

Case Report of Polyradiculopathy, Hearing Loss, and Ataxia as Presentation of Neurobrucellosis

Aysha A. Alshareef, MD, SAUDI BOARD NEUROLOGY

*Department of Internal Medicine,
Faculty of Medicine, King Abdulaziz University
Jeddah, Saudi Arabia
kdraysha@hotmail.com*

Abstract. A case report of a 46-year-old male presented with lower limb weakness with lower motor neuron signs, hearing loss; nerve conduction study demonstrated axonal polyradiculoneuropathy. CSF study showed (low glucose, high protein with lymphocytosis), brucella titer in the blood was borderline, polymerase chain reaction and culture for tuberculosis were negative. The patient initially was managed with an anti tubercular treatment. The weakness improved, but the patient continues to have hearing loss. Several months later his gait became ataxic; brucella titer at the blood was repeated 1/160; CSF brucella culture were negative; CSF brucella agglutination titer came back very high 1:1280, and anti brucella regimen were started. The patient showed significant improvement within few months after the treatment.

Keywords: Neurobrucellosis, CSF brucella titer, Polyradiculopathy, Ataxia, Hearing loss.

Introduction

Brucellosis is an infection caused by intracellular bacteria of the genus *Brucella*. *B. melitensis* is the most virulent and most widely encountered of all the species^[1]. The natural reservoir of *Brucella* is of domestic animals such as sheep, goats, cattle, camels, dogs and pigs. The disease is transmitted to humans by direct contact or through the consumption of

Correspondence & reprint request to: Dr. Aysha Alshareef
P.O. Box 80215, Jeddah 21589, Saudi Arabia
Accepted for publication: 01 August 2009. Received: 26 May 2009

raw meat, milk or milk products of the infected animals^[1-3]. Although it has been eradicated in most European and North American countries, it is still an important public health problem throughout the world, in particular in the Mediterranean region including Turkey, the Arabian Peninsula, the Indian subcontinent, Mexico and some parts of Central and South America^[1,4,5]. When brucellosis affects the nervous system, it is known as neurobrucellosis. Neurobrucellosis can occur in the form of acute meningitis, meningoencephalitis, cerebellitis, myelopathy, cranial neuropathy or radiculopathy. If not treated early, neurobrucellosis can result in severe neurological morbidity and sequels, which can be irreversible^[6]. Neurobrucellosis is categorized according to the clinical manifestation; that is, central nervous system or peripheral nervous system involvement or a combination^[7]. This case report describes a male presented with lower limb weakness, hearing loss and ataxia, diagnosed as neurobrucellosis. It also includes a review of literature related to similar cases.

Case report

A 46 year old male presented to the outpatient clinic with a history of progressive lower weakness for 7 m duration. The weakness started initially as difficulty in climbing stairs. Gradually the patient became unable to walk without assistance. He reported a history of numbness of the lower limbs, and hearing loss on both ears. He denied any history of headache, convulsion, double vision, swallowing or speech difficulty, no history of urinary and bowel incontinence.

During this illness he lost 50 kg. There was a history of a mild on-and-off fever and h/o night sweating. Thus, he likes to drink raw milk frequently. He gave a history of contact of tuberculoses patient, on examination, vitally he was stable, no lymphadenopathy, chest, cardiovascular, and abdominal exams. All were within normal limits. Neurological exams revealed normal higher function test. Speech exams were normal. Cranial nerves exams were normal apart from bilateral sensory neural hearing loss; motor exam were completely normal in the upper limb while lower limb exam reveled wasting; power grade of 3/5 proximally and distally; absent reflexes, and planter response is down going bilateral. Sensory exam and coordination exam were normal; nerve conduction study revealed axonal polyradiculoneuropathy CSF study

revealed (WBC 157 cell/cubic mm, RBC 2cell /cubic mm), lymphocytosis 96%, protein 5.1, glucose 1.9 g/dl; cytology screen demonstrate inflammatory cells but no malignant cells; bacterial culture were negative; brucella titer IN THE BLOOD were borderline 1/160; gram stain, acid fast bacilli stain; polymerase chain reaction (PCR) for tuberculosis were negative.

Thoraco lumbar magnetic resonance image revealed a high signal intensity of T4 and T5 vertebra, which is suggestive of infective spondylitis. Other work-up including ESR, CBC, liver function and renal function tests; tumor markers (PSA, CEA, CA19), thyroid function test, Vitamin B12, bone marrow aspiration and biopsy. HIV serology, anti nuclear antibodies; magnetic resonance image (MRI) of the brain, bone scan, CT chest, abdomen, pelvis all were within normal limit; anti tuberculosis medication was started empirically (Rifampicin, INH, Pyridoxine, Pyrazinamide).

