

Case Report

Neurobrucellosis presenting as a pituitary abscess: a case report and review of literature

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Abstract: Brucellosis, a zoonotic disease caused by infection with *Brucella melitensis*, has a pan-global presence. Neurobrucellosis is a rare complication of the disease. Herein, we presented our experience with a case of neurobrucellosis in a 31-year-old man who presented with a pituitary abscess. Surgical resection of the abscess was performed, and standard combined antibiotic regimen was administered postoperatively. Neurobrucellosis may pose a diagnostic challenge owing to its rarity and the non-specific clinical and radiological findings. Detailed history taking and systematic laboratory examinations of serum and cerebrospinal fluid are keys to an early diagnosis of the condition. Treatment compliance and appropriate surgical intervention are other important aspects of management of neurobrucellosis that confer a favorable prognosis.

Keywords: Neurobrucellosis, pituitary abscess, surgery, antibiotics

Introduction

Brucellosis, caused by *Brucella melitensis*, is one of the most common zoonotic diseases with a pan-global presence. The most common routes of infection in humans are through consumption of raw meat and unpasteurised milk or by direct contact with infected animals [1, 2]. After entering human body, the pathogens multiply inside the phagocytic cells and eventually cause clinical symptoms. Affected patients may exhibit a broad spectrum of clinical manifestations and complications. These include undulant fever, hepatosplenomegaly, lymphadenectasis, abortion, orchitis, spondylitis, arthritis, endocarditis, encephalitis, and asthenia [3]. Involvement of the central nervous system (CNS), also referred to as neurobrucellosis (NB), is a rare but serious complication of brucellosis [4-6].

Neurobrucellosis is usually underdiagnosed, and especially in non-pastoral areas differentiating NB from other infectious diseases is often challenging. In this paper, we present our experience with a case of NB who presented with a pituitary abscess.

Case report

A 31-year-old man presented with a history of fever and headache for one week and developed a mental aberration for one day. The patient had a history of long-term direct contact with animal flocks. Six months later, he was diagnosed as a case of brucellosis, for which no systemic treatment was received. One week prior to admission, he developed fever with a peak temperature of 39°C. He also complained of intermittent headache. One day prior to admission, a sudden onset of psychiatric symptoms including, restlessness, shouting, rambling speech, symptoms suggestive of auditory and visual hallucinations and lack of normal response to questions was observed. Physical examination showed neck stiffness. Brain magnetic resonance imaging (MRI) showed a sellar mass with a diameter of 39×35×31 mm. The mass had a heterogeneous appearance; the front part appeared hyperintense on T1 weighted images (T1WI) and hypointense on T2 weighted images (T2WI); the posteroinferior part appeared hypointense on T1WI and hyperintense on T2WI. The optic chiasma was significantly compressed; no obvious signs of oede-

