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# *Candida albicans* Peritonitis After Urethrostomy in a Dog

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**Abstract :** A 7-year-old castrated male Maltese developed anemia, ascites with peritonitis, and vomiting after urethrostomy. A microbial culture test of the peritoneal fluid indicated *Candida albicans*. Antifungal therapy was administered with intravenous fluconazole combined with antibacterial therapy. The patient recovered completely 37 days after referral admission.

***Key words*** **:** *Candida albicans*, dog, fluconazole, peritonitis.

## Introduction

*Candida* spp. is a group of dimorphic fungi that is part of the normal flora of the oral, gastrointestinal, upper respiratory tract, and urogenital mucosa of humans, dogs, and cats (5,27). The genus *Candida* includes approximately 200 species of asexual yeast, of which 20 have been implicated as infectious agents in animals or humans (5,26,27). The commensal organism becomes pathogenic when conditions favor excessive growth or when a patient's immune system is compromised (5,27). Cutaneous candidiasis (11), systemic candidiasis (1,3,7,8,12,19,20), *Candida* spp. cystitis (25), intestinal candidiasis (21), *Candida albicans* meningitis (2), Mycotic endophthalmitis (14), and *Candida* peritonitis (22) have all been reported in the veterinary literature. Peritonitis associated with *Candida albicans* has been reported in only two cases (19,22). This current report presents a case of *Candida albicans* peritonitis after urethrostomy.

## Case

A 7-year-old castrated male Maltese dog, weighing 7.6 kg, was presented to the Veterinary Medicine Teaching Hospital, Chungnam National University, with chief complaints of anorexia and lethargy. The patient underwent a urethrostomy for the removal of obstructive calculi in the urethra 7 days ago. After surgery, postoperative management included enrofloxacin (Baytril® 50inj, Bayer HealthCare, Korea) given at 5 mg/kg body weight (BW) q12h subcutaneously for 3 days and meloxicam (Metacam®, Bohringer Ingelheim Vetmedica, USA) given at 0.1 mg/kg BW q24h subcutaneously for 3 days. The patient was then discharged with carprofen (Rimadyl®, Pfizer Animal Health, USA) at 2.2 mg/kg BW q12h orally for 4 days and cephalexin (Phalexin, Dong Wha Pharm Co., Ltd., Korea) at 30 mg/kg BW q12h orally for 4 days.

Physical examination revealed a heart rate of 120/min with a weak pulse. Dry, pale mucous membranes, prolonged capillary refilling time, and prolonged skin tenting were presented. The overall hydration status was 8% dehydrated, and the body temperature was within the reference interval (RI) (38.0°C).

Blood examination revealed macrocytic normochromic anemia with a red blood cell count of $1.7 \times 10^6/\mu l$ (RI: 5.5 to $8.5 \times 10^6/\mu l$). The reticulocyte production index was 2.1, which was indicative of regenerative anemia. The hematocrit level was 12.2% (RI: 35.0 to 55.0%), and the white blood cell count was $55.07 \times 10^3/\mu l$ (RI: 6.0 to $17.0 \times 10^3/\mu l$), with 69% segmented neutrophils, 7% band forms, 12% monocytes, 4% lymphocytes, 8% eosinophils based on white blood cell differential counts. The platelet count was within the reference interval. The serum biochemical evaluation revealed borderline low normoalbuminemia with albumin recorded at 2.4 g/dl (RI: 2.4 to 3.5 g/dl). The remainder of the examination, including urinalysis, was unremarkable.

A whole blood transfusion was initiated after the screening tests. After the completion of the blood transfusion, the red blood cell count was $3.51 \times 10^6/\mu l$ (RI: 5.5 to $8.5 \times 10^6/\mu l$), and the hematocrit level was 26.5% (RI: 35.0 to 55.0%). To restore hydration, 0.9% normal saline with potassium supplementation was administered intravenously for 7 days. Two days after admission, tachypnea (50 breaths/min) and vomiting were presented. Abdominal radiography revealed decreased serosal detail. Ultrasonography confirmed the presence of hypoechogenic fluid around the interlobar space of the liver, within the peritoneal cavity, and in the region cranial to the bladder (Fig 1). Ultrasonography-guided abdominocentesis yielded a small amount of brown to red sero-purulent peritoneal fluid.

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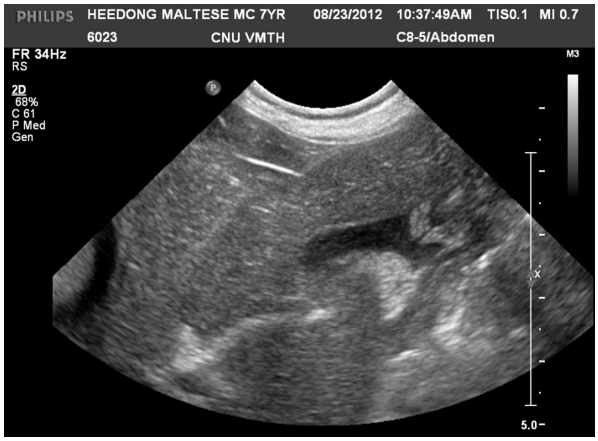


**Fig 1.** Abdominal ultrasonography revealed presence of hypoechogenic fluid within peritoneal cavity around interlobar space of liver.