The patient follow-up revealed partial improvement in the weakness, but the hearing loss did not improve. Few months later, however, his gait became unsteady, and neurological exam demonstrated cerebellar signs bilateral with truncal ataxia. Follow-up MRI on the brain were normal; repeated agglutination titer for brucellosis species was borderline elevated 1:160; CSF study was repeated and revealed glucose 2.5 mmol/L, protein 1.85 g/dl, RBC :36 cell /cubic mm, WBC: 37 with lymphocytic predominates 91%. CSF culture for bacterial brucella, tuberculosis were negative, while CSF brucella titer result was significantly elevated 1/1280. Therapy with IV (intravenous) amikacin, doxycycline Rifampicin and Co-trimoxazole was instituted. Follow-up agglutinin titer of brucella species after one week post anti brucella regimen was 1/600. The patient dramatically improved within few months after treatment.

Discussion

Brucellosis is a disease caused of infection with Gram-negative microorganisms of the genus *Brucella*^[8]. It is a zoonosis transmittable to humans. All *Brucella* infections are led by direct or indirect exposure (e.g., milk or milk products and raw meat) to animals^[9]. The disease starts with nonspecific symptoms such as fever, sweats, malaise, anorexia, headache, and back pain. The diagnosis has been made from a

history of previous symptoms of the disease, culture of the organisms from the blood or cerebrospinal fluid, and serologic testing^[8]. Long-term antimicrobial therapy has been regarded as an effective treatment strategy for brucellosis^[9]. Among the most commonly involved systems are the hepatobiliary system and the skeletal system^[8] because *Brucella* are in the gastrointestinal tract. However, nervous system involvement is not common. The incidence has been reported to be between 3 and 25% of the cases of generalized brucellosis^[10].

Brucellosis is a systemic infectious disease. The infection spreads hematogeneously to the tissues rich in elements of the reticuloendothelial system including liver, bone marrow, lymph node and spleen. It may also localize in other tissues including joints, central nervous system (CNS), the heart and kidneys^[11-13]. Nervous system complications of neurobrucellosis include meningitis, encephalitis, brain abscess, epidural abscess, demyelization syndromes and meningo-vascular syndrome. Meningitis has been reported as the most frequent presentation, occurring in about 50% of the cases^[14]. A high cure rate can be achieved by treatment with triple combination, which otherwise, would result in high mortality and morbidity. There are four species of *Brucella* that can infect humans: *B. melitensis*, *B. abortus*, *B. suis* and *B. canis*; all are gram-negative coccobacilli. After ingestion of the *Brucella* bacillus, a brief bacteraemia phase appears and *Brucella* diffusely colonizes the lymphoreticular system, with proliferation of macrophages and lymphocytes. Soon afterwards granulomas form^[15-17].

Neurobrucellosis has neither a typical clinical picture nor specific CSF findings. Blood and bone marrow culture are the best diagnostic methods but are not always successful^[17-19]. A history of ingestion of untreated milk or milk products, symptoms and signs not typical of known neurological disease, a serum agglutination titer > 1:160 and a CSF agglutination titer > 1:80, abnormal CSF with increased protein and lymphocytic pleocytosis, and improvement with appropriate therapy are diagnostic criteria^[16-18].

Central nervous system involvement, neurobrucellosis can be seen in both the acute and chronic stages and occurs in $5 \pm 10\%$ of diagnosed cases. In acute infection, neurological involvement is nonspecific and includes headache, fatigue, and myalgia. In chronic infection, as in our case, the clinical presentation is diverse and mimics

other neurological diseases such as meningitis, meningoencephalitis, myelopathy, myelitis, cerebellitis, polyradiculitis, and mononeuritis. Most patients present with involvement of cranial nerves, commonly the optic, oculomotor, abducent, facial, trigeminal and vestibulocochlear^[15,20]. There seems to be a predilection for the vestibulocochlear nerve, but optic nerve involvement is uncommon^[20]. In endemic areas any suspicious nervous system symptom should be investigated for neurobrucellosis as it may easily be misdiagnosed any neurological syndrome, brucellar spinal root involvement may cause a lower type of motor neuron lesion. In this regard, our case is a lower motor neuron type lesion with its nerve root involvement. A Guillain–Barré like syndrome with symmetrical polyradiculopathy and no sensory loss has been reported by Bahemuka *et al.*^[21] and five cases of polyradiculoneuropathy have been previously reported by Kochar *et al.*^[22]. Besides, Shakir *et al.*^[5] reported 19 cases of neurobrucellosis, six of which were in the form of proximal polyradiculoneuropathy. However, in our case the diagnosis of polyradiculoneuropathy was made with clinical and electromyography examinations which revealed axonal polyradiculoneuropathy.

