy (SAMPR), along with the electromyographic pseudomyopathic changes, and their histopathological correlation.

Case presentation: A 24-year-old man presented with gradually progressive bilateral lower limb weakness for three weeks that progressed to a loss of ambulation in seven weeks. He had no ocular, facial, or sphincteric weakness and no sensory symptoms. He showed normal cognitive, cranial nerve, and upper limb exams. His lower limb power was medical research council (MRC) grade 3 proximally, and 4 distally. His reflexes were grade 2+ in the upper limbs and grade 0 in the lower limbs. The nerve conduction studies were normal. Electromyography (EMG) showed active denervation with a short-duration motor unit potential (MUP) and early recruitment. MRI showed a diffuse enhancement of the lumbosacral nerve roots. Cerebrospinal fluid (CSF) showed a protein of 2.7 g/L and a white blood cells (WBC) count of 420 cells per microliter. Muscle biopsy revealed neurogenic changes with secondary degenerating and regenerating fibers, explaining the small and short MUPs in the EMG. CSF grew Brucella after fourteen days of incubation. Serum showed high antibody titers for the Brucella species "Melitensis" and "Abortus". The patient started to walk again, ten months after starting a course of antibiotics.

Conclusion: Neurobrucellosis can present primarily as SAMPR, sparing the sensory system. SAMPR, with ongoing degenerating and regenerating muscle fibers, may explain the pseudomyopathic changes found in electromyographic studies.

1. Introduction

Brucellosis is one of the most common infectious diseases worldwide, with 500,000 new cases occurring every year (Dreshaj et al., 2016). It is endemic in many countries, such as in the Mediterranean areas, parts of South and Central America, and Eastern and Western Africa (Dreshaj et al., 2016). It is caused by intracellular Gram-negative bacteria of the *Brucella* genus. It is transmitted to humans by contact with fluids of infected animals (sheep, cattle, goats, pigs, or other animals) or derived food products such as unpasteurized milk and cheese.

Brucellosis is a multisystem disease that commonly presents with febrile illness and constitutional symptoms, along with a variable spectrum of clinical manifestations. Nervous system involvement may occur in 5–12% of brucellosis cases (Ertem et al., 2012; Dreshaj et al., 2016; Al-Sous et al., 2003). Peripheral nervous system involvement occurs in 41% of neurobrucellosis cases. Polyradiculoneuropathy has been reported in 15 cases (Al-Sous et al., 2003; Ertem et al., 2012).

We present a case of subacute polyradiculopathy due to neurobrucellosis, with pure motor symptoms and sparing of the sensory

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nerves on electrodiagnostic testing. Electromyography and muscle biopsy showed neurogenic changes with secondary myopathic changes.

2. Case presentation

The patient was a 24-year-old man who complained of a 3-week history of gradual, progressive, asymmetrical, bilateral, proximal more than distal lower limb weakness that was affecting his left side slightly more than his right. He struggled with walking, climbing stairs and standing from chairs, and he progressed to loss of ambulation in seven weeks since his symptoms started. He had mild subjective weakness in his hand grip. There were no sensory symptoms, no ocular, facial, or bulbar weakness. He had no sphincteric control symptoms, no lower back pain, or cognitive dysfunction. He reported unintentional weight loss of ten kilograms over a two-month period. He reported no other constitutional symptoms, no recent febrile illness, and no night sweat. He had ingested raw camel milk three months before the onset of his symptoms. There was no family history of any neurological disorders. He showed a normal cognitive and cranial nerve examination. The motor examination was normal in the upper limbs.

In contrast, the lower limb power showed nearly symmetrical power with medical research council MRC grade 4+ at hip flexion and knee extension, 3+ at knee flexion, and 4− at ankle dorsiflexion. He had absent lower limb reflexes, flaccid tone, and a downgoing plantar response. His sensory and cerebellar examinations were normal. He had a waddling gait and no scapular winging.

