

Short Communication

Acute Calculous Cholecystitis Caused by *Candida lusitanae*: an Unusual Causative Organism in a Patient without Underlying Malignancy

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SUMMARY: Candidiasis of the gallbladder is an uncommon cause of acute cholecystitis. Candidal cholecystitis is seen especially in patients with malignancies. In the present case, we report that acute calculous cholecystitis was caused by *Candida lusitanae* in a 33-year-old patient without underlying malignancy. According to our review of the literature, this is the first report of acute cholecystitis caused by *C. lusitanae*.

In more than 90% of patients with acute cholecystitis, gallstones are impacted in the cystic duct. In the presence of cholecystitis and cholelithiasis, an appreciable number of various bacteria may be found in the bile and walls of the gallbladder. Usually, the organisms found in the biliary tract are the normal intestinal flora: namely, enteric Gram-negative bacilli, including *Escherichia coli*, *Klebsiella/Enterobacter*, and *Proteus* spp., as well as the enterococci (1). Candidiasis of the gallbladder is an uncommon cause of acute cholecystitis. According to our review of the literature, this is the first report of acute cholecystitis caused by *Candida lusitanae*. In the present case, we report that acute calculous cholecystitis was caused by *C. lusitanae* in a patient without underlying malignancy.

A 33-year-old female, who was neither an alcoholic nor a smoker was admitted for right upper-quadrant abdominal colic, with pain radiating to the back, and vomiting which had been present for 2 days. Over the course of 2 years, she had suffered from several episodes of abdominal colic. She had a sectio caesarea 9 months before the admission. On admission, the body weight of the patient was 94 kg (body mass index 39 kg/m²). Her temperature was 38.3°C, blood pressure was 140/90 mmHg, pulse rate was 100 beats/min, and respiratory rate was 24/min. Remarkable findings on physical examination included tenderness over the right upper-abdominal quadrant with a positive Murphy's sign, but without rebounding pain. Laboratory examinations revealed a leukocyte count of $9.12 \times 10^9/L$, with 74.5% neutrophils, a hemoglobin level of 13.3 g/dL, and a platelet count of $257 \times 10^9/L$. Serum chemistry results revealed the following values: glucose level, 118 mg/dL; sodium, 141 mmol/L; potassium, 4.49 mmol/L; blood urea nitrogen, 10.74 mg/dL; and creatinine, 0.67 mg/dL. Results of a liver function test performed on admission were as follows: aspartate aminotransferase, 19 IU/L; alanine aminotransferase, 21 U/L; total bilirubin 1.0 mg/dL (normal range, 0.2-1.6 mg/dL); direct bilirubin, 0.19 mg/dL (normal range, 0-0.3 mg/dL); alkaline phosphatase, 76 IU/L (normal range, 10-100 IU/L); and gamma glutamyl transferase, 43 IU/L (normal range, 8-61 IU/L). The initial C-reactive pro-

tein concentration was 21.26 mg/dL (normal value, <0.5 mg/dL). Erythrocyte sedimentation rate was 94 mm/h. The amylase and blood gas analyses were within normal limits. Ultrasound showed three gallstones in the gall-bladder lumen. There was no gallbladder thickening, which is sensitive but less specific for diagnosing acute cholecystitis. Because liver and bile ducts were normal by sonography, we did not perform further examination such as computed tomography and magnetic resonance cholangiopancreatography. Blood cultures were negative. Ceftriaxone administration was begun at 2 g/day. However, no recovery from fever or other clinical signs was observed. Then, open cholecystectomy was performed. The gallbladder was removed. In the examination of the cholecystectomy specimen, the surgeon found that the ductus cysticus was stenotic and the bile density had increased. The gallstones are shown in Figure 1. The post-cholecystectomy specimens were cultured on blood agar (Oxoid, Basingstoke, UK), EMB agar (Difco, Detroit, Mich., USA), and Sabouraud dextrose agar (Difco). The Petri dishes were incubated at 37°C for 48 h. The bile cultures were negative for bacteria (aerobic and anaerobic). However, the cultures yielded yeast that was subsequently identified as *C. lusitanae* by API 32 CAUX kits (Bio-Merieux SA, Marcy l'Etoile, France). Gallstone specimens also yielded *C. lusitanae*. According to results of the cultures, fluconazole (400 mg/day) was added to ceftriaxone treatment. Pathological examination of the gallbladder specimens showed that the tumor was composed of fascicles of plump spindle cells intermixed with numerous neutrophils and chronic inflammatory cells, including plasma cells, lymphocytes, eosinophils, and macrophages. The spindle cells were arranged in fascicles with a moderate amount of intercellular collagen demonstrable

