# Brucellosis Induced Ascites, Cholestasis and Elevated Serum CA 125 Level: Case Report

## Brusellaya Bağlı Asit, Kolestaz ve Yükselmiş Serum CA 125 Düzeyi

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**ABSTRACT** Gastrointestinal complications of brucellosis are randomly reported, ascites and cholestasis being particularly rare. A 25-year-old female patient with a history of fever, weakness, jaundice, nausea and sweating was admitted to our clinic. The physical examination revealed a temperature of 39.3°C, hepatosplenomegaly and moderate free ascites in the abdomen. Initial laboratory investigation revealed mild anemia, biochemical findings of cholestasis, hypoalbuminemia, elevated serum CA 125 level, increased lymphocyte count in ascidic fluid and low (0.9 g) serum-ascites albumin gradient. After comprehensive evaluation, *Brucella melitensis* induced ascites, intrahepatic cholestasis and elevated serum CA 125 level were detected. We observed complete clinical and laboratory improvement at the end of anti-brucellosis treatment.

**Key Words:** Brucellosis; ascites; cholestasis; CA-125 antigen

**ÖZET** Brusellozun gastrointestinal komplikasyonları nadir olarak bildirilmiştir, asit ve kolestaz özellikle nadirdir. Ateş, halsizlik, sarılık, bulantı ve terleme öyküsü olan 25 yaşındaki kadın hasta kliniğimize kabul edildi. Fizik muayenede 39,3°C ateş, hepatosplenomegali ve batında orta derecede serbest asit saptandı. İlk laboratuvar araşırmasında hafif anemi, kolestazın biyokimyasal bulguları, hipoalbuminemi, yükselmiş serum CA 125 düzeyi, asit sıvısında artmış lenfosit sayısı ve düşük (0,9 g) serum-asit albumin gradienti görüldü. Kapsamlı değerlendirmeden sonra *Brucella melitensis*'e bağlı asit, intrahepatik kolestaz ve yükselmiş serum CA 125 düzeyi bulundu. Anti-brusella tedavisinin sonunda tam klinik ve laboratuvar düzelme gözledik.

**Anahtar Kelimeler:** Bruselloz; asit; kolestaz; CA-125 antijeni

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Brucellosis is a zoonotic disease still prevalent in most areas of the developing world. Human brucellosis is known for presenting with protean manifestations. It is a multisystemic disease in which the clinical spectrum may be quite different according to the involved area. Complications can be very diverse depending on the specific site of the infection.[1,2] The focal complications of brucellosis frequently cause problems in the differential diagnosis. Gastrointestinal complications of brucellosis range from the most frequently seen hepatitis to reported cases of colitis and pancreatitis. Still, ascites cases directly attributed to brucellosis in the presence or absence of predisposing factors are extremely rarely reported in the literature.[3,4]

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We report a rare case of brucellosis with massive ascites, intrahepatic cholestasis and elevated serum CA 125 level.

## CASE REPORT

Twenty five-year-old female patient with fever, weakness, jaundice, nausea and sweating was admitted to our clinic. The physical examination revealed a temperature of 39.3 $^0$C, a blood pressure of 110/70 mmHg, a pulse rate of 110/min, a respiratory rate of 20/min, a regular heart rate and clear lungs on auscultation. The liver was palpable 5 cm below the right costal margin and the spleen was palpable 3 cm below left costal margin. There was moderate free ascites in the abdomen. There was no edema on the lower extremities.