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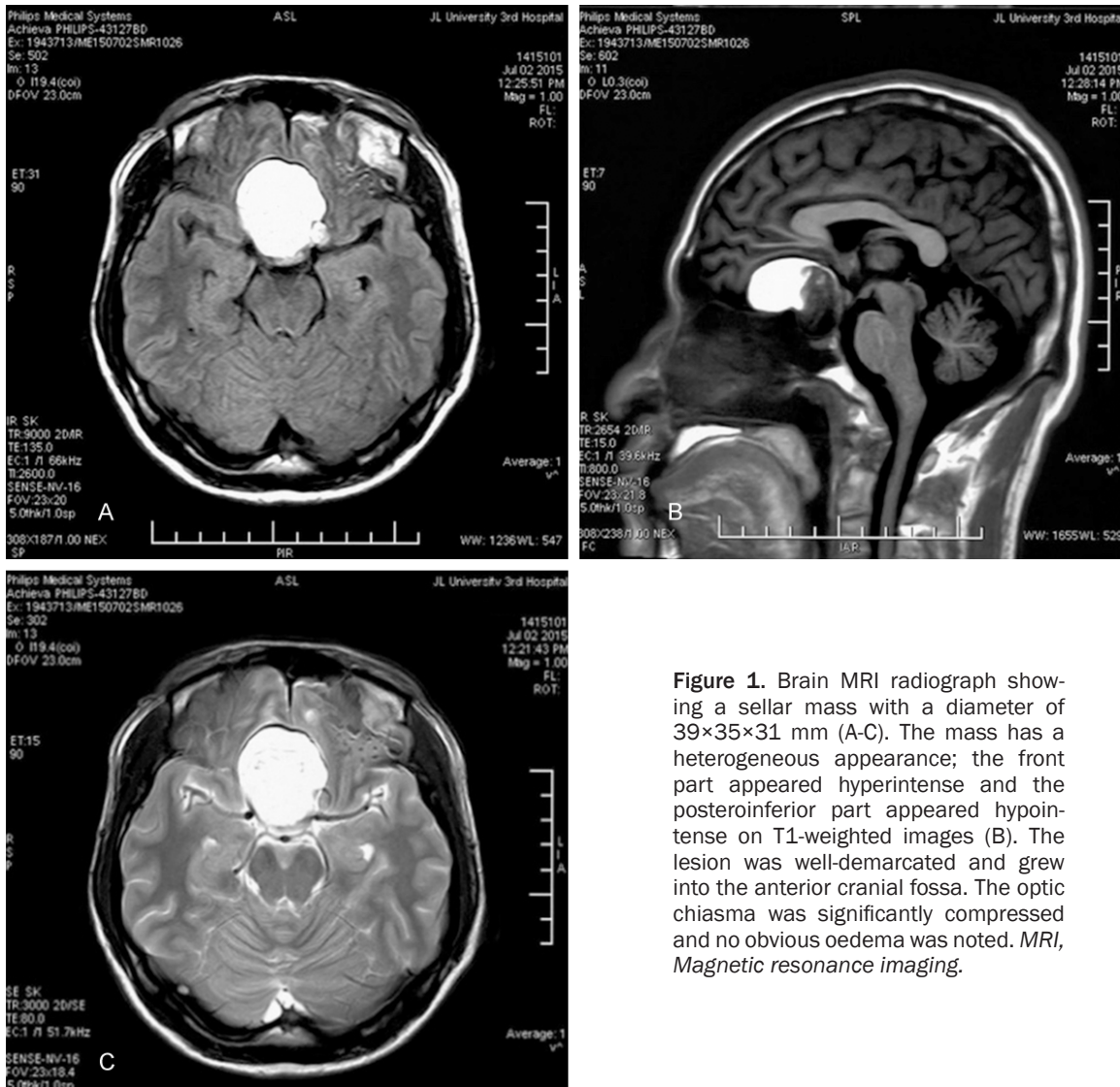


Figure 1. Brain MRI radiograph showing a sellar mass with a diameter of 39×35×31 mm (A-C). The mass has a heterogeneous appearance; the front part appeared hyperintense and the posteroinferior part appeared hypointense on T1-weighted images (B). The lesion was well-demarcated and grew into the anterior cranial fossa. The optic chiasma was significantly compressed and no obvious oedema was noted. MRI, Magnetic resonance imaging.

ma were noted (Figure 1A-C). Laboratory investigations revealed a significant increase in serum growth hormone level (10.3 ng/mL; normal range 0.003-0.971 ng/mL), while other endocrine hormone levels were normal.

A preoperative diagnosis of pituitary abscess was made. Craniotomy was performed using the right frontotemporal approach. Intraoperatively, the mass appeared yellow, viscous and tofukasu-like, and it severely compressed the pituitary and optic chiasma. Histopathological examination revealed degeneration and myxoid changes, as well as scattered acute or chronic inflammatory cells. Immunohistochemical examination was not consistent with a neoplastic lesion. Serum agglutination test showed a high titre (> 1:300). However, *Brucella* was not

detected in the serum, cerebrospinal fluid, or in the lesion pus.

On the first postoperative day, the laboratory test of cerebrospinal fluid demonstrated an increased pressure (> 300 mmH₂O), an increased protein level (0.92 g/L; normal range 0.15-0.45 g/L), increased leukocytes (66×10⁶/L; normal range 0-8×10⁶/L) and erythrocytes (300×10⁶/L; normal range 0×10⁶/L) levels, and an increased proportion of monocytes (86%). The Pandy test was positive; the glucose and chloride levels were normal.

Postoperatively, headache and psychiatric symptoms were completely relieved; the patient developed transient diabetes insipidus that recovered following administration of desmo-