The investigations showed a normal complete blood count, electrolytes, creatinine, urea, magnesium, phosphate, calcium, erythrocyte sedimentation rate (ESR), C-reactive protein, total bilirubin, alkaline phosphatase, and lipase. His creatine kinase level was 153 U/L (reference range (RR): 0–195 U/L). Antinuclear antibodies (ANA) was positive at 1:80, and double-stranded DNA was negative. Serum protein electrophoresis demonstrated no monoclonal protein. Human immunodeficiency virus (HIV) serology, Venereal Disease Research Laboratory (VRDL) test, Hepatitis C antibody, and Hepatitis B surface antigen tests were all negative.

Electrophysiologic studies, performed one month after the onset of weakness, identified preserved bilateral common peroneal, tibial, left median and ulnar compound motor action potentials (CMAPs), as well as, bilateral sural, superficial peroneal, left median and ulnar sensory nerve action potentials (SNAPs). There was no prolongation in F-waves' latency. Electromyography (EMG) showed fibrillation potentials (grades 1–2), positive sharp waves (grades 1–2), and short-duration voluntary motor unit potentials (1–2 ms), with an amplitude in several motor units ranging between 0.1 and 0.2 millivolts, and an early recruitment at the bilateral iliopsoas, left vastus lateralis, and right semitendinosus muscles (Supplementary Videos 1–3). The EMG was normal in the tibialis anterior, gastrocnemius, and left biceps and triceps muscles.

At this point, both muscle biopsy and lumbosacral MRI were ordered. Lumbar spine MRI showed smooth and diffuse enhancement of the nerve roots in the cauda equina (Fig. 1, A-B). At five weeks from the onset of weakness, a muscle biopsy was performed on the left semitendinosus muscle. The muscle biopsy showed several angulated fibers and target and targetoid fibers, which were suggestive of neuropathic (denervation) pathology (Fig. 1, C-F); additionally, there were many degenerating and few regenerating fibers, which are considered secondary myopathic changes (Fig. 1, C-F).

Shortly after admission, six weeks after the onset of weakness, a lumbar puncture was performed, and the cerebrospinal fluid (CSF) analysis showed an elevated protein (2.74 g/L, normal 0.15–0.45 g/L), normal glucose, and elevated leukocytes (420×10^6/L), with 90% lymphocytes without erythrocytes. Negative CSF studies included fungal and bacterial cultures, polymerase chain reaction (PCR) for herpes simplex virus, Epstein–Barr virus, varicella-zoster virus, and enterovirus. Due to a high CSF protein level and lymphocyte count, a lumbar puncture was performed three more times. It consistently showed elevated protein levels (1.89, 3.73, and 4 g/L, respectively), normal glucose, and high leukocyte counts (192 and 315×10^6/L, respectively). In contrast, the CSF cytology showed few atypical lymphocytes, and flow cytometry showed CD4 T lymphocytes. Only after fourteen days of incubation did the CSF culture show substantial Brucella growth. The serum Brucella Melitensis antibody value was 1:320 (negative if <1:8), and serum Brucella Abortus antibody was 1:80 (negative if <1:8).

Based on these results, the patient was started on a four-month course of amikacin and ceftriaxone, and a one-year course of doxycycline and rifampicin. Before starting the treatment, the patient lost ambulation, and ten months after treatment, he was able to walk independently. NCS was repeated five months after onset of his symptoms, and it showed a drop in common peroneal CMAP with preserved sural and right superficial peroneal SNAPs (Table 1).

