

Case Report

A case of childhood Brucellosis with neurological involvement and epididymo-orchitis

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Abstract

Brucellosis is a common zoonotic infection worldwide caused by *Brucella* species. Central nervous system involvement is a serious complication of brucellosis, and the clinical presentation is quite heterogeneous. The genitourinary system may be affected. Epididymo-orchitis is the most common type of urinary tract involvement, which can cause serious complications. Herein, we present a case of brucellosis in a child with a rare combination of epididymo-orchitis and neurobrucellosis not encountered previously in the literature.

Key words: *Brucella*; epididymo-orchitis; neurobrucellosis; child.

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Introduction

Brucellosis is an important zoonotic disease across the world. Clinical signs are highly variable, with mild to moderate severity, because all the organs and tissues can be affected by the microorganism [1]. The clinical diagnosis should always be confirmed by bacteriological or serological tests because of the lack of any pathognomonic signs and symptoms of the disease. Chronicity, complications, and relapses can occur when the disease is not treated in a timely and effective manner. *Brucella*-related central nervous system involvement and epididymo-orchitis are rare findings, especially in children [2,3]. In this article, we report a case of a successfully treated childhood brucellosis that, to our knowledge, was not published previously in the literature.

Case Report

A previously healthy 15-year-old male patient was admitted to our clinic with a three-month history of weakness, intermittent headache, and high fever, in addition to scrotal swelling and pain for a week in August 2013. Epididymo-orchitis and splenomegaly was detected before his admission to our hospital, Ankara Hematology Oncology Children's Training and Research Hospital, which is located in the center of Turkey. A five-day treatment with cefotaxime and amikacin was administered at another center. Personal

and family history were unremarkable for any disease, but the patient was a member of a family living in a village engaged in animal husbandry, and he consumed unpasteurized milk and milk products. On physical examination, the motor and mental development of the child was compatible with that of his peers, and his general condition was good despite a 39°C fever and headache. Examination of the neurological system and all other systems was normal, but on genitourinary system examination, the left scrotum was severely edematous, hyperemic, and painful compared to the right. In laboratory studies, hemoglobin was 14.3 g/dL (N: 11–14 g/dL), white blood cell count was 6,700/μL (N: 5,000–12,000/μL), and platelet count was 314,000/μL (N: 150–450×10³/μL). Erythrocyte sedimentation rate was 66 mm/h (N: 0–20 mm/h), and C-reactive protein was 10 mg/dL (N: 0–0.8). The results of blood chemistry including amylase level were within normal limits. There were 13 leukocytes/high power field (HPF) on urine microscopy. On scrotal color Doppler ultrasound examination, the size of the left testis and epididymis was significantly increased, with decreased echogenicity compared to the right testis; a rough and heterogeneous view and increased vascularization without an arterial and venous flow problem was present. There were no torsion and no masses, and the picture was interpreted by the radiologists as

compatible with infectious inflammatory involvement. There was only mild hepatomegaly and splenomegaly on abdominal ultrasound. TORCH and mumps serologies in blood, and acid-fast bacteria in the urine staining were negative. The slide agglutination test was positive, as was the tube agglutination test, with 1/320 titer for *Brucella*. Because of the severe headaches despite normal neurological examination, computed tomography and magnetic resonance imaging of the brain were performed; both were normal. The headache was thought to be associated with neurological involvement of *Brucella*, and cerebrospinal fluid (CSF) samples were taken. The results of lumbar puncture yielded abundant lymphocytes in all areas on direct examination; protein 76.3 mmol/L (N: 15–45 mmol/L), glucose 48 mg/dL with 86 mg/dL simultaneous blood sugar, and *Brucella* tube agglutination of CSF was positive as 1/160 titer. Blood and CSF cultures via the automated Bactec method (Becton-Dickinson, Sparks, USA) and urine culture were negative. Rifampicin and doxycycline combination therapy was started with ceftriaxone treatment. Headache and scrotal findings completely disappeared during the first week of treatment. In the third week of treatment, the patient's acute-phase reactants returned to normal limits, CSF results were all normal, and the *Brucella* agglutination test of CSF was negative with a negative culture. Ceftriaxone treatment was stopped based on these results and the patient was discharged on the twenty-fourth day of hospitalization, but doxycycline and rifampin combination therapy was continued after his discharge. The patient is currently in the fourth month of treatment, which is planned to be completed after six months. The child has not had any problems reported during outpatient follow-up visits to date.