Initial laboratory investigations revealed hematocrite level as 33.6%, hemoglobin as 11.1 g/dL, white blood cell count as 5710/mm$^3$, platelet count as 170,000/mm$^3$, alanine aminotransferase (ALT) as 163 U/L (range: 10-40 U/L), aspartat aminotransferase (AST) as 595 U/L (range: 10-35 U/L), gamma glutamyl transferase as 821 U/L (GGT) (range: 9-64U/L), alkaline phosphatase (ALP) as 899 U/L (range: 40-150 U/L), total bilirubine as 4.6 mg/dL (range: 0.2-1.2 mg/dL), lactate dehydrogenase as 1,091 U/L (LDH) (range 125-243 U/L) and albumine as 1.6 g/dL. On the thirtieth day of treatment, laboratory investigations revealed hematocrite 32.4%, hemoglobin 10.6 g/dL, white blood cell count 5,870/mm$^3$, platelet count 297,000/mm$^3$, ALT 25 U/L, AST 32 U/L, GGT 66 U/L, ALP 126 U/L, total bilirubine 0.9 mg/dL, LDH 267 U/L and albumine 3.7 g/dL. Erythrocyte sedimentation rate, serum urea, creatinine, sodium, potassium, calcium, amylase and prothrombine time were normal. Serum markers for hepatitis A virus, hepatitis B virus and hepatitis C virus and Salmonella as well as serum antinuclear antibodies, smooth muscle antibodies, antimitochondrial antibodies and anti LKM-1 antibodies were negative. The examination of ascites yielded a cell count of 682/mm$^3$ (lymphocytes 69%), and serum-ascites albumin gradient was 0.9 g/dL. There were no malignant cells in the cytological examination of ascidic fluid. The Wright serum agglutination test for *Brucella melitensis* was positive in a titer of 1/320. *Brucella melitensis* was isolated from the blood culture. Serum CA 19-9 and carcinoembryonic antigen levels were within the normal ranges and serum CA 125 level was 152 U/ml (normal <35 U/mL).

Chest X-ray was normal. Abdominal ultrasound revealed hepatomegaly (right lobe measuring 160 mm in diameter), splenomegaly (long axis measuring 165 mm in diameter) and moderate free peritoneal fluid. An abdominal computerized tomography (CT) showed mild hepatosplenomegaly with diffuse, ill defined, small, round and hypodense lesion 5-7 mm in diameter and moderate amount of intraperitoneal fluid (Figure 1).

The patient was administered tetracycline 1 g/day for 30 days and streptomycine 1 g/day for 21 days. Body temperature returned to normal on the fifth day of treatment. The clinical picture rapidly improved, the biochemical findings of cholestasis completely disappeared and serum CA 125 level returned to normal level (17 U/mL). She was not administered any drug such as rifampisin after completion of one-month treatment. Her control abdominal CT three days after completion of treatment showed complete resolution of ascites and lesions localized to the liver, and near-complete normalization of hepatosplenomegaly (Figure 2).

An informed consent was obtained from the patient.

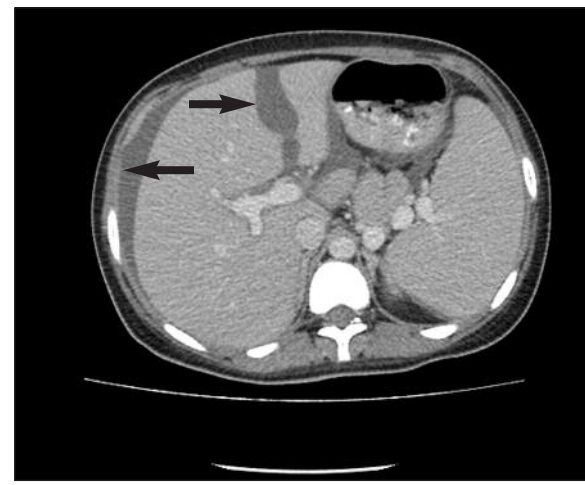

**FIGURE 1:** Abdominal CT before treatment shows hepatosplenomegaly and ascites (arrow).

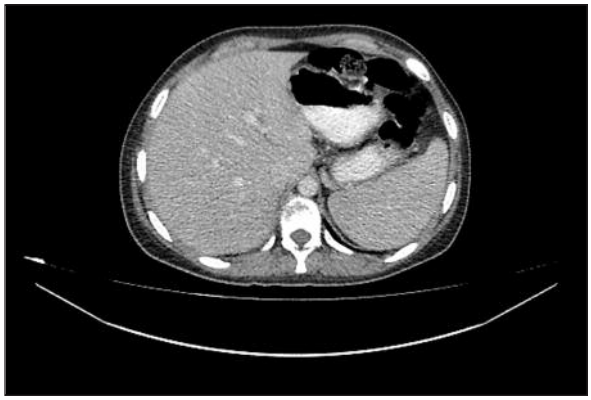

**FIGURE 2:** Abdominal CT three days after completion of treatment shows complete resolution of ascites and near complete normalization of hepatosplenomegaly.

