Caso clinico

Case reports

Acute brucellosis associated with leukocytoclastic vasculitis and splenic infarct

Brucellosi acuta associata a vasculite leucocitoclastica e infarto splenico

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INTRODUCTION

Brucellosis in humans is globally the most prevalent multisystem bacterial infection of zoonotic origin with lethal complications. It is still an important public health problem in the Eastern and Southeastern regions of Turkey. Although its prevalence varies by countries, over 500,000 new cases occur annually [1]. Brucellosis is transmitted to humans through direct contact due to the profession, and through the consumption of non-pasteurized milk and dairy products or animal meat. Brucellosis most commonly involves the locomotor, gastrointestinal, haematologic, cardiovascular, respiratory and central nervous systems, respectively. Skin involvement is not common, and leukocytoclastic vasculitis is also quite rare. Although the enlarged spleen is a very common finding, there are also a few cases of splenic infarct reported in the literature [2, 3]. In this paper, we present a case of acute brucellosis associated with leukocytoclastic vasculitis and splenic infarct.

CASE REPORT

A 17-year-old male patient living in a city located in the Southeastern region of Turkey presented to the outpatient clinic with fever, malaise, loss of appetite, pain in the knee joints, abdominal pain (epigastric and in the abdominal left upper quadrant) and rash on legs although he had no health problems until four weeks ago. For the previous two weeks, he had an obvious fever, with chills, shivering and sweating mainly in the evening. During history-taking, the patient reported neither cough, weight loss, haematochesia, haematuria nor insect bites. His history showed consumption of non-pasteurized dairy products but no systemic diseases and no drug or substance addiction. His physical examination indicated a body temperature of 39.2°C, epigastric sensitivity, dullness to percussion over Traube's space, millimetric palpable purpura extending from the distal of the knees in the right and left legs to

Figure 1 - Extensive purpuric lesions on patient's leg.

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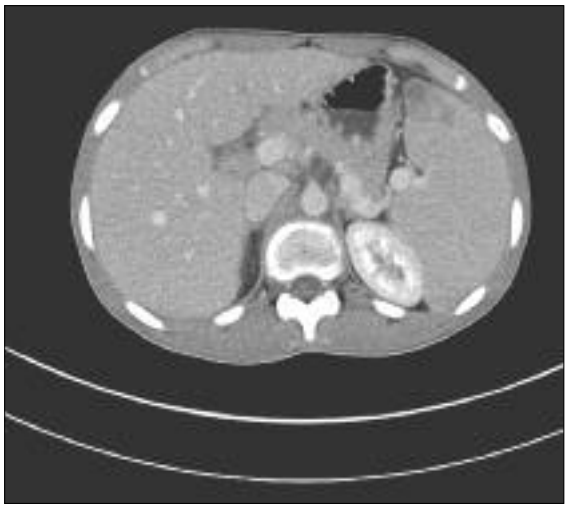

Figure 2 - Contrast enhanced abdominal computed tomography showing 3,5x2,5 cm- triangular hypodense area that could not be enhanced in the arterial phase at the lower pole.

the dorsum of feet and ankles (Figure 1). Abdominal guarding and rebounding were not detected and the heart sounds were normal without any murmurs.

The laboratory findings showed 12.2 g/dl of haemoglobin (normal: 12.5-16 g/dl), 32 mm/hour of erythrocyte sedimentation rate (normal: 0-20), 40.8 mg/L of C- reactive protein (normal: 0-5), while the routine haemogram, biochemical and urinary test results were normal. Peripheral smear didn't indicate any atypical cells. Hepatitis B surface antigen and Rose Bengal tests were found to be positive in the serological examination. Anti-HCV and anti-HIV were negative. Brucellosis tube agglutination test was found to be positive with a value of 1/320. No proliferation was found in any of the three blood cultures sampled. The abdominal ultrasound examination performed due to patient's epigastric pain didn't show any pathology except some lymph nodes in the portal area, with the largest one sized 25x16 mm, and enlarged spleen (177 mm). Upper gastrointestinal endoscopy yielded normal findings. Contrast enhanced computed tomography that was performed due to the persistent abdominal pain showed enlarged spleen and suspected triangular splenic infarct of around 3,5 x 2,5 cm that was hypodense in the arterial phase series at the lower pole (Figure 2). Samples were taken from the rash on both legs for biopsy due to the preliminary diagnosis of vasculitis following dermatological consultation that was requested due to the palpable purpura on legs. The patient was diagnosed with leukocytoclastic vasculitis based on the findings of the pathological examination (Figure 3).

