A case of brucellosis presenting with status epilepticus and coma

Status epileptikus ve koma ile seyreden bir bruselloz olgusu

Mahmut Katı[1], Irfan Binici[2], Fazilet Duygu[3], Mehmet Asoglu[4], Yener Tumay[5]

[1]Harran University, School of Medicine, Department of Psychiatry, Sanliurfa

[2]Yuzuncu Yil University, School of Medicine, Department of Infectious Diseases and Clinical Microbiology, Van
[3]Tokat State Hospital, Department of Clinical Infectious Diseases, Tokat
[4]Balikligol State Hospital, Department of Psychiatry, Sanliurfa
[5]Sanliurfa Training and Research Hospital, Department of Neurology, Sanliurfa

Corresponding author: Mahmut KATI, Harran University Faculty of Medicine, Department of Psychiatry 63200, Sanliurfa, Tel: +90 (414) 318 30 00, Facsimile: +90 (414) 313 96 15, E-mail: mahmutkati@harran.edu.tr

Abstract
In this paper, a case of brucellosis presenting with status epilepticus, coma, encephalitis, hepatitis, pancreatitis, disseminated intravascular coagulation (DIC), renal and muscular involvement is presented. A 23-year-old male patient recovered with medical treatment without sequel.
Key words: Brucellosis, coma, encephalitis, status epilepticus

Özet
Bu yazıda status epileptikus, koma, ensefalit, hepatit, pankreatit, yaygın damar içi pıhtılaşma, böbrek ve kas tutulumu ile seyreden ve medikal tedavi ile sekelsiz olarak iyileşen 23 yaşında erkek hasta olgusu sunuldu.
Anahtar kelimeler: Bruselloz, koma, ensefalit, status epileptikus

Introduction

Brucellosis is a zoonotic disease which may be manifested by multisystemic involvement such as hematopoetic, endocrine, cardiovascular, gastrointestinal, genitourinary, musculoskeletal, ophtalmologic, respiratory, neuropsychiatric and soft tissue during its course (1, 2). In this paper, a case brucellosis is presented with multisystemic involvement.

Case report

A 23 year-old-male patient was referred to a local heath center with complaints of headaches, fever, generalized joint and muscle pains, loss of appetite and dysartria. He was interpreted as to have respiratory tract infection for which an antibiotic treatment was started. Although he continued the treatment for 3 days, his complaints did not subside. Because of increasingly somnolence followed by blurred consciousness and at last coma, he was admitted to our emergency department. Upon the evaluation of Rose Bengal test from blood as positive, he was hospitalized in the department of Infectious diseases with preliminary diagnosis of neurobrucellosis. He had the history of fresh cheese consumption continuously with the knowledge that his brother had experienced brucellosis one year ago. He had no chronic disease, a history of alcohol or drug consumption, any operation or seizures. On physical examination, body temperature was 39,8 ºc, pulse rate 108/minute, blood pressure 130/70 mmHg, breath rate 24/minute, signs of meningeal irritation were negative. On laboratory examination, urine pH was 5, density 1017, protein >300 mg/dl, 9 erythrocytes, 2 leukocytes, and 5 renal epithelial cells were present on each microscopic area (magnification 40x10). In hemogram, white blood cell (WBC) was 10.900/mm3, hemoglobin (Hb) 4.7 g/dl, platelet count 19000/mm3, prothrombin time (PT) 17 sec, partial prothrombin time (PTT) 26.2 sec, erythrocyte sedimentation rate (ESR) 56 mm/hour. In his biochemistry, alanin amino transferase (ALT) was 52 U/l, aspartate serum transferase (AST) 146 U/l, amylase 522 U/l, pancreatic amylase 155 U/l, lipase 101 U/l, total bilirubin 3.74 mg/dl, direct bilirubin 0.87 mg/dl, creatin kinase myocardial band (CK-MB) 100 U/l, creatin kinase (CK) 659 U/l, lactate dehydrogenase (LDH) 3094 U/l, sodium (Na) 132mmol/l, potassium (K), 3.15mmol/l, calcium (Ca) 8 mg/dl, urea 105 mg/dl, creatinine 2.52 mg/dl, uric acid 15 mg/dl, C-reactive protein CRP) 71 mg/l, fibrinogen 322 mg/dl, D-dimer 3.59 micg/dl. Serologies for viral hepatitis A, B, C, E, toxoplasmosis, infectious mononucleosis, herpes simplex virus, cytomegalovirus and human immunodeficiency virus, blood film for malaria, salmonella agglutination tests, and tuberculin test results were negative. Brucella standard agglutination test (SAT) was evaluated positive at a titer of 1/2560. Cranial tomography and abdominal ultrasonography findings were unremarkable.

