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An unusual case of neurobrucellosis presenting with unilateral abducens nerve palsy: clinical and MRI findings

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ABSTRACT
Brucellosis is an endemic zoonotic disease in which neurobrucellosis occurs in 5–10% of cases. Variable clinical and radiological manifestations of neurobrucellosis can mimic those of other diseases. In this report, we present unusual clinical and magnetic resonance imaging (MRI) findings in a patient with neurobrucellosis and unilateral abducens nerve palsy. Her MRI showed punctate leptomeningeal enhancement of the cerebellum on contrast-enhanced T1-weighted images, and a focal area of hyperintensity in the splenium of the corpus callosum on T2-weighted images.

Key words: • *brucellosis* • *abducens nerve* • *magnetic resonance imaging*

Brucella is an intracellular bacterium that causes a chronic granulomatous infection similar to tuberculosis, requiring combined and protracted antibiotic treatment (1). Brucellosis is a zoonotic disease, endemic in certain geographic parts of the world, such as the Middle East, Central Asia, and Mediterranean countries (2–4). Humans are affected as secondary hosts through the consumption of infected unpasteurized milk products, direct contact with infected animal parts, and the inhalation of infected aerosolized particles (1, 5). Neurobrucellosis (NB) occurs in 5–10% of cases, and affects the central or peripheral nervous system (CNS, PNS) (6). Variable clinical manifestations and imaging abnormalities of NB can mimic other neurologic diseases (2). Herein, we report the unusual clinical and magnetic resonance imaging (MRI) findings of a patient with NB presenting with unilateral abducens nerve palsy.

Case report

A 24-year-old female patient was referred to our hospital complaining of sore throat. Presumed to have acute tonsillitis, she was given antibiotic therapy including procaine penicillin. On the fourth day of therapy; she developed diplopia with left lateral gaze, nausea, vomiting, joint pain, and jaundice, and was hospitalized immediately afterwards. She disclosed a history of consumption of unpasteurized milk and milk-products. It was also noted that her father had been treated for brucellosis 10 years ago.

General physical examination revealed fever and icteric sclera, but no sign of hepatomegaly. Neurological examination did not reveal any abnormalities except for left abducens nerve paralysis.

Laboratory findings revealed mild anemia, and elevated aspartate aminotransferase (AST), alanine aminotransaminase (ALT), alkaline phosphatase, lactate dehydrogenase (LDH), gamma glutamyl transpeptidase (GGT), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) levels. Serum bilirubin was also slightly increased. Blood culture was positive for *Brucella* spp., and the serum agglutination test for Brucella was positive at 1/1280. Lumbar puncture revealed a clear cerebrospinal fluid (CSF) with increased pressure (25 cm^2 H_2O). CSF protein level was 41 mg/dL (normal range, 15–45), and glucose and chloride levels were within normal limits. In addition, 80 cells/mL were detected in CSF, with a high proportion of lymphocytes. Wright and Coombs tests were both positive at a titer of 1/10. Rose-Bengal test was negative, but monoclonal IgG was detected in CSF.

Cranial MRI was performed on a 1.5 T Signa Horizon MRI system (GE Medical Systems, Milwaukee, Wisconsin, USA). Post-contrast T1-weighted images (TR/TE, 460/14 ms) revealed unusual leptomeningeal enhancement in the cerebellar hemispheres that was predominantly located peripherally (Fig. 1), although other sequences including the

