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Case report

Isolated intracranial hypertension: a rare presentation of neurobrucellosis

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Abstract

Brucella melitensis infection is endemic in the eastern and south-eastern Anatolia regions of Turkey. We report an unusual case of brucella meningitis presenting with bilateral papilla stasis, diplopia and absence of other neurological involvement. Diagnosis was made by positive culture of *Brucella* spp. with a BACTEC 9120 system with inoculation of the patient's cerebrospinal fluid (CSF). This is the first report of isolation of *Brucella* spp. from CSF on a BACTEC 9120 system for diagnosis of meningitis. This case demonstrated that brucella meningitis may present with very slight symptoms, and inoculation of CSF into BACTEC bottle besides conventional cultures improves the detection of *Brucella* in endemic areas such as Turkey.

Keywords: *Brucella*; Bilateral papilla stasis; Diplopia; Meningitis; BACTEC

1. Introduction

Brucella melitensis infection is endemic in the eastern and south-eastern Anatolia regions of Turkey [1]. The habit of consuming raw milk and unpasteurized milk products is widespread in these regions. The disease is commonly seen in people consuming unpasteurized milk or milk products and in those living in close contact with animals and their products. These organisms might cause neurobrucellosis, which was first described by Hughes in 1896 [1]. Clinically it presents as meningoencephalitis in the acute form and polyradiculopathy, myelitis, cerebellar syndrome or cranial nerve involvement in the chronic form [1–8].

Brucellosis is diagnosed with high certainty through conventional bacteriological methods when *Brucella* spp. are recovered from blood, bone marrow or other tissues using rapid culture techniques such as the BACTEC system or the DuPont isolator, by which incubation time for recovery of brucellae is decreased. Presumptive diagnosis can be made serologically by rose bengal and standard tube agglutination (STA) tests. High or increased titers of specific *Brucella* antibodies are indicative of active brucellosis.

Here, we report an unusual case of brucella meningitis presenting with bilateral papilla stasis, diplopia and absence of other neurological involvement.

2. Case report

A 38-year-old woman presented with diplopia, headache, vomiting and artralgia for 2 months, with no fever or sweating. Bilateral papilla stasis was found on fundus examination. She was admitted to the hospital. Her mental status was normal. There was no neck stiffness, Kernig's sign or any neurologic deficits on physical examination. All the other possible etiologies of bilateral papilla stasis such as intracranial tumor, malignant hypertension, diabetic papillopathy, poisoning/toxicity, and optic neuritis were adequately excluded with history, neurological and opthalmological examination and neuro-radiological imaging. White blood cell count (5500 mm^3), hemoglobin (11.5 mg/dl), and erythrocyte sedimentation rate (20 mm/h) were within normal limits. Leukocyte formula revealed 64% lymphocytes, 24% neutrophils and 12% monocytes. Blood chemistry was within normal range.

Cranial computerized tomography, magnetic resonance (MR) imaging and MR angiography were normal. Lumbar puncture (LP) was performed, and the opening pressure was

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300 mmH_2O. Cerebrospinal fluid (CSF) examination revealed 80 lymphocytes per mm^3, with 0.20 mg/l protein and 0.53 mg/l glucose (serum glucose: 124 mg/l). No microorganisms were seen on Gram and methylene blue stains of CSF. The CSF sample was cultured routinely on blood agar, chocolate agar, eosin-methylene-blue agar (EMB) and sabouraud dextrose agar medium (Oxoid, Oxoid Ltd., Basingstoke, Hampshire, UK) incubated at 37 °C under 5% CO_2 atmosphere. There was no growth on routine media after 48 h incubation. Two days later, LP was repeated for the second CSF examination. Leukocyte count, protein and glucose levels were the same as the first CSF results. Opening pressure was 280 mmH_2O. CSF cultures were repeated on routine conventional agar. Simultaneously, a 1-ml CSF sample was inoculated into blood culture medium (BACTEC 9120, Becton-Dickson, automatic blood culture system) and into a blood culture bottle, BACTEC 9120. The culture of CSF was also negative on plate agar medium, but BACTEC tubes yielded positive growth signals by the fifth day of incubation. These positive tubes were subcultured on sheep blood agar, chocolate agar and EMB at 37 °C in 5% CO_2 atmosphere for at least 48 h. Small whitish colonies appeared on blood and chocolate agar only after 48 h and no growth on EMB agar. The colonies yielded Gram-negative coccobacilli, and they were positive for oxidase and urease tests and not utilized glucose, lactose and sucrose sugars of triple sugar iron agar. *Brucella* identification was made according to the above data together.

At first, the serologic test for *Brucella* was positive, with a titer of 1/80. One week later, the titer increased to 1/160. Serologic testing in CSF was not studied, due to uncertainty declared by the manufacturer.

After isolation and identification of *Brucella* spp. from CSF, therapy with doxycycline (100 mg twice a day), rifampin (600 mg/day orally) and trimethoprim-sulfamethoxazole (TMP-SMX) (160 mg twice a day) was instituted. Doxycycline was not tolerated and was stopped after the fifth day. Treatment was continued with TMP-SMZ and rifampin. The patient's condition improved, diplopia disappeared, and the CSF leukocyte count decreased to 40 per mm^3 at 2 weeks after initiation of therapy. Papilla stasis and intracranial hypertension returned to normal within 4 weeks. After 4 weeks, she was discharged from the hospital and advised to continue the anti-brucella medication. CSF returned to normal within 5 months. The therapy was stopped after CSF results returned to normal; she was very healthy, and no relapse was seen after 6 months following therapy.