## DISCUSSION

Brucellosis is the most common zoonoses in the world. Human brucellosis was once thought to be predominantly transmitted through animal contact. However, it is now being realized increasingly that animal products such as milk and meat products also play important roles in the disease transmission. Human brucellosis has protean manifestations. However, the most common presenting symptom is fever. The symptoms and signs most commonly reported are fever, fatigue, malaise, chills, sweating, headache, myalgia, arthralgia and weight loss. Complications can be diverse depending on the specific site of the infection. Bone and joint involvement are the most frequent complications of brucellosis.[1,2] Isolated epidydimoorchitis, vasculitis and primary peritonitis caused by brucellosis have been reported previously.[5-7]

The gastrointestinal system is one of the less frequently affected sites in brucellosis. Liver and/or spleen involvement is seen in approximately 30-60% of the cases. Although a mild abnormality in liver biochemical profile is common, it does not denote a frank hepatitis, but rather an overreaction of the reticuloendothelial system of this organ. Frank hepatitis is a well-recognized complication of brucellosis often in the form of granulomatous hepatitis.[8] There have been reports of hepatic abscess, acute abdomen, cholecystitis and pancreatitis attributed to Brucella infection.[1,9] Ascites has been reported both in the patients with chronic liver disease, and in previously healthy patients.[3,4,10] In our patient, there was no known predisposing factor that can precipitate the development of ascites. We did not perform ascidic fluid culture for bacterial infection. However, presence of elevated leukocyte count in the ascidic fluid may be the result of a generalized peritoneal immune reaction to infection or direct peritoneal invasion by *Brucella melitensis*. Additionally, presence of hypoalbuminemia may be an important factor in the development of ascites. Complete clinical and radiological improvement after anti-brucellosis treatment confirmed the diagnosis of brucellosis-induced ascites in our patient.

The term of cholestasis indicates blockage or stasis of bile. Cholestasis is not a disease but a symptom of many diseases. It is defined as a pathologic state of reduced bile formation or flow. The mechanism of cholestasis can be broadly classified into intrahepatic, where an impairment of bile formation occurs, and extrahepatic, where impedance to bile flow occurs after it is formed.[11] Cholestatic liver disease is characterized by a predominant elevation of serum alkaline phosphatase, gamma glutamyl transferase and bilirubine levels. The presence of cholestasis is reported in 3% of large brucellosis series. There are several case reports in the literature about Brucella-induced cholestasis.[11,12] Our patient had characteristic laboratory findings compatible with intrahepatic cholestasis and had also diffuse microabscess- like lesions on the abdominal CT. Intrahepatic cholestasis may be the result of intrahepatic bile flow blockage caused by diffuse intrahepatic microabscesses.

CA 125 is a coelomic epithelial antigen produced by various tissue types such as ovarian cells and mesothelium. It has been found to be elevated in the serum of patients with ovarian carcinoma, peritoneal tuberculosis, chronic liver disease, advanced leukemia with serosal involvement, and in the patients with various gastrointestinal malignancies.[13-17] We did not find any information in the literature regarding the CA 125 level in the brucellosis cases. In our case, CA 125 level was elevated before treatment as much as 4.3 folds of upper limit of normal, and it returned to normal level after treatment. This con-

comitant normalization with complete resolution of ascites suggests that peritoneal infection caused by *Brucella melitensis* may induce overexpression of CA 125 from peritoneal mesothelial tissues.

In conclusion, brucellosis should be considered in the differential diagnosis in case of fever, intrahepatic cholestasis, ascites and elevated serum CA 125 level.

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