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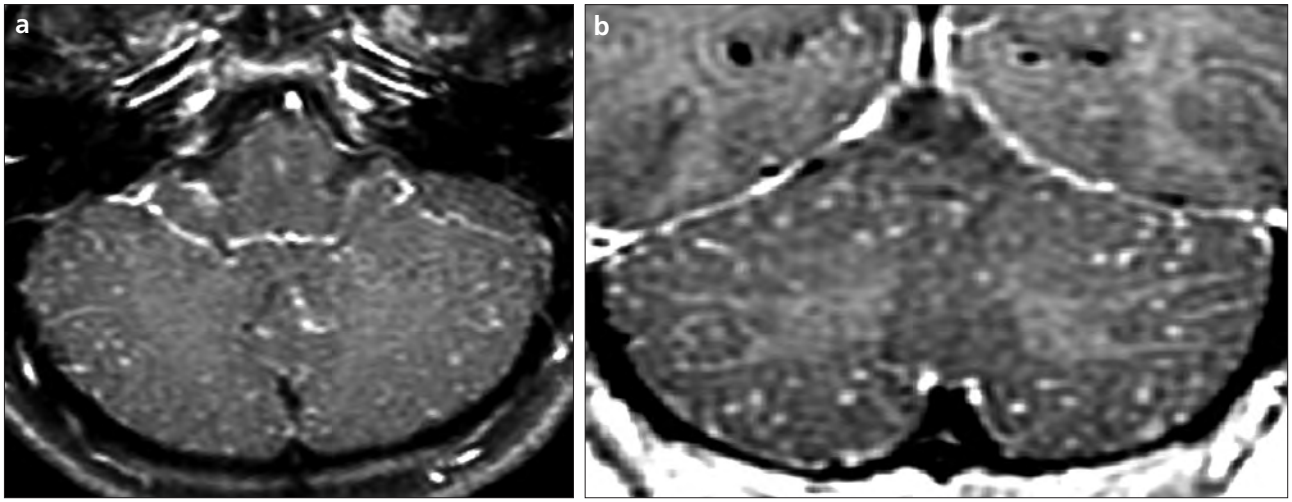

Figure 1. a, b. Axial **(a)** and coronal plane **(b)** contrast-enhanced T1-weighted MR images show unusual leptomeningeal enhancement in the cerebellar hemispheres that was located predominantly peripherally.

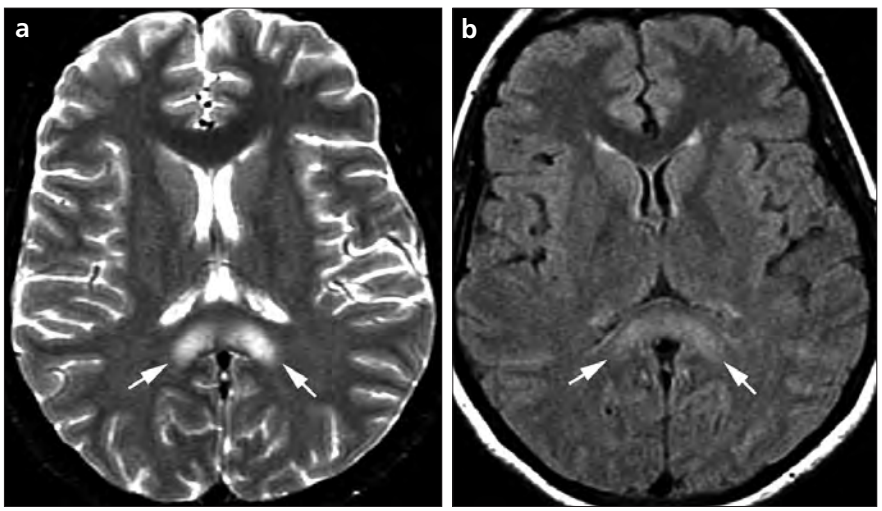

Figure 2. a, b. Axial plane T2-weighted **(a)** and FSEIR **(b)** MR images show an area of increased signal intensity at the splenium of the corpus callosum *(arrows)*.

FSEIR sequence did not show any abnormality in the cerebellum. Although special thin-sliced sequences intended for detailed visualization of cranial nerves were not obtained during cranial MRI, no enhancement of the left abducens nerve was noted, grossly. Additionally, a focal area of increased signal intensity at the splenium of the corpus callosum was detected on both T2-weighted (TR/TE, 4700/95 ms) and FSEIR (TR/TE, 8002/97 ms) sequences (Fig. 2), although diffusion-weighted MRI was normal. On the postcontrast MR images, the focal callosal lesion did not show contrast enhancement.

The patient was diagnosed with NB, by clinical, radiological, and laboratory findings. Following treatment with trimethoprim-sulfamethoxazole, doxycycline, and rifampicin, the patient's fever resolved. At the 3-month follow-up visit, ESR and serum biochemical values were within normal limits, and CSF tests were normal (Wright, Coombs, Rose Bengal, and Brucella IgM). Neurological examination was unremarkable. Control contrast-enhanced cranial MRI was also normal, except for persistent focal high intensity at the splenium on T2-weighted and FSEIR images.