3. Discussion

We present a case of acute weakness due to nerve and nerve root disease without sensory involvement, which is referred to as subacute motor polyradiculopathy (SAMPR). In our Brucella case, weakness was the chief complaint, with no definite sensory symptoms, and NCS and EMG showed some features that are typically associated with myopathy; however, a muscle biopsy revealed neurogenic changes with secondary myopathic features. An MRI of the lumbosacral spine confirmed the involvement of nerve roots. To specify the etiology, a CSF culture grew Brucella after fourteen days of incubation. Here, we will focus our discussion on 1) the EMG myopathic features that could occur in SAMPR and its possible explanation on muscle biopsy; 2) the different causes of acute motor polyradiculopathy (AMPR) and SAMPR, and their electrodiagnostic and radiological findings, and finally; 3) the clues that may help physicians to differentiate between the various etiologies of cauda equina nerve root enhancement.

Neurogenic conditions are usually characterized by large-amplitude and long-duration motor units on needle electromyography. However, small units with short duration could be associated with neurogenic conditions. These units occur due to the drop of some muscle fibers from the motor units, either anatomically or physiologically, which may occur due to atrophy of part of the muscle fibers (Daube and Rubin, 2009). This commonly occurs due to degeneration or necrosis of some muscle fibers, which our case exhibited in the muscle biopsy. Another explanation for short-duration MUPs is newly re-innervated motor units, commonly known as nascent MUPs. However, this is usually associated with reduced recruitment and reflects more chronic changes. In our case, the histological features indicative of underlying neurogenic pathology are the angulated fibers as well as the target and targetoid fibers. Usually, the presence of degenerating, necrotic fibers and regenerating fibers are associated with myopathic disorders; however, when these occur in a neurogenic process, they are commonly referred to as myopathic changes in neuropathy (Dubowitz and Sewry, 2007). The possible mechanism that allows a neuropathic process (including proximal pathology at the anterior horn cell or nerve root level) to produce muscle fiber degeneration (before Wallerian degeneration takes place) is the impairment in anterograde and retrograde axonal transport. This leads to variable damage to the very distal part of the axon after

