Acute Neurobrucellosis: Syndrome of Inappropriate Antidiuretic Hormone Secretion and Parkinsonism Presentation

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Received: April 6, 2014; Accepted: May 15, 2014

1. Introduction

Brucellosis is a zoonotic infection, which is considered as one of the most widely spread animal-human infections, worldwide (1). Brucellosis can be transmitted to human hosts through numerous pathways, yet the consumption of unpasteurized dairy products is still the most common way (2). Even though the disease can be found all over the world, some areas are considered as high risk regions for brucellosis, such as the Middle East, South and Central America, and Mediterranean Basin (3). In general, Brucella species infect the reticuloendothelial system, yet they can infect any organ of the body, which can result in serious complications with poor treatment and misdiagnosis, especially in endemic areas (4). Neurobrucellosis is found in less than 5% of brucellosis cases and has various clinical presentations in both central and peripheral nervous system; meningoencephalitis and aseptic meningitis are considered as the most common forms of nervous system involvement so far (5). Neurobrucellosis should be considered when neurological problems cannot be explained by other etiology especially in endemic areas (6).

2. Case Presentation

A retired 78-year-old man who had been healthy was admitted to our unit as he had experienced a few hours of decreased consciousness. His problems started with a dull headache in the occipital region four days earlier accompanied with nausea, vomiting, anorexia, bradycardia, restless tremor and rigidity. He referred to the clinic after three days, where a head CT scan and MRI was obtained, which revealed no structural or anatomic abnormalities; he developed a sudden fever 12 hours after admission. Except for tamsulosin use he wasn’t under any kind of prescription and use of illicit drugs. The only suspicious point in his history was regular use of unpasteurized dairy products for many years. On physical examination he was febrile with axillary temperature of 38.6°C, pulse rate of 114 beat/min and respiratory rate of 16/min. The rest of the physical examination was normal, yet the neurological examination revealed an old man with a semi-consciousness state, without nuchal rigidity and papilledema, and both Kernig’s and Brudzinski’s signs were negative. The patient’s lab tests were normal except for mild anemia and hyponatremia (Na = 125 mEq/L); liver function tests were slightly elevated, erythrocyte sedimentation rate (ESR) was 10 mm/h, C-reactive protein [CRP] was 5 mg/dL. Rapid plasma regain (RPR), HIV, and viral hepatitis serology tests were negative. Even with appropriate treatment with 3% hypertonic saline, the patient was still hyponatremic, and his sodium levels was between 125 mEq/L and 129 mEq/L. The patient received intravenous empirical treatment for meningitis with 2 g ceftriaxone, 1 g vancomycin, and 2 g ampicillin, plus a single dose of 700 mg acyclovir. The second brain CT had normal results, cerebrospinal Fluid (CSF) samples were collected and revealed high protein (150 mg/dL), with lymphocytic pleocytosis (WBC = 65 cell/μL, 91% lymphocyte) and low glucose (20 mg/dL). The PCR of CSF
was negative for mycobacterium tuberculosis and HSV1-2. Serum agglutination tests were positive; Wright t/640 and 2ME t/40. The brucellosis antibody test was positive for IgG (IgG = 165.4 Ru/mL) and CSF-PCR was positive for brucellosis.

The patient’s treatment was switched to doxycycline 200 mg/q12h, oral rifampin 600 mg/d and intravenous ceftriaxone 2 g/q12h for 2 weeks. After this treatment all of the patient’s symptoms subsided even his uncontrolled hyponatremia and parkinsonism signs and he gained back his health. After discharge, the ceftriaxone was changed to trimethoprim/sulfamethoxazole (160/800), 2 tablets/q12h. The three-antibiotic treatment was continued for 12 weeks with weekly follow ups.

3. Discussion

Brucella species are gram-negative, aerobic, encapsulat- ed coccobacilli, which include B. melitensis, B. abortus, B. canis and B. suis. These species can infect humans (1). The first Brucella stain isolated in Iran was B. abortus, which was isolated from a bovine fetus, during the year 1944 (7). Besides, in 1950, the first B. melitensis was isolated (8). These two species are the only species isolated in Iran with B. melitensis having greater prevalence (5). Brucellosis has high incidence in Iran with a rate of about 0.73-141.6 per 100000 individuals, per year (9, 10). The main sources of infection are ingestion of contaminated dairy products, direct contact with infected animals, conjunctival in- oculation and inhalation of contaminated aerosols (10).

There are various risk factors associated with brucellosis, which can be modified by education programs; these in- clude, having an infected individual in the household, and animal’s death or abortion in family holding and raising animals also considered to be a risk factor related to animals. Educated individuals seem to have a protective factor against brucellosis (11). Neurobrucellosis is a rare presentation of brucellosis which occur by direct or indirect mechanisms (12). Neurobrucellosis has many signs and symptoms including, headache, fever, sweats, weight loss, meningeal irritation signs, confusion, hepato- splenomegaly, convulsion disorder, dysarthria and diplo- pia (13). The most common clinical manifestation of NB is aseptic meningitis or meningoencephalitis (5, 9), but it can also manifest as polyradiculoneuritis, Guillain-Barre syndrome, brain abscess (14) and Parkinson’s disease (15). Theoretically, any central nervous disorder can lead to antidiuretic hormone release which leads to syndrome of inappropriate antidiuretic hormone secretion (SIADH) and hyponatremia (16).

NB diagnosis is done by isolating the Brucella bacteria from blood or CSF which is considered as the gold standard, but cultures are negative in > 50% of the cases (9, 15). Cerebrospinal fluid analysis usually reveals lymphocytic pleocytosis, high protein levels and hypoglycorrhachia, except for cerebellar syndrome, which only results in high protein level (9, 16). Agglutination tests such as Coombs test and Rose-Bengal test are used for diagnosing NB, but their sensitivity is less than enzyme-linked immuno- sorbent assay (ELISA); real time PCR assay is a powerful tool for detecting and diagnosing NB (17).

Neurobrucellosis treatment includes the following medications, doxycycline, rifampicin, ceftriaxone, trimethoprim-sulfamethaxozol, streptomycin and ciproflox- acin, which have been found to have high effectiveness against NB (18). Treatment duration depends on the patient’s condition; the duration of treatment is 24 weeks (19). Even for our patient who was an elderly with chronic use of unpasteurized dairy products, NB was without systemic involvement and the treatment was only for 12 weeks due to rapid response to the treatment. The prognosis is favorable, with mortality rate being less than 5.5%. However, there are reports of permanent bilateral hearing loss and myelopathy (20). Regarding our patient, even with presentation of acute brucellosis as NB and symptoms of SIADH and Parkinsonism, he regained all of his functions as before the illness.

Neurobrucellosis is a rare presentation of brucellosi- sis and has a variety of symptoms. This disease should be considered when neurological problems can’t be explained by other etiology or when patients do not re- spond to treatments, especially in endemic areas.

Acknowledgements

We thank all the nursing staff and the personnel of Gholhak laboratory for their precious helps.

References