3. Discussion

About 18 000 new cases of brucellosis are diagnosed per year in Turkey, and the prevalence of seropositivity in the Turkish population varies from 2.6% to 14.4%, according to geographical region [1].

Neurological complications of brucellosis are quite rare, with an incidence reported to be 1.7–10% [1,2]. Although depression and mental confusion are common in brucellosis, direct invasion of the central nervous system (CNS) occurs in less than 5% of cases [12].

In a classical review on this subject, Shakir et al. [2] divided neurobrucellosis into two main categories according to the mode of presentation. The first is an acute presentation with meningoencephalitis, and the second a chronic form affecting both the peripheral and the CNS [2,4]. The chronic peripheral form includes proximal polyradiculoneuropathy, whereas the central form comprises a diffuse CNS involvement, predominantly involving spinal cord or cerebrum with or without cranial nerve palsies [2].

Al Deeb et al. [5] report 13 neurobrucellosis cases, which were subdivided into five categories: forms of acute meningoencephalitis, meningovascular involvement, CNS demyelination, peripheral neuropathy, and finally papilledema and increased intracranial pressure.

The common symptoms of chronic brucellosis are headache and lassitude, neither of which is due to direct CNS infection, which is quite rare [2]. Involvement of the CNS can be due to direct effects of bacilli, cytokines or endotoxins on peripheral nerves, spinal cord, meninges and brain. The neurological signs of brucellosis can also be secondary to the vertebral involvement or abscess formation in the brain. The nervous system can be involved in various stages of brucellosis, i.e. at the onset of illness, during the course of illness or during convalescence or months after recovery from acute infection [4].

Zaidan and Al Tahan [8] described a patient with increased intracranial pressure and papilledema without hydrocephalus. But in that case, cerebral venous thrombosis was the main cause. In the case we describe, cranial computerized tomography, MR and MR angiography excluded this diagnosis.

Diaz Espejo et al. [9], reported an exceptional case of neurobrucellosis, presenting with chronic intracranial hypertension together with destruction of the sella turcica.

Meningitis is the most common manifestation of neurobrucellosis [1–11]. CSF analysis reveals a lymphocytic pleocytosis, elevated protein content and low to normal glucose level. But in our patient, there was no neck stiffness, Kernig's sign or any neurological deficits on physical examination, and blood and CSF chemistry were within normal range. CSF examination revealed 80 lymphocytes per mm^3, with 0.20 mg/l protein and 0.53 mg/l glucose (serum glucose: 124 mg/l) and intracranial opening pressure was 300 mmH_2O. It is an unusual case of brucella meningitis, presenting with diplopia, bilateral papilla stasis and absence of other neurological involvement.

Isolation of the organism from blood or bone marrow proves presence of the disease. In brucella meningitis, Gram stains are usually negative, and cultures are positive in less than one quarter of the cases [12]. Over the last decade, the use of a blood culture system for the culture of normally

sterile body fluid other than blood has gained increasing acceptance [13]. Currently, it was found that it is more accurate and efficient in detecting brucellosis. It can also be used for detection of other slow-growing bacteria like *Kingenella*. Yagupsky reported 1072 synovial fluid culture procedures in the BACTEC 9240 blood culture system, and 15 of them (0.14%) were positive for *B. melitensis* [1]. The BACTEC system can improve isolation of the bacteria, especially slow-growing bacteria like *Brucella* spp. Bone marrow and synovial fluid inoculation in the BACTEC system were previously used for diagnosis of brucellosis [13,14]. This is the first report of isolation of *Brucella* spp. from CSF by the BACTEC 9120 system for diagnosis of meningitis.

In the BACTEC culture system, the mean detection time for *Brucella* was reported to be 2–7 days [15–17]. In our case, an automated blood culture system, BACTEC 9120, *Brucella* spp. was identified on the fifth day after inoculation, although cultures of CSF were negative on conventional plate agar media. Automated BACTEC culture systems can isolate *Brucella* spp. in a fast and efficient way for bloodstream infection. The isolation time for brucellae may be reduced by these systems to 4–7 days instead of 3 weeks. The isolation time of 5 days was as rapid as that reported for blood, bone marrow and synovial fluid in the literature [13–16].

There is no unanimity of opinion regarding the optimal regimens for brucella meningitis [12]. There is still no consensus on type and number of antimicrobials and duration of therapy for brucella meningitis. Most authorities recommend the use of doxycycline in combination with two or more other drugs, with treatment continued for many months, depending on the response [12]. In our case, treatment was started with doxycycline and TMP-SMX and rifampin, but doxycycline was discontinued because of intolerance. Treatment of neurobrucellosis remains controversial. Some authors of studies recommend therapy with two drugs [18,19]. For that reason, we did not start other antimicrobials in addition to rifampin and TMP-SMX. The patient's response to this regimen was good and the lymphocyte count in CSF was decreased within 2 weeks. The therapy was continued until no leukocytes in CSF were observed.

To conclude, based on the case reported here, we think that in endemic areas of brucellosis, in the presence of bilateral papilla stasis, one must consider and rule out neurobrucellosis even without focal neurological deficits or other common symptoms. In addition, in endemic areas like Turkey, besides conventional cultures, CSF should be inoculated into a BACTEC blood culture system for certain and rapid diagnosis of neurobrucellosis.

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