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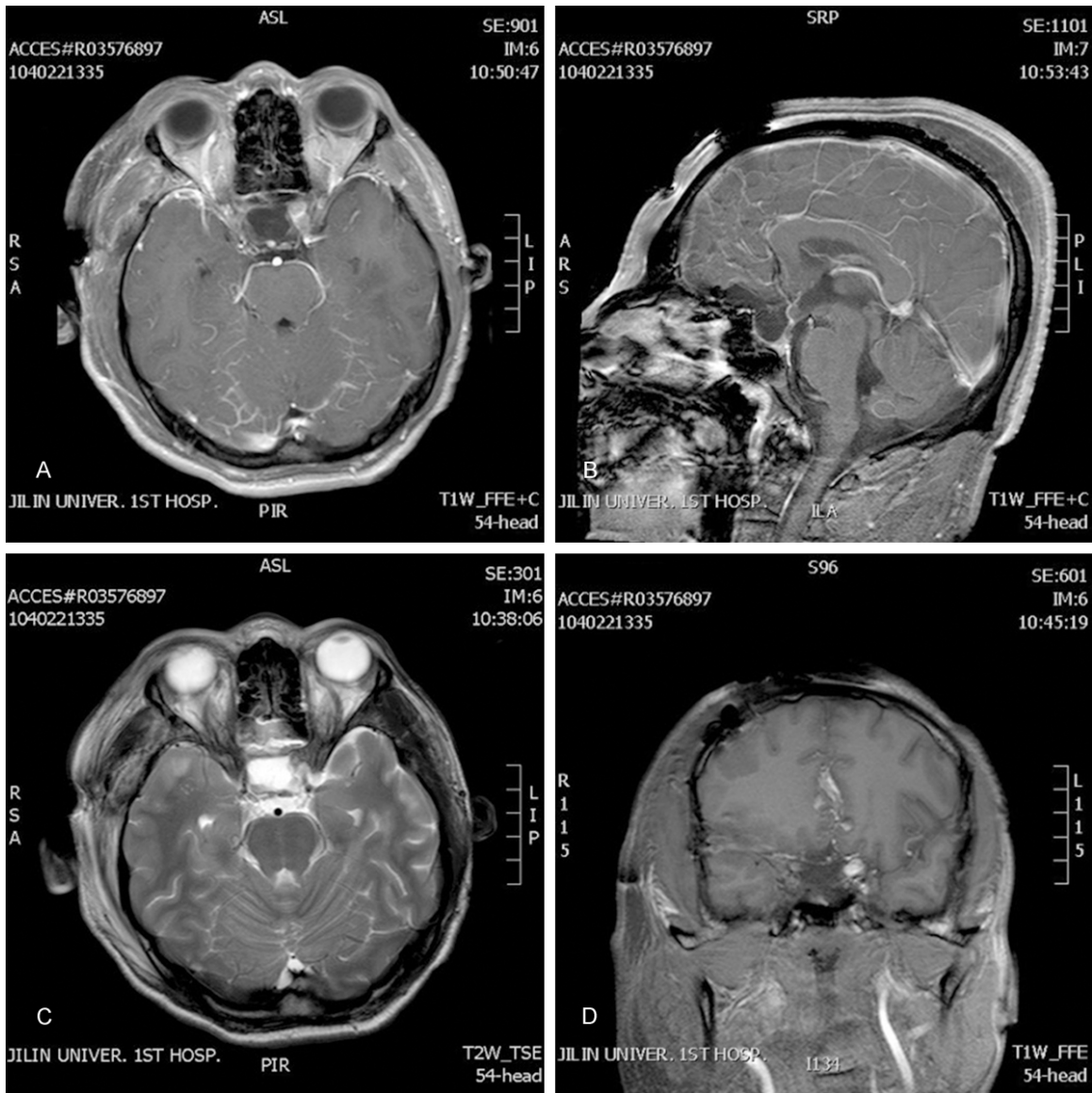


Figure 2. Postoperative MRI confirmed a gross total resection. *MRI, Magnetic resonance imaging.*

pressin acetate for one week. Postoperative magnetic resonance imaging (MRI) confirmed the gross total resection of the pituitary abscess (Figure 2). A diagnosis of NB was made, and a combined antibiotic protocol was prescribed (doxycycline [100 mg, twice daily], rifampicin [600 mg, once daily], and ceftriaxone [2000 mg, twice daily]). In the following days, the temperature fluctuated between 37.6°C and 38.8°C. Considering the evidence of cerebrospinal fluid infection, ceftriaxone was replaced by meropenem (2000 mg, three times a day) and continuous lumbar cistern drainage was performed.

At the time of discharge, his temperature and laboratory examination of cerebrospinal fluid were normal. He was advised to continue treatment with doxycycline, rifampicin and ceftriaxone for 6 weeks. During a follow-up period of 10 months, the patient was asymptomatic and laboratory and radiological examinations were all normal.

Discussion

Brucellosis is an infectious and allergic zoonotic disease caused by infection with bacteria of the genus *Brucella*. It is widespread in more

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than 170 countries. The annual incidence of brucellosis is estimated to be > 500,000 cases; the prevalence rates exceed 10 cases per 100,000, with considerable geographical variability [7, 8]. Neurobrucellosis is a rare form of brucellosis with diverse transmission routes, and it is vulnerable to misdiagnosis. NB affects approximately 1.7-10% of all cases of brucellosis, and is associated with a high mortality rate of up to 7% [9].