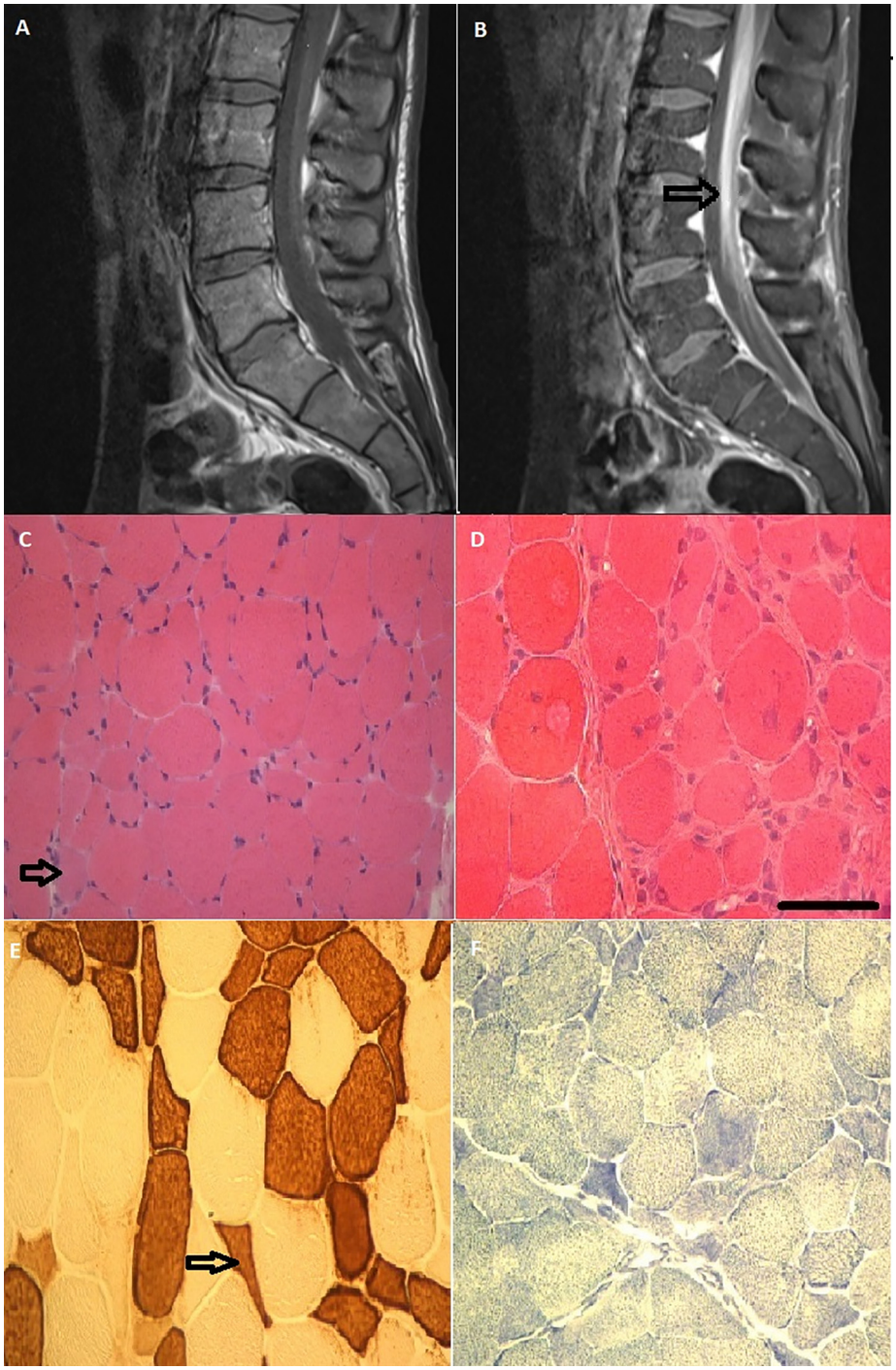

Fig. 1. MRI lumbosacral spine and Muscle biopsy. A) Pre-contrast MRI lumbosacral spine showing no hyperintensity signal B) post-contrast MRI showing cauda equina nerve roots enhancement. (C-F) Partial denervation with myopathic change. C) (H&E-×200) shows scattered angulated, degenerated, and regenerated fibers (arrow); D) shows (H&E-×400) many degenerating fibers E) Myosin heavy chain (MHCs) shows atrophic angulated fibers (arrow) F) Succinic dehydrogenase (SDH) shows target/targetoid fibers.

it branches off the main axonal trunk (Williamson and Cleveland, 1999; Zhang et al., 1997; Krakora et al., 2012). Subsequently, some muscle fibers undergo degeneration, and fewer muscle fibers contribute to the motor unit potential. We believe that the histopathological correlation of the small short motor units seen on EMG in our case is due to the segmental necrosis and degeneration of some muscle fibers.

There are a few causes of SAMPR described in the literature. Lyme disease has been reported in two cases to cause AMPR, presenting with acute weakness mimicking Guillain–Barre syndrome (Scelsa et al., 1996), both of which showed high CSF protein levels and pleocytosis. The diagnosis was confirmed based on positive serology. Both patients exhibited weight loss but no fever, and the second case had hyperreflexia suggestive of myeloradiculoneuropathy. Acute human immunodeficiency virus (HIV) infection has been reported in four cases of SAMPR, affecting lower limbs only with no associated cytomegalovirus infection (Benatar and Eastman, 2000). These HIV and Lyme disease cases had similar electrodiagnostic findings to our case, including normal sural and median sensory nerve action potentials and normal F-waves

Table 1
Nerve conduction study.