Discussion

Brucella is still an important human pathogen, and is endemic in the undeveloped countries of the world. Following ingestion of contaminated products, hematogenous dissemination can occur, resulting in uptake of the bacteria by the reticuloendothelial system, and eventually, involvement of any organ (4).

Brucellosis is a disease with protean manifestations, although fever is an invariable feature. Malodorous perspiration and constitutional symptoms are generally present. Lymphadenopathy, hepatomegaly, and splenomegaly are often seen. Although osteoarticular disease, involvement of the reproductive system, and hepatitis are commonly seen, CNS is involved in only 5–7% of cases in most studies (1).

NB can develop at any stage of the disease (6). Several clinical forms of brucellosis affecting the CNS have been reported, including meningitis, meningoencephalitis, myelitis, radiculoneuritis, cranial nerve involvement, and demyelinating or vascular disease (3, 4, 6, 7). Thus, the presentation of NB is diverse (6). The most common type of NB affecting the CNS is chronic meningoencephalitis in which lymphocytic pleocytosis and high protein levels are detected in the CSF (8). Because Brucella is a slow-growing bacterium, CSF and blood cultures can be negative, so the diagnosis is generally made by serological methods. Brucella antibody seen in CSF is diagnostic (5).

Al Sous et al. claim that the clinical-radiologic correlation in NB is variable (2). They divide the imaging findings of NB into four categories: normal, inflammation (abnormal enhancement), white matter changes, and vascular changes. Inflammation is recognized by granulomas, or abnormal enhancement of the meninges, perivascular

space, or lumbar nerve roots (2). In our case, we noted both inflammation (cerebellar leptomeningeal enhancement) and white matter changes (corpus callosum hyperintensity on T2-weighted images). The inflammatory process, which presented as abnormal enhancement, disappeared on follow-up MRI after the treatment; however, the hyperintensity at the splenium did not disappear.

Although T2-hyperintensity of the splenium has been described in diverse clinical settings (e.g., epilepsy, use of antiepileptic drugs or metronidozole, and Marchiafava-Bignami disease), our patient did not have any of these conditions. Thus, splenial T2-hyperintensity in our patient was thought to result from an alternative mechanism. CNS demyelination can be a rare feature of NB (6, 8–10). In 1963, Fincham et al. reported that the white matter changes in NB were sequelae of demyelination, as confirmed by pathologic study (9). Marconi supported this claim with autopsy evidence that demyelination in a patient with NB was similar to that seen in lesions of multiple sclerosis (11). The nature of these white matter changes is not known, but they may be due to an autoimmune reaction (2). In addition to resembling that of multiple sclerosis or vasculitis, the white matter involvement of NB can mimic that of other inflammatory or infectious diseases such as acute disseminated encephalomyelitis or Lyme disease (2, 12). In our case, the persistent callosal signal change was also thought to be secondary to demyelination.

As a result of basal meningitis, involvement of one or more cranial nerves is seen in more than 50% of the NB cases. The vestibulocochlear nerve is the cranial nerve most frequently involved in NB (3). Isolated cranial nerve involvement in NB is a very rare condition; there are only a few reports of isolated abducens nerve palsy (13–15). The pathogenesis of abducens nerve palsy is speculative. Extension of meningeal infection, and possible vasculitic processes are the possible etiologies (13).

In addition to NB, other possible casues of cranial nerve palsies in patients with brucellosis include pseudotumor cerebri and side effects of tetracyclines, which are often used to treat brucellosis (15). Our patient also had unilateral (left) abducens nerve palsy. Because she had signs of basal meningitis as well as positive serological tests for brucellosis in the CSF, the etiology of cranial nerve involvement was presumed to be a result of basal meningitis, rather than pseudotumor cerebri. The medical literature would support a good prognosis with regard to cranial nerve involvement in our patient. Accordingly, her ocular symptoms regressed completely after therapy.

In conclusion, NB is a treatable disease with a favorable outcome. The diagnosis of NB depends mostly on high clinical suspicion in endemic countries. One should keep in mind the diverse clinical or radiological presentations of NB, particularly in young patients with neurological abnormalities. Imaging findings of NB are variable, and can mimic those of other demyelinating, infectious, or inflammatory conditions.

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