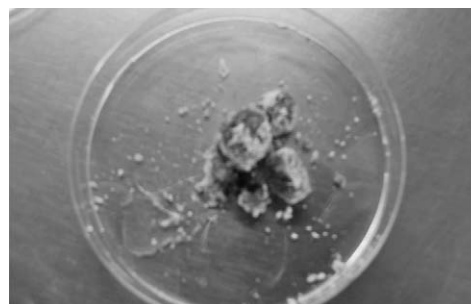


Fig. 1. The gallstones specimens.

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with Masson trichrome stain. Immunohistochemically, the spindle cells stained positively for smooth muscle actin and vimentin but were negative for S-100 and CD68. Pathological diagnosis was inflammatory pseudotumor according to these results. Ceftriaxone plus fluconazole treatment was stopped, and the patient was discharged at the 10th day of operation.

There are more than 150 species of *Candida*, but only nine are regarded as frequent pathogens for humans. They are *C. albicans*, *C. guilliermondii*, *C. krusei*, *C. parapsilosis*, *C. tropicalis*, *C. pseudotropicalis*, *C. lusitaniae*, *C. dubliniensis*, and *C. glabrata* (2). According to previously published data, infections with *Candida* and other fungal species are seen in patients with underlying malignancy, diabetes mellitus, and AIDS. Moreover, patients receiving corticosteroids, antibiotics, or parenteral hyperalimentation also seem to be at high risk of developing a secondary fungal infection (3). Candidal cholecystitis, usually following extrahepatic biliary tract obstruction, is infrequently reported, and the causative agent is usually *C. albicans* (4-10). Domagk et al. (3) reported seven cases of candidal biliary tract infection, of which *C. albicans* was the causative agent in six. Domagk et al. (3) also reported a case of common bile duct candidiasis caused simultaneously by *C. albicans* and *C. glabrata*. A case of candidal liver abscesses and concomitant candidal cholecystitis in a 37-year-old patient without underlying malignancy was reported by Lai et al. (11). In their case, the proposed entry route of infection was a retrograde ascent from the biliary tract, and bile and aspirated pus culture repeatedly tested positive for *C. albicans* and *C. glabrata*. McGuire et al. (12) reported a case of gangrenous cholecystitis secondary to *C. tropicalis* infection in a patient with leukemia.

Although uncommon, *C. lusitaniae* is of clinical importance because of its intrinsic or secondary (acquired) resistance to amphotericin B. It is typically found in patients with hematological malignancies and patients in intensive care units (13). The patient had not hematological malignancy. However, she was grossly overweight. Obesity may have predisposed her to acute cholecystitis caused by *C. lusitaniae*.

The management for candidal cholecystitis is not well established. Surgical drainage or cholecystectomy is considered adequate treatment for isolated candidal cholecystitis in non-neutropenic patients, but the addition of antifungal therapy is required in critically ill or immunocompromised patients, or patients with extra-biliary tract candidiasis (9,14). Buchner et al. (15) reported that factors that restrict the use of fluconazole include pretreatment with azoles and involvement of resistant species like *C. krusei*. In addition, the fluconazole concentration in the bile was equal to or slightly

higher than serum concentrations reported in the study conducted by Bozzette et al. (16). Our patient was treated with open cholecystostomy plus fluconazole.