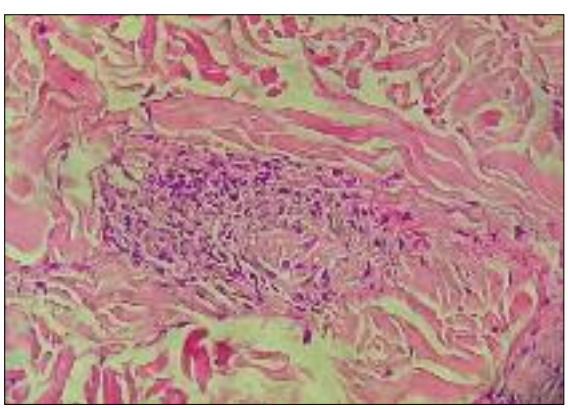

Figure 3 - Skin biopsy from the leg showed eosinophilic fibrinoid degeneration at the blood vessel wall and luminal occlusion as well as inflammatory cell infiltration containing leukocytes with polymorphic nuclei and lymphocytes around the vessels.

After the tube agglutination test was found to be positive with a value of 1/320, the patient was treated with 200 mg/day doxycycline and 600 mg/day rifampicin for six weeks. Echocardiography performed to rule out infective endocarditis had a normal finding. The patient was followed up via physical examination and intermittent ultrasonography against ruptures by administering intravenous hydration and analgesics. The mesenteric-portal system arterial Doppler ultrasonographic examination of the patient indicated normal splenic artery and vein. Cardiac murmur was not present in physical examination and the echocardiography finding was normal; thus, infective endocarditis was ruled out. Haematologic tests requested to evaluate his predisposition to coagulation (Protein C an S level, Anti-thrombin III level, JAK mutation, Factor V Leiden mutation, factor II mutation, anticardiolipin antibodies) yielded no abnormal findings. Hepatitis B surface antigen was positive, while HBV DNA and Anti-Delta antibody was negative. Liver enzymes were normal before and after the antibiotic treatment but he was followed up as an inactive carrier. ANA, RF, pANCA, cANCA, VDRL tests were negative in the patient with vasculitic rash, and the complement components 3 and 4 levels were within the normal range. In the follow-up, haematuria and proteinuria were not found in the repeated urinary tests.

Following the fifth day of antibiotic treatment, the patient didn't have high fever; while the rash on legs was completely resolved on day eight. The patient was discharged on day fourteen following his hospitalization. His treatment was completed in six weeks, he didn't have any complaints at month four but he is presently under follow-up without any complications.

DISCUSSION

As a systemic infection, brucellosis may involve any organ or system of the body. Like in the other multisystem diseases, brucellosis is characterized by many symptoms and findings, which makes diagnosis difficult. Locomotor, gastrointestinal, haematologic, cardiovascular, respiratory and central nervous systems are most commonly involved in brucellosis.

Skin involvement in brucellosis is very rare, which was reported to range from 0,7% to 6% in various series [4-6]. There are four types of brucellosis-associated skin lesions, which, by the order of prevalence, are widespread papulonodular lesions (the most prevalent), erythema nodosum-like lesions, widespread maculopapular lesions and widespread purpuric lesions [5]. Skin lesions associated with brucellosis might be manifested in the first episode of the infection, during its relapse and as an independent symptom [7, 8]. Skin lesions usually respond to treatment, while it has also been reported to be resolved spontaneously [8]. Buzgan et al. from Turkey reported a case series of 1028 patients with 2.4% of skin involvement. Maculopapular-urtcarial rash, petechia-purpura, erythema nodosum-likelesions are the types of skin lesions reported respectively according to their prevalence [6]. Other causes of leukocytoclastic vasculitis in our case were explored. He was not taking any medicine. Serological tests yielded negative anti-HCV, anti HIV, VDRL results. ANA, RF, anticardiolipin antibodies were negative in the rheumatologic tests, while the complement components 3 and 4 levels were found to be normal. Haematuria and proteinuria were not found in the repeated urinary tests. There wasn't any endoscopic or clinical finding of gastrointestinal involvement. These clinical and laboratory findings enabled us to rule out the systemic rheumatologic and infectious diseases that caused the leukocytoclastic vasculities in our patient. Although the pathogenesis of the vasculitic lesions associated with brucellosis is not fully understood, hypersensitivity reaction in small blood vessels to brucellosis antigens is inculpated [8, 9]. Like in our patient, mixed infiltration of small blood vessels in the dermis by neutrophils and lymphocytes, leukocytoclasis, edema in the endothelium and fibrinoid necrosis are the pathological findings consistent with the hypersensitivity reaction. Furthermore, presence of perivascular immune deposits in some cases is also consistent with the role of immunologic reactions triggered by brucellosis [8, 9].