The hearing loss and ataxia, although it is uncommon but there are some case reports^[23-28], the initial partial improvement of the weakness most likely related to Rifampicin effect. The effect of brucellosis on the nervous system can be because of the direct effect of bacilli, cytokines, or endotoxins on peripheral nerves, spinal cord, meninges, and the brain^[22]. Although the exact pathology is not totally resolved, a demyelination lesion is possible to account for some of the features^[5]. Most of the reported cases of neurobrucellosis showed correlation between the brucella titer in the CSF and blood. The blood titer usually is greater or equal to the CSF titer, which does not exist in our case in which the CSF titer is significantly high in/out of proportion to the blood titer level, which indicates that any case suspicious of neurobrucellosis with low or borderline brucella blood titer. CSF titer should be done to confirm the diagnosis. There are no specific antibiotic regimens and duration of treatment for neurobrucellosis. The duration of treatment varies from 8 weeks to 2 years. Rifampicin, Doxycycline and Trimethoprim/Sulfamethoxazole have been found effective with good central nervous system penetration and synergistic actions^[9]. Our case received IV amikacin, Rifampicin, Doxycycline and Co-trimoxazole.

Conclusion

In conclusion, brucellosis may resemble a variety of neurological syndromes, including polyradiculopathy, ataxia, cranial neuropathy, including hearing loss, Therefore, a complete work-up for brucellosis including culture and agglutination titer test should be done in the blood and CSF to rule out or confirm the presence of brucellosis.

References

- [1] **Bingöl A, Yüçemen N, Meço O.** Medically treated intraspinal "Brucella" granuloma. *Surg Neurol* 1999; **52**(6): 570-576.
- [2] **Duyur B, Erdem HR, Ozgocmen S.** Paravertebral abscess formation and knee arthritis due to brucellosis in a patient with rheumatoid arthritis. *Spinal Cord* 2001; **39**(10): 554-556.
- [3] **Gür A, Geyik MF, Dikici B, Nas K, Cevik R, Sarac J, Hosoglu S.** Complications of brucellosis in different age groups: a study of 283 cases in southeastern Anatolia of Turkey. *Yonsei Med J* 2003; **44**(1): 33-44.
- [4] **Geyik MF, Gür A, Nas K, Cevik R, Saraç J, Dikici B, Ayaz C.** Musculoskeletal involvement of brucellosis in different age groups: a study of 195 cases. *Swiss Med Wkly* 2002; **132**(7-8): 98-105.
- [5] **Shakir RA, Al-Din AS, Araj GF, Lulu AR, Mousa AR, Saadah MA.** Clinical categories of neurobrucellosis. A report on 19 cases. *Brain* 1987; **110**(Pt 1): 213-223.
- [6] **Vajramani GV, Nagmoti MB, Patil CS.** Neurobrucellosis presenting as an intramedullary spinal cord abscess. *Ann Clin Microbiol Antimicrob* 2005; **4**: 14.
- [7] **Heindel W, Lanfermann H, du Mesnil R, Fischbach R.** [Infections of the cervical spine] *Aktuelle Radiol* 1996; **6**(6): 308-316.
- [8] **Miller JR, Jubelt B.** *Bacterial Infections*. In: Rowland LP (ed). *Merritt's Neurology*, 10th edn. Philadelphia: Lippincott, Williams & Wilkins, 2000. pp 103-107.
- [9] **Young EJ.** *Brucella Species*. In: Mandell GL, Bennet JE, Dolin R (eds). *Mandell, Douglas, and Bennet's Principles and Practice of Infectious Diseases*. Philadelphia: Churchill Livingstone, 2000. pp. 2386-2393.
- [10] **Shakir RA.** Neurobrucellosis. *Postgrad Med J* 1986; **62**(734): 1077-1079.
- [11] **Coskun E, Süzer T, Yalçın N, Tahta K.** Spinal extradural compression caused by granuloma of brucellosis. *Scand J Infect Dis* 1998; **30**(3): 311-313.
- [12] **Harman M, Unal O, Onbaşı KT, Kıymaz N, Arslan H.** Brucellar spondylodiscitis: MRI diagnosis. *Clin Imaging* 2001; **25**(6): 421-427.
- [13] **Ozates M, Ozkan U, Bükte Y, Ceviz A, Sari I, Simsek M.** Lumbar epidural brucellar abscess causing nerve root compression. *Spinal Cord* 1999; **37**(6): 448-449.
- [14] **al Deeb SM, Yaqub BA, Sharif HS, Phadke JG.** Neurobrucellosis: clinical characteristics, diagnosis, and outcome. *Neurology* 1989; **39**(4): 498-501.
- [15] **Thomas R, Kameswaran M, Murugan V, Okafor BC.** Sensorineural hearing loss in neurobrucellosis. *J Laryngol Otol* 1993; **107**(11): 1034-1036.
- [16] **McLean DR, Russell N, Khan MY.** Neurobrucellosis: clinical and therapeutic features. *Clin Infect Dis* 1992; **15**(4): 582-590.