In conclusion, candidiasis of the gallbladder is uncommon cause of acute cholecystitis. Candidal cholecystitis is seen especially in patients with malignancies. According to our review of the literature, this is the first report of acute calculous cholecystitis caused by *C. lusitaniae*.

REFERENCES

1. Levison, M.E. and Bush, L.M. (2000): Peritonitis and other intra-abdominal infections. p. 821-856. In Mandell, G.L., Bennett, J.E. and Dolin, R. (ed.), Principles and Practice of Infectious Diseases. 5th ed. Churchill Livingstone, N.Y.
2. Edwards, J.E. (2005): *Candida* species. p. 2938-2957. In Mandell, G.L., Bennett, J.E. and Dolin, R. (ed.), Principles and Practice of Infectious Diseases. 6th ed. Churchill Livingstone, N.Y.
3. Domagk, D., Fegeler, W., Conrad, B., et al. (2006): Biliary tract candidiasis: diagnostic and therapeutic approaches in a case series. Am. J. Gastroenterol., 101, 2530-2536.
4. Santos, L.D., Rogan, K.A. and Kennerson, A.R. (2004): Cytologic diagnosis of suppurative cholecystitis due to *Candida albicans* and actinomyces. A report of 2 cases. Acta Cytol., 48, 407-410.
5. Ambros Checa, A. and Ortega Carnicer, J. (1998): Acute acalculous cholecystitis due to *Candida albicans*. Med. Clin., 111, 38-39.
6. Lopez Onrubia, P., Bastida Vila, M.T., Martinez Martinez, J.A., et al. (1995): Acute cholecystitis and wound infection due to *Candida albicans*. Eur. J. Clin. Microbiol. Infect. Dis., 14, 253.
7. Shah, M.D., Berman, W.F., Turner, M.A., et al. (1993): *Candida albicans* cholecystitis. Am. J. Gastroenterol., 88, 1792-1793.
8. Cobo, J., Quereda, C., Antuna, A., et al. (1992): Acute cholecystitis caused by *Candida albicans*. Enferm. Infect. Microbiol. Clin., 10, 119-120.
9. Hiatt, J.R., Kobayashi, M.R., Doty, J.E., et al. (1991): Acalculous candida cholecystitis: a complication of critical surgical illness. Am. Surg., 57, 825-829.
10. Scheele, J. and Kujath, P. (2006): *Candida peritonitis* in a patient with necrotising cholecystitis and pancreatitis. Mycoses, 49, 340-342.
11. Lai, C.H., Chen, H.P., Chen, T.L., et al. (2005): Candidal liver abscesses and cholecystitis in a 37-year-old patient without underlying malignancy. World J. Gastroenterol., 11, 1725-1727.
12. McGuire, N., Hutson, J. and Huebl, H. (1992): Gangrenous cholecystitis secondary to *Candida tropicalis* infection in a patient with leukemia. Clin. Infect. Dis., 14, 367-368.
13. Dismukes, W.E., Pappas, P.G. and Sobel, J.D. (eds.) (2003): Clinical Mycology. Oxford University Press, N. Y.
14. Morris, A.B., Sands, M.L., Shiraki, M., et al. (1990): Gallbladder and biliary tract candidiasis: nine cases and review. Rev. Infect. Dis., 12, 483-489.
15. Buchner, T., Fegeler, W., Bernhardt, H., et al. (2002): Treatment of severe *Candida* infections in high-risk patients in Germany: consensus formed by a panel of interdisciplinary investigators. Eur. J. Clin. Microbiol. Infect. Dis., 21, 337-352.
16. Bozzette, S.A., Gordon, R.L., Yen, A., et al. (1992): Biliary concentrations of fluconazole in a patient with candidal cholecystitis: case report. Clin. Infect. Dis., 15, 701-703.