A nasogastric tube was inserted into the patient and combined treatment consisting of rifampicin (2x300 mg/day enteral), doxycycline (2x100 mg/day enteral)

and ceftriaxone 4 gr/day intravenous (IV) was started. 2 units of whole blood and 2 units of fresh frozen plasma were given for the severe anemia and thrombocytopenia. On the second day of his hospitalization, because tonic and clonic generalized convulsions developed while he was in coma, diazempam was started IV in order to stop convulsions. Phenytoin (3x100 mg/day IV) was also added to the treatment. Because the convulsions started again 1 hour later, diazepam was repeated, but the convulsions did not cease. The continuing convulsions were interpreted as status epilepticus for which phenytoin ceaselessly in infusion (100 mg per 100 ml isotonic fluid IV) was started. However, despite the continuous infusion for 10 minutes, because the convulsion did not abate yet, the patient was anesthetized by means of midazolam and thiopental and connected to a ventilation apparatus. By means of this application, epileptic convulsions of the patient hardly ceased 1 hour later. When the patient was extubated the following day, hemogram revealed Hb 6.7 g/dl, and platelets 38.000/mm3; but 4 hours later Hb decreased to 6.4 g/dl, and platelets to the level of 12.500/mm3. 2 units of whole blood and 2 units of fresh frozen plasma were repeated. On the fourth day of hospitalization, he recovered his consciousness, Hb increased to 9.2 g/dl and platelets to 30.000/ mm3, owing to the paranoid behaviors, auditory hallucinations and aggressive behaviors, haloperidol and biperidene lactate was added to the treatment. On the fifth day of hospitalization, potassium replacement was performed because blood potassium reduced to 2.9 mmol /l. Because potassium did not come to normal despite replacement, whether there is potassium loss was investigated in 24 hours urine, but there was no loss with urine. Despite the replacement treatment in daily requited doses continuously, potassium was about 2.5 mmol /l. On the sixth day of hospitalization, his body temperature, pulse rate and breath rate came to normal. But while levels of LDH, CK and CK-MB at admission were respectively as 3094 U/l, 659 U/l, and 100 u/l, they increased to levels of 5286 U/l, 6410 U/l, and 184 U/l respectively. On same day, because the convulsions appeared again in the patient, valproate (3x500 mg/day orally) was added to the treatment. The convulsion of the patient stopped, but his general status deteriorated; platelets count fell under 10.000/mm3 and developed gross hematuria, melena, epistaxis and generalized petechia on the body. One unit of platelet suspension was given to him. Cranial magnetic resonance imaging which was taken for the purpose of investigation of intracranial bleeding was evaluated as normal. High levels of urea, creatinine and uric acid on admission increased, to levels of 107 mg/dl, 2.7 mg/dl and 20 mg/dl, respectively. Renal functions were followed up without any additional treatment. Levels of ALT, AST, total bilirubin, direct bilirubin, PT and D-Dimer increased to 105 U/l, 169 u/l, 6.07 mg/dl, 2.87 mg/dl, 19.5 sec and 6.45 micg/dl respectively versus 52 u/l, 146 U/l, 3.74 mg/dl, 0.87 mg/dl, 17 second and 3.59 mcg/dl on admission levels, respectively. Fibrinogen decreased to 298 mg/dl from 322 mg/dl on admission, and the patient because unconscious again. One unit of whole blood was given to him because platelet suspension could not be found. On the tenth day of hospitalization, platelet count increased to a level of 23.000/mm3. Hematuria, melena and epistaxis disappeared, and he regained his consciousness the following day. In the lumbar puncture performed on the fifteenth day of hospitalization when platelet count came to a level of 50.000/mm³, no cell was seen in cerebrospinal fluid (CSF). CSF glucose and protein was normal. Brucella Wright, and Wright with Coomb's performed from the CSF and acid-fast bacilli were found negative. Electroencephalography (EEG) of the patient revealed findings compatible with encephalitis. On the seventeenth day of hospitalization developed seizures of crying this ceased two days later. His general status improved, hypopotasSemia recovered, thus potassium replacement was stopped. Proteinuria, pyuria and renal epithelial cells disappeared. Bone barrow biopsy performed when platelet count increased to 135.000/mm3 was unremarkable. On the twentieth day of hospitalization, all laboratory findings were normalized /fibrinogen 307 mg/dl, Hb 9 gr/dl, platelets counts 246.000/mm³, WBC 4.640/mm³, PT 15.2 sec, PTT 29.5 sec, D-dimer 0.88 micg/dl, ESR 33 mm/h, ALT 26 U/L, AST 16 U/l, amylase 86 U/l, pancreatic amylase 30 U/l, lipase 40 U/l, total bilirubin 0.21 mg/l, CK_MB 12 U/l, and urea 16 mg/dl, creatinine 0.57 mg/dl, LDH 377 U/l,CK 21 u/l, and uric acid 2.6 mg/dl). Haloperidol and biperiden was stopped and valproate dose was gradually lessened. Ceftriaxone was completed to one month, and then discontinued, and the patient was released from the hospital continuing on rifampicin and doxcycline treatment. On the follow-up controls, the patient had no complaints and his treatment was completed to 2 months and ceased. No complaints occurred during his follow-ups during one year.

