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# Portal vein thrombosis and liver abscess due to *Lactococcus lactis*

## Ailevi Akdeniz Atefli olan bir vakada *Lactococcus Lacti*s'e ikincil portal ven trombozu ve karaci¤er absesi

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*A 26-year-old man was admitted with fever and abdominal pain. Abdominal ultrasonography and Doppler ultrasound eventually revealed portal vein thrombosis and a pyogenic liver abscess (17x11x11 cm). Lactococcus lactis was isolated from a culture of the abscess material. This organism is not a common pathogen in humans. This is the first published description of portal vein thrombosis and pyogenic liver abscess due to L. lactis.*

**Key words:** Portal vein thrombosis, liver abscess, *Lactococcus lactis*

*26 yaşındaki erkek hasta ateş ve karın ağrısı nedeni ile kliniğe kabul edildi. Ateşi devam eden hastada abdominal ve Doppler ultrasonografi ile portal ven trombozu ve pyojenik karaciğer absesi (17x11x11 cm) saptandı. Abse materyalinden yapılan kültürde insanlar için tipik bir patojen olmayan Lactococcus lactis üretildi. Bu yazıda, L. Lactis'e ikincil portal ven trombozu ve pyojenik karaciğer absesi gelişen ilk vaka sunulmuştur.*

**Anahtar kelimeler:** Portal ven trombozu, karaci¤er absesi, *Lactococcus lactis*

## INTRODUCTION

Pathogens causing pyogenic liver abscess (PLA) and portal vein pylephlebitis usually originate from an infectious focus in the abdomen like biliary disease, colon or appendix (1-3). *Lactococcus spp.* are not recognized as important pathogens in humans, but the literature provides evidence that they can cause infection, particularly in immunocompromised hosts (4). To our knowledge, this is the first reported case of PLA and portal vein pylephlebitis due to *Lactococcus lactis.*

## CASE REPORT

A 26-year-old male was admitted with fever (39°C) of three-days' duration associated with icteric sclera and tenderness at the epigastrium and upper-right quadrant of the abdomen. The liver extended 4 cm below the costal margin at the mid-clavicular line.

Laboratory findings on admission were as follows: hemoglobin 15.6 g/dl; white blood cell (WBC) count 13,700/mm$^3$; aspartate aminotransferase (AST) 80 U/L; alanine aminotransferase (ALT) 148 U/L; alkaline phosphatase (ALP) 509 U/L; gammaglutamyl transferase (GGT) 325 U/L; lactate dehydrogenase (LDH) 516 U/L; bilirubin 4.80 mg/dl (conjugated/unconjugated 2.93/1.87 mg/dl); total protein 7 g/dl; albumin 4 g/dl; erythrocyte sedimentation rate (ESR) 40 mm/h, serum fibrinogen 808 mg/dl; and serum C-reactive protein 96 mg/L. Testing of coagulation parameters showed prothrombin time 12.7 s, activated partial thromboplastin time 25 s, and international normalized ratio 1.02. Urinalysis revealed bilirubin ++, urobilinogen +++, and proteinuria 48 mg/day, and microscopic examination of urine sample showed 5-6 erythrocytes per high-power field.

Chest x-ray was normal. Abdominal ultrasonography (USG) revealed normal hepatic parenchyma, and the length of the liver was 15.5 cm at its maximum.

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Further testing was done to investigate fever etiology. Serology results for hepatitis A, B and C virus, Epstein-Barr virus, cytomegalovirus, herpes simplex 1 and 2 viruses, parvovirus B-19 and *Borrelia burgdorferi* were negative. An agglutination test for brucellosis was also negative. No bacteria were isolated from blood, urine or bone marrow cultures. Throat and stool cultures grew no pathogenic bacteria. Acid-fast bacilli staining, culturing and polymerase chain reaction analysis of bone marrow and urine samples revealed no infection with Mycobacterium tuberculosis, and a tuberculin skin test was negative. The findings on abdominal and thoracic computed tomography (CT), echocardiography, and double-contrast barium enema for colon assessment were unremarkable.

Throughout the first three weeks in hospital, the fever and abdominal pain persisted, and liver enzyme levels and ESR remained elevated. On the 23rd day after admission, abdominal USG was repeated in an attempt to identify the origin of the continued fever and investigate presence of pylephlebitis. This revealed a heterogeneous, hypoechoic mass measuring 17x11x11 cm in the right lobe of the liver with a few surrounding hypoechoic foci. Subsequent portal Doppler USG demonstrated a thrombus in the portal vein and hepatosplenomegaly. The findings of these two examinations were key to the diagnosis of liver abscess and portal vein thrombosis (PVT). Further testing of serum protein C, protein S and anti-thrombin levels was done to probe the mechanism underlying PVT. The patient's protein C level was below normal at 49% (normal range, 70-140%), whereas his protein S and anti-thrombin III levels were within normal limits.

Abdominal CT confirmed the Doppler USG results. A catheter was placed percutaneously under ultrasound guidance to drain the abscess, and the patient was started on empirical treatment with intravenous meropenem (3 g/day), teicoplanin (400 mg/day) and metronidazole (2.250 g/day). A heparin infusion was administered to treat the PVT. On the third day of treatment, the fever subsided and the patient's body temperature normalized.