- [17] **Cotran RS, Kumar V, Robbins SL.** *Infectious Disease.* In: Robbins SL (ed) Pathologic Basis of Disease, 4th ed. Philadelphia: Saunders, 1994. pp 364-365
- [18] **al Deeb SM, Yaquub BA, Sharif HS, Phadke JG.** Neurobrucellosis: clinical characteristics, diagnosis, and outcome. *Neurology* 1989; **39**(4): 498-501.
- [19] **Solomon HM, Jackson D.** Rapid diagnosis of *Brucella melitensis* in blood: some operational characteristics of the BACT/ALERT. *J Clin Microbiol* 1992; **30**(1): 222-224.
- [20] **Tali ET, Keskin T, Öznür II, Simonson T, Yuh WT.** MRI of brucella polyneuritis in a child. *Neuroradiology* 1996; **38** (Suppl 1): S190-192.
- [21] **Bahemuka M, Shemena AR, Panayiotopoulos CP, al-Aska AK, Obeid T, Daif AK.** Neurological syndromes of brucellosis. *J Neurol Neurosurg Psychiatry* 1988; **51**(8): 1017-1021.
- [22] **Kochar DK, Agarwal N, Jain N, Sharma BV, Rastogi A, Meena CB.** Clinical profile of neurobrucellosis--a report on 12 cases from Bikaner (north-west India). *J Assoc Physicians India* 2000; **48**(4): 376-380.
- [23] **Valenza G, Kallmann B, Berend A, Mlynski R, Nöckler K, Kurzai O, Frosch M, Abele-Horn M.** Isolation of *Brucella melitensis* from a patient with hearing loss. *Eur J Clin Microbiol Infect Dis* 2006; **25**(1): 67-68.
- [24] **Kaygusuz TO, Kaygusuz I, Kilic SS, Yalcin S, Felek S.** Investigation of hearing loss in patients with acute brucellosis by standard and high-frequency audiometry. *Clin Microbiol Infect* 2005; **11**(7): 559-563
- [25] **Tuncer I, Akdeniz H, Uygan I, Türkdöğän K, Cekici S, Durmuş A.** A brucellosis case with ascites, hearing loss and pancytopenia. *Turk J Gastroenterol* 2002; **13**(3): 168-171.
- [26] **Sahin E, Yilmaz A, Ersöz G, Uğuz M, Kaya A.** Multiple cranial nerve involvement caused by *Brucella melitensis*. *South Med J* 2009; **102**(8): 855-857.
- [27] **Thomas R, Kameswaran M, Murugan V, Okafor BC.** Sensorineural hearing loss in neurobrucellosis. *J Laryngol Otol* 1993; **107**(11): 1034-1036.
- [28] **Tuncel D, Uçmak H, Gökçe M, Utku, U.** Neurobrucellosis. *Eur J Gen Med* 2008; **5**(4): 245-248.

تقرير حالة داء البروسيلات العصبي وفقدان السمع وضعف الأقدام

عائشة عبدالملك الشريف

قسم الباطنة، كلية الطب، جامعة الملك عبدالعزيز

جدة - المملكة العربية السعودية

المستخلص. داء البروسيلات العصبي يسبب عدم التوازن، وضعف في الأقدام، وفقدان السمع، وعدم التوافق بين نتيجة الأجسام المضادة في الدم والسائل النخاع الشوكي. وفي هذه الورقة نعرض حالة رجل يبلغ من العمر خمسة وأربعين عامًا يعاني من ضعف مزمن في القدمين، وفقدان السمع، وعدم التوازن، ولقد أوضحت التحاليل الطبية وجود زيادة في نسبة الأجسام المضادة في الدم، وفي عينة بذل النخاع الشوكي لبكتيريا البروسيلات، ولقد أعطي علاج البروسيلات مما أدى إلى شفائه.