Discussion

Brucellosis is a zoonotic disease which may be seen almost all over the world (3). Transmission to human is generally via gastrointestinal route and the disease disseminates from there to lymphatics as well as to all parts of the body by hematogenous route. We could not find any predisposing factor to result in multysystemic involvement and severity of the prognosis in our patient. The diagnosis of the disease is usually possible when presents with classical symptoms and signs, but the diagnosis may be difficult especially in multisystemic involvement and/or in unconscious

patients. The disease is still diagnosed with serologic tests on the whole (4). Our case was also diagnosed with brucella SAT test, which was positive at titer of 1/2560. The reason why brucella could not isolated from the culture was attributed to usage of antibiotic prior to his hospitalization. The presentation of neurobrucellosis includes meningitis, encephalitis, meningoencephalitis, myelitis, subarachnoid haemorrage, radiculoneuritis, involvement of cranial and peripheral nerves, intraserebral and epidural abscesses and meningovascular syndromes (3, 5). The patient can be brought to medical attention as in our case. Neurological complications of brucellosis may occur either related to the acute-febrile state that appears in occult disease or related to actual invasion and localization of the pathogen in the central nervous system (CNS) (6). Although encephalitis was diagnosed with EEG from the patient in our presented case, the negativity of brucella SAT performed from CSF and protein in the CSF made us consider that encephalitis may be related to brucella toxins. Upto our knowledge, a neurobrucellosis case presenting with status epilepticus has not been reported yet upto now in the literature. In this regard, our case has the characteristic of being the first case presented in the literature. Delirium, hallucinations, dementia, manic and paranoid behaviors, neurasthenia, depression and psychotic reactions may be counted among psychiatric presentations of brucellosis (3). Also in our case there was a picture consisting of delirium, hallucination and paranoid behaviors. In addition, during the course of brucellosis, renal insufficiency, pyelonephritis, renal abscess, interstitial nephritis, renal calcification, renal granuloma and glomerulonephritis may be seen (7). In our presented case, renal involvement was proven by, elevations of urea, creatinine and uric acid and meaningful existence of proteinuria, hematuria and renal epithelial cells in urine. Renal biopsy was considered to be performed, but the bad general status of the patient, and the thrombocytopenia did not allow us to do this; meanwhile when the platelet count came to normal level and his general status improved, his renal functions were also improved. Hematologic complications of brucellosis show a wide spectrum ranging from a mild anemia to pancytopenia (8). Hematologic abnormalities in brucellosis may be related to the depression of the bone narrow, granuloma formation in the bone marrow with haemophagocytosis. These all findings improve with treatment in a short time (9). In our case, severe anemia and thrombocytopenia which was present at the beginning was normalized when his several statuses improved. Because our patient was in coma on admission and in bad general status, examination of the bone marrow could not be performed. The bone marrow biopsy performed once the patient recovered from coma and his general status improved was evaluated as normal. It can be considered that the bone marrow may have been depressed during the infection but afterwards improved with the treatment. An exceptional condition in our case was the continuous platelet consumption during the disease course. While the low levels of Hb gradually arose after the treatment, platelet count continuously fell below the level of 10.000 mm^3, despite multiple platelet transfusions and resulted in multiple bleeding. Platelet destruction was considered to develop secondary to brucellosis in peripheral circulation. As in gram negative bacterial septicemia, development of disseminated intravascular coagulopathy (DIC) may be seen as a haematologic complication (3). The existence of meaningful elevation of D-dimer and PT and thrombocytopenia and hypofibrinogenemia shows the development of DIC. The most frequently involved organ in the gastrointestinal system is liver and usually it is encountered during the course of brucellosis. A mild degree elevation, rarely a moderate, in hepatic function tests is present. Hepatosplenomegaly has been reported in more than half of the patients (10). In our case, there was an elevation in transaminases with bilirubinemia (especially in direct bilirubin), but no hepatosplenomegaly. Development of acute pancreatitis due to brucellosis has been quite rarely reported. The contribution of radiologic imaging methods to diagnosis of acute pancreatitis is limited. Highly elevated amylase, pancreatic amylase and lipase levels made us consider acute pancreatitis due to brucellosis in our case (11, 12). Amylase and lipase levels fell to normal in our case at the end of the first month. Elevation of LDH, CK and transaminases, together with the elevation of CK-MB may be associated with muscular involvement ad/or myocarditis but neither echocardiography nor biopsy could be performed, thus this has not gained certainty. As a mater of fact, electrocardiogram and echocardiography does not help always in diagnosis of myocarditis. Definite diagnosis of myocarditis is made by biopsy which is not routinely performed (4).

In conclusion, in brucellosis cases with multisystemic involvement, treatment of complications is important and life-saving as specific anti-brucellar treatment. Taking to in consideration that brucellosis may result in all kind of complications, it should also be considered in differential diagnosis of status epilepticus.

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