Gram staining of the drained abscess material revealed neutrophils and Gram-positive cocci. A sample of the abscess contents was cultured on 5% sheep-blood agar and incubated at 35°C. At 48 hours, the plates showed growth in the form of smooth alpha-hemolytic colonies. Microscopic examination of these colonies revealed short chains of Gram-positive cocci. Testing showed these were catalase-negative, and the isolated organism was identified as *L. lactis* (BBL Crystall ID systems, Becton Dickinson Co., USA). When we investigated possible exposure to this bacterium, the patient reported that he did not ingest raw milk or any other dairy products produced with raw milk. Based on the antibiotic sensitivity testing, the teicoplanin and metronidazole were stopped and the patient continued taking meropenem. On the 12th day of treatment, the intravenous heparin therapy was changed to subcutaneous administration of low molecular weight heparin. In the following days after starting antibiotics, the patient's WBC count, ESR, and serum levels of fibrinogen and liver enzymes had all returned to normal.

Periodic re-examination with USG and Doppler USG demonstrated regression of the abscess but no change in the PVT. On the 45th day of antibiotic treatment, meropenem was discontinued based on the patient's clinical status, laboratory parameters and USG findings. The patient was discharged from hospital, at which time the low molecular weight heparin was switched to oral warfarin. This therapy was continued for six months. No clinical or laboratory abnormalities were detected at regular rechecks in the outpatient clinic; however, Doppler USG at sixth month showed persistent minimal heterogeneity in the parenchyma of the right liver lobe and still PVT.

## DISCUSSION

In the setting of PVT, serum levels of protein C, protein S and anti-thrombin III are likely to be decreased due to increased consumption during the coagulation process. Primary coagulopathies are associated with low levels of all three of these molecules. Our patient exhibited low protein C at the time PVT was diagnosed, but his protein C, protein S and anti-thrombin III levels were all in the normal range during follow-up in the outpatient clinic, confirming that the patient had no coagulation abnormalities.

Biliary tract abnormalities are known to be the most common causes of hepatic abscess, but the liver can also be seeded with bacteria via suppurative pylephlebitis. Our patient had a thrombus in his portal vein and a PLA. This combination suggests that the abscess was secondary to pylephlebitis. We did an extensive work-up to try to identify an intraabdominal infection source that might explain pylephlebitis and/or PLA; however, no

such focus was found. Previous reports have documented colonization of the streptococcal bacterium *L. lactis* in the abdomen, and hematogenous dissemination from such a site is possible. When a streptococcal agent is identified as the pathogen in PLA, the potential for hematogenous dissemination should be considered (5).

Abdominal pain and fever are the most common presenting symptoms of both pylephlebitis and PLA. Leukocytosis and elevated levels of acute-phase reactants may also be seen in both conditions. Serum liver enzymes may be elevated in pylephlebitis and PLA, with particularly high levels of ALP and GGT (6, 7). Jaundice is rare in pylephlebitis, but is frequently seen in cases of pylephlebitis accompanied by liver abscess. Patients may exhibit leukocytosis with a left shift, anemia and increased liver enzyme levels. The pattern of elevation of liver enzymes may be either parenchymal (AST, ALT), or cholestatic (ALP, GGT) (6, 8).

*Lactococcus lactis* is a Gram-positive bacterium that is phylogenetically close to the genus Streptococcus. *L. lactis* is one of the most important microorganisms used in the dairy industry. It is essential for milk acidification, and *Lactococcus spp*. are also used as starter cultures for the production of fermented dairy products such as cheese, buttermilk, sour cream and yogurt. Lactococci are also used in probiotics (9). *Lactococcus spp*. are not recognized as important pathogens in humans, but the literature provides evidence that they can cause infection, particularly in immunocompromised hosts (4, 10). Bovines are the natural hosts for *L. lactis*, and humans can become infected by ingesting contaminated raw milk or fermented dairy products. *L. lactis* may colonize the human gastrointestinal tract after ingestion, and then cause infection by gaining access to sterile body sites. L. lactis is considered to be non-pathogenic unless it is involved in fermentation. The appendix is a frequent site of pathogenic activity for *L. lactis*. In humans, this agent has been associated with endocarditis, cerebellar abscess, arthritis and necrotizing pneumonitis (11-15). *Lactococcus spp*. have also been isolated from clinical samples of human blood, skin lesions and urine (13). Nakarai et al. reported a pediatric patient with liver abscess due to *L. lactis cremoris* (16), and Antolin and colleagues also reported liver abscess caused by the same pathogen in an immunocompetent adult patient (10). Our case is only the second case in the literature that features a PLA caused by *L. lactis* in an adult patient.

In the last two decades, the treatment for PLA has changed significantly. Surgical drainage has been replaced by percutaneous drainage procedures. Today, percutaneous aspiration with ultrasound or CT guidance is the first-line approach for draining liver abscesses. Computed tomography facilitates the diagnosis, and therefore has reduced the delay in diagnosing these lesions. Percutaneous needle aspiration with antibiotic therapy is the recommended approach for patients with unilocular abscess (3). In our case, we achieved good results with percutaneous abscess drainage and antibiotic therapy.

In conclusion, our case demonstrates the importance of keeping an open mind when evaluating a patient with fever. *Lactococcus lactis* should be kept in mind as a cause of liver abscess. If a fever persists, other causes, particularly pylephlebitis and solid-organ abscess, should be investigated thoroughly, as mortality risk is high when these conditions are not promptly diagnosed.

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