Discussion

Brucellosis is a widespread and potentially life-threatening multisystem zoonotic disease caused by intracellular Gram-negative bacteria of the genus *Brucella*, and can affect people at any age, including children. Turkey is an endemic country for brucellosis, and *Brucella* seroprevalence varies from 1.3% to 26.7% in many studies from various regions of the country [4]. Consumption of raw milk and milk products and, to a lesser extent, contact with infected animals or their waste material are the main routes of infection [5]. Signs and symptoms are quite variable and can be confused with many other diseases due to a lack of pathognomonic clinical signs [1]. The diagnosis of brucellosis is based on potential exposure,

clinical features suggestive of brucellosis, and serological tests with or without positive culture, the last of which is the gold standard of the diagnosis. Serologic tests such as slide agglutination test, serum agglutination test, microagglutination test, indirect Coombs (antihuman globulin) test, enzyme-linked immunosorbent assay (ELISA), indirect fluorescent antibody test (IFA), or immunochromatographic lateral flow assay are the main tools of brucellosis diagnosis in the absence of a positive culture [5,6]. Serum titers of tube agglutination test for $\geq 1/160$ are considered to be positive for brucellosis in Turkey [3]. In our case, consumption of unpasteurized milk and cheese was the potential route of transmission; many farming families who live in rural areas and engage in animal husbandry in Turkey consume unpasteurized cheese. Brucellosis was diagnosed by serological methods not accompanied by any culture growth due to the strong clinical suspicion and a positive history of exposure.

Neurobrucellosis is a rare but severe complication and is rarely seen in children; prevalence has been found to be approximately 1% [7]. While a minority of cases admit with typical signs of meningitis, which is the most common clinical form of neurobrucellosis, its presentation is usually non-specific and may mimic various pathologies, which make diagnosis difficult and necessitates a high index of suspicion [1,8]. Diagnosis of neurobrucellosis is confirmed by positive CSF culture, antibodies against *Brucella* in CSF at any titer via standard agglutination test or Coombs test, or the presence of meningeal involvement signs in laboratory such as lymphocytic pleocytosis, elevated protein content, and reduced CSF/plasma glucose rate without evidence of culture or serology in CSF [9]. Positive detection of at least one of these findings is sufficient for diagnosis [1,8]. In our patient, there was a severe headache unexplained by any other reason in the imaging modalities. A lumbar puncture was performed, and obvious pleocytosis and elevated protein level with normal CSF biochemistry and positive *Brucella* antibody titers were determined. The lack of positive CSF culture is thought to be associated with the cefotaxime treatment the patient received for five days at the previous center. Treatment of neurobrucellosis is controversial and there is currently no consensus. Although there are differences in various studies, a treatment regimen of three to nine months' duration with an average of six months and dual-triple combination therapy is recommended; the combination can include rifampicin, doxycycline, TMP-SMX, ceftriaxone, and aminoglycosides

[1,8,10]. We administered a three-week triple combination therapy with ceftriaxone, doxycycline, and rifampin to the patient, who had a favorable clinical response to treatment at the end of the first week. Laboratory response was supported by normal acute phase reactants and negative CSF *Brucella* agglutination test in the third week of therapy.

Brucella epididymo-orchitis (BEO) is a focal complication and has been reported in 2%–20% of patients with brucellosis [11]. BEO can cause serious complications, and therefore must be considered in the differential diagnosis of acute scrotal disease in endemic areas. Genitourinary complications have rarely been documented in the medical literature, and published articles describing cases of brucellar epididymo-orchitis are few in number, especially in children [11,12]. The presumptive diagnosis of BEO can be made via serological testing and can be supported by cultures of epididymal aspirate, scrotal tissue, or sperm. BEO can mimic many other diseases, including tuberculosis and testicular malignancy, both of which should be considered in the differential diagnosis. Ultrasonography plays an important role in the diagnosis, especially for exclusion of the possibility of an abscess or tumor. The duration of antibiotic therapy for BEO varies considerably. Treatment includes antibiotics administered for a minimum period of six weeks [11,13]. In our patient, after ruling out other common causes of epididymo-orchitis, BEO was diagnosed with positive serum serology for *Brucella* and with the support of ultrasound findings. There was a significant clinical response within approximately one week of the initiation of therapy.

Conclusion

Neurobrucellosis may not be a typical presentation in brucellosis, and diagnosis should be considered with high clinical suspicion in patients with nervous system complaints in all cases with brucellosis. Epididymo-orchitis and neurobrucellosis are rare manifestations of brucellosis, especially in children. BEO might be seen in children, especially in the adolescent age group, and it should be kept in mind and included in the differential diagnosis of acute scrotal disease. This successfully treated case is presented because the combination of these two findings had not been previously reported in the literature.

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