The neurological impairment in NB is primarily caused by the inflammatory-immune response to the endotoxin. The infected monocytes and lymphocytes are known to be resistant to apoptosis, which results in prolonged survival of the bacteria thereby increasing the risk of central nervous system involvement [10]. Additionally, the endotoxin induces an allergic inflammation with a characteristic monocytic infiltration in chronic infection. Focal neurological symptoms may be the only sign of NB (peripheral nerve involvement is common), or it can be one of the systemic symptoms in chronic Brucellosis [4, 6]. Gul *et al.* retrospectively analyzed 187 cases of NB, and found three cases that presented as cerebellar abscess, spinal abscess and epidural abscess, respectively [11].

Meningitis, meningoencephalitis or encephalitis is the most common clinical manifestation of NB. Other neurological symptoms include peripheral neuropathy, neuritis of multiple nerve roots and myelitis [12]. Most patients present with cranial nerve involvement; the vestibulocochlear, oculomotor, abducent, facial, trigeminal and optic nerves being more commonly involved. There seems to be a particular predilection for vestibulocochlear nerve involvement in NB [13, 14]. Cases of neurobrucellosis presenting with neurovascular signs such as transient ischemic stroke and subarachnoid haemorrhage are also on record [15]. There are some other infrequent manifestations as well, such as Guillain-Barre syndrome and pituitary abscess [5, 16].

Specific radiological findings that may suggest a diagnosis of NB are still lacking. In a study of neuroimaging data pertaining to 23 cases of brucellosis by Al-Sous *et al.*, the main radiological findings included inflammation, white matter impairment, and vascular injury [17]. The first NB case with a sellar lesion was described by Çiftçi *et al.* in 1998 [18].

The standard diagnostic criteria of NB include: 1) epidemiological contact history: close contact with livestock or livestock products, or living in brucellosis-affected area; 2) neurological symptoms; 3) abnormalities in cerebrospinal fluid detected by laboratory examinations: increased protein level or mild-to-moderately elevated lymphocyte count; glucose and chloride levels may be normal in the early stages (mimicking viral encephalitis) and decreased in the later stages (mimicking tuberculous meningitis); 4) positive findings in immunological tests of the serum, bone marrow or cerebrospinal fluid: isolation of *Brucella*, positivity to the *Brucella*-specific antibodies, or serological agglutination titres > 1:160; 5) improvement in clinical or laboratory indices with standard treatment for *Brucella*; 6) other suspected diseases excluded [19].

In the present case, the patient had a history of long-term contact with animal flocks, and exhibited severe psychiatric symptoms and neck rigidity. Brain MRI study revealed a sellar mass, and the titre of serum agglutination test (> 1:300), both of which were consistent with a diagnosis of NB. Additionally, the improvement in clinical and laboratory indices following standard antibiotic treatment protocol for brucellosis further favored the diagnosis.

Although the isolation of *Brucella* in serum or bone marrow is the gold standard for diagnosis of brucellosis, in 14% of the brucellosis cases in a study by Gul *et al.*, the organism was isolated from the cerebrospinal fluid [11]. In most cases, the diagnosis is established based on the combination of clinical manifestations, results of serum agglutination test and cerebrospinal fluid examination. Due to the rarity of NB and the difficulty in bacterial isolation, a prompt definitive diagnosis is challenging. Due to the abnormalities in cerebrospinal fluid detected by laboratory examinations, a probable intracranial infection postoperatively should be taken into consideration as well; identifying NB from postoperative infection may be difficult. Currently, the standard treatment for NB involves use of multiple antibiotics that can achieve high intracellular concentration and can traverse the blood-brain-barrier [7, 20]. Completion of full treatment course should be emphasized. The widely-used protocol includes doxycycline (200 mg/day) and rifampicin (600-900 mg/day), in combination with other antibi-

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otics like ceftriaxone, aminoglycosides or quinolones. The combination treatment regimen should be administered for at least six weeks [21]. And furthermore we recommended a much longer treatment course of more than four months to prevent recurrence of NB. Hormone medications can be used in patients with serious complications such as meningitis, osteomyelitis, or endocarditis [22].

With the indiscriminate use of anti-inflammatory drugs and antibiotics, the characteristic clinical presentation of undulant fever is uncommon. Moreover, misuse of these medications tends to mask the symptoms and contribute to a delayed diagnosis of brucellosis. The documented recurrence rate of brucellosis is in the range of 5-10%, and thus a long-term regular follow-up is a key element of its management [23].

Pituitary abscess is a rare manifestation of NB, which may be difficult to diagnose owing to the non-specific clinical and radiological features. A comprehensive history-taking and systematic laboratory investigation of serum and cerebrospinal fluid can facilitate an early diagnosis of this disease. Adherence to the recommended combined-antibiotic therapy is effective and confers a favorable prognosis.

Disclosure of conflict of interest

None.

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