	Study 1 at one month	Study 2 at five months	Normal range
Motor nerves			
Peroneal at EDB, left			
DL (ms)	5.4	Not recordable	≤6.5
Amp (mV) at the ankle	2.6	Not recordable	≥ 2
Amp (mV) below the knee	2.2	Not recordable	≥ 2
CV (m/s)	45	Not recordable	≥40
Amp (mV) above the knee	2.5	Not recordable	≥ 2
CV (m/s)	55	Not recordable	≥40
F waves (ms)	Absent	Not recordable	≤53
Tibial at AH, left			
DL (ms)	3.5	5.2	≤ 6
Amp (mV) at the ankle	8.8	7.5	≥ 4
Amp (mV) at the knee	8.3	5.7	≥ 4
CV (m/s)	49	36	≥40
F waves (ms)	43	49	≤53
Peroneal at EDB, Right			
DL (ms)	5.4	9.8	≤6.5
Amp (mV) at the ankle	2.8	0.63	≥ 2
Amp (mV) below the knee	2.4	0.61	≥ 2
CV (m/s)	44	28	≥40
Amp (mV) above the knee	2.4	0.61	≥ 2
CV (m/s)	45	35	≥40
F waves (ms)	49	Not recordable	≤53
Tibial at AH, Right			
DL (ms)	3.5	5.7	≤ 6
Amp (mV) at the ankle	13.2	9.2	≥ 4
Amp (mV) at the knee	10.1	6.2	≥ 4
CV (m/s)	44	32	≥40
F waves (ms)	43	56	≤53
Sensory nerves			
Sural, right			
DL (ms)	3.6	4.5	≤ 4
Amp (μV)	12	26	≥ 6
CV (m/s)	46	40	≥40
Sural, left			
DL (ms)	3.7	3.6	≤ 4
Amp (μV)	13	9.8	≥ 6
CV (m/s)	52	49	≥40
Superficial peroneal, right			
DL (ms)	3.4	4.3	≤4.4
Amp (μV)	12.6	9.2	≥ 6
CV (m/s)	50	40	≥40
Superficial peroneal, left			
DL (ms)	3.5	4.5	≤4.4
Amp (μV)	8.1	2	≥ 6
CV (m/s)	47	37	≥40

Amp: amplitude, CV: conduction velocity, DL: distal latency, ms: milliseconds, mV: millivolts, μV: microvolts, m/s: meter per second.

latency throughout the illness. At the same time, there were drops in motor action potentials. Neurosyphilis is another cause of SAMPR in immunocompetent patients (Corabianu et al., 2003). Noninfectious causes of AMPR/SAMPR include post-bariatric surgery and medication such as pembrolizumab; however, these causes are not associated with high white blood cell counts and often present with no elevation in CSF protein levels (Landais, 2014; Sepulveda et al., 2017). On the other hand, brucellosis may cause SAMPR with normal white blood cell count in CSF (Oliveri et al., 1996). Additionally, in the late stages of the neurobrucellosis, Brucella titer in the blood could be normal with negative Brucella culture from CSF. In such cases, the CSF Brucella titer could be the only evidence for diagnosis (Alshareef, 2009). The absence of sensory involvement in brucellosis has been reported by Goktepe et al. (Goktepe et al., 2003).

The causes of cauda equine nerve root enhancement are varied, and a few clues may help to differentiate these different etiologies. Guillain–Barre syndrome is a common cause of cauda equina nerve root enhancement; however, this occurs without an elevation in CSF cell counts (Gorson et al., 1996). Leptomeningeal carcinomatosis causes nodular rather than smooth nerve root enhancement on MRI, and it is frequently associated with positive malignant cells in cytology studies (Alkhotani et al., 2016). Another cause of nerve root enhancement is intravascular lymphoma (Abuzinadah et al., 2012). A clue to intravascular lymphoma is the presence of an IgG κ monoclonal protein in CSF protein electrophoresis, and the elevation in CSF white blood cells is minimal.

In conclusion, our case emphasizes the importance of considering brucellosis in the differential diagnoses of SAMPR, particularly in areas where it is endemic. This work also describes the myopathy-like features that can be observed in the EMG analysis in such cases, which could be due to the presence of degenerating and regenerating muscle fibers.

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Appendix A. Supplementary data

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