Splenic infarct is associated with haematologic and thromboembolic diseases, whereas its association with infectious diseases is very rare. Splenic infarct associated with the infectious disease of brucellosis is quite uncommon with only a few cases [2, 3]. We explored protein C and S deficiency, factor V Leiden mutation, factor 2 mutation, JAK-2 mutation and anti-phospholipid antibody that might cause hypercoagulability in our patient, but we didn't find any pathology. Infective endocarditis was ruled out because the cardiac examination didn't indicate murmurs and echocardiography had a normal finding. Pain in the left upper quadrant of the abdomen that patient presented is the most common symptom of splenic infarct. It might, however, be asymptomatic in some patients. Furthermore, nausea and abdominal bloating are the other symptoms. Some vascular complications such as arterial or venous thrombosis and skin vasculitis are observed in patients with brucellosis [8, 10, 11].

Endothelial lesions caused by the local germ cell infiltration and septic embolism that lead up to hypercoagulability are inculpated for the physiopathogenesis of these vascular complications [2]. Diagnosis is made via the radiological imaging methods. Abdominal computed tomography showing low-density lesions like in our patient is supportive of the diagnosis [2]. Our patient had a positive clinical response to medication (antibiotics, intravenous hydration, analgesics). During the follow-up of our patient, we didn't find any complications that required surgery due to infarct such as sepsis, abscess, haemorrhage and formation of persistent pseudocysts. There have been reports of cases developing splenic abscess and haemorrhage that are life-threatening complications [12, 13]. Complete clinical response has been achieved in these cases with only antibiotic treatment thanks to early diagnosis like in our patient

without any need for surgery. The patient didn't develop any complications during both his stay at hospital and follow-up period after his discharge.

In conclusion, it should be remembered that this disease with multisystem involvement might also be presented with atypical clinical findings in endemic regions without any typical symptoms and findings. Splenic infarct and leukocytoclastic vasculities are rarely concomitant in the course of brucellosis. In order to rule out the splenic infarct and complications, contrast enhanced radiological tests (CT or MRI) should also be planned in addition to abdominal ultrasonography within the normal range. If the diagnosis of splenic infarct is made and treated as early as possible, this will prevent the development of life-threatening complications.

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Keywords: brucellosis, cutaneous, leukocytoclastic, splenic infarction, vasculitis.

SUMMARY

Brucellosis is globally the most prevalent multisystem infection of zoonotic origin, while it is still one of the most important public health problems in Turkey as non-pasteurised milk and dairy products are consumed. Early diagnosis is vital to prevent the possibly lethal complications caused by the disease. However, diagnosis might be delayed as the disease does not have a single and typical manifestation and presents with various symptoms of different systems. Brucellosis and associated splenic infarct have rarely been studied, there being few cases in the literature. One of the rare involvements in this disease is dermatological involvement, which has been found in less than 10% of brucellosis cases. In this study, we discuss a 17-year-old male patient who was admitted to our hospital due to fever, abdominal pain, arthralgia and rash on legs, diagnosed with brucellosis through brucellosis tube agglutination test and found to have splenic infarct upon examination and leukocytoclastic vasculitis according to the skin biopsies in the light of the present literature.

RIASSUNTO

La brucellosi costituisce, a livello mondiale, la zoonosi multisistemica maggiormente prevalente; in Turchia, questa patologia è uno dei più importanti problemi di salute pubblica a causa del consumo di latte e derivati non pastorizzati. La diagnosi precoce è essenziale per prevenire le possibili complicanze fatali della malattia. Tuttavia, la diagnosi può essere ritardata in quanto la malattia, che non ha una manifestazione unica e caratteristica, si presenta con vari sintomi, a carico di sistemi diversi. La brucellosi e l'infarto splenico ad essa associato sono stati studiati solo raramente, essendo presenti in letteratura solo pochi casi. Uno dei rari coinvolgimenti di questa malattia è quello dermatologico, che è stato riscontrato in una percentuale inferiore al 10% dei casi di brucellosi. In questo studio, presentiamo il caso di un paziente maschio di 17 anni giunto presso il nostro ospedale con febbre, dolore addominale, artralgia e rash alle gambe e per il quale veniva posta diagnosi di brucellosi, mediante test di agglutinazione, ma anche di infarto splenico, sulla base di ulteriori indagini e della presenza di vasculite leucocitoclastica, in accordo alle biopsie cutanee e alla luce della letteraura corrente.

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