Microscopic examination of the peritoneal fluid revealed the presence of numerous degenerative neutrophils with intracellular and extracellular yeasts (Fig 2). To confirm the presence of fungal organisms, a periodic acid-Schiff (PAS) stain was performed, and multiple yeasts, pseudohyphae, and degenerative neutrophils were observed (Fig 2). Fluid samples were submitted for microbial culture and microbial susceptibility tests. While awaiting the culture results, antibacterial therapy was initiated with amoxicillin/clavulanic acid (Clavamox®, Pfizer Animal Health, Australia) at 20 mg/kg BW q12h orally and metronidazole (Flasinyl®, CJ Cheil jedang, Korea) at 12.5 mg/kg BW q12h orally. Antifungal therapy included fluconazole (Flukan, Korea United Pharm. Inc., Korea) at 5 mg/kg BW q24h intravenously. The peritoneal fluid was submitted to Neodin Veterinary Science Institute (Seoul, Korea) for bacterial and fungal culture and was positive for *Candida albicans* which was grown on Sabourausd dextrose agar, identified on germ tube test and confirmed by VITEK 2 system (bioMérieux).

The patient stopped vomiting 5 days after admission. Therefore, the antifungal therapy was changed to oral fluconazole (Fugazole, Shinpoong Pharma Ltd., Korea) given at 5 mg/kg BW q24h. Additional administration included famotidine (Famotidine, Krown Pharma Ltd., Korea) at 0.5 mg/kg BW q12h orally and silymarin (Legalon®, Bukwang Pharma Ltd., Korea) at 10 mg/kg BW q12h orally as supportive therapy.

Seven days after admission, clinical signs were improved, and abdominal radiography revealed no signs of ascites and peritonitis. Blood examination revealed thrombocytosis ($805 \times 10^3/\mu l$; RI: 120 to $600 \times 10^3/\mu l$) and a red blood cell count of $3.74 \times 10^6/\mu l$ (RI: 5.5 to $8.5 \times 10^6/\mu l$). The hematocrit level was 27.6% (RI: 35.0 to 55.0%). At that time, the patient was discharged with oral fluconazole, silymarin, and famotidine for 10 days, as described above.

At 16 days after admission, blood examination revealed continuing thrombocytosis ($1003 \times 10^3/\mu l$; RI: 120 to $600 \times 10^3/\mu l$). Antithrombotic minimal dose aspirin (Aspirin, Hanmi Pty Ltd., Korea) at 0.5 mg/kg twice per day was prescribed. The white blood cell count was within the normal range.

Three weeks after admission, blood examination, serum biochemical profiling, electrolyte analysis, and urinalysis were performed. Blood examination revealed anemia with a red blood cell count of $3.57 \times 10^6/\mu l$ (RI: 5.5 to $8.5 \times 10^6/\mu l$). The platelet and white blood cell counts were within the reference intervals. The remaining examinations were unremarkable. Therefore, fluconazole was discontinued for the patient. Aspirin was also discontinued at this time.

An abdominal ultrasonographic examination was repeated at 37 days from admission. The peritonitis and ascites were no longer detectable. The platelet count was within the normal range. At this time, all clinical signs related to peritonitis and anemia were resolved.

## Discussion

This report presents a case of infectious peritonitis with *Candida albicans*. Of the *Candida spp.*, *C. albicans* is most commonly identified in both humans and dogs (10,21). In humans, 90% of fungal peritonitis cases are caused by *Candida* spp. The other cases are attributed to *Aspergillus spp*.

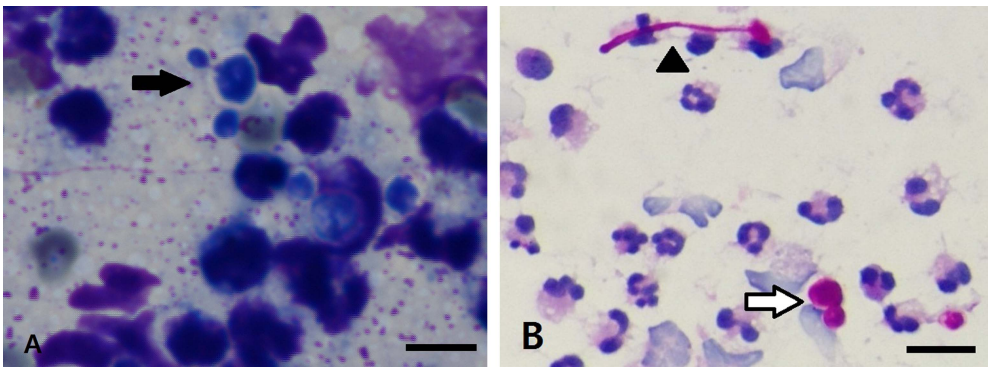


**Fig 2.** Numerous degenerative neutrophils with cocci and intracellular, extracellular yeasts (arrow) were observed, Peritoneal fluid smear, 1,000×, Dip Quick stain, Bar 10 μm (A), and multiple yeasts, pseudohyphae (arrow head) and budding yeasts (open arrow) were observed with degenerative neutrophils, Peritoneal fluid smear, 1,000×, PAS stain, Bar 10 μm (B).

(5%) and *Penicillium spp.* (5%) (15). To our knowledge, reports classifying the etiologic agents of fungal peritonitis have not been published in the veterinary literature.

Several risk factors for *Candida* infections in dogs, cats, and humans include the administration of broad-spectrum antimicrobials and corticosteroids, diabetes mellitus, acidic urine pH, indwelling urinary catheters, provision of nutrition parenterally, and the placement IV and urinary catheters (5,19,22,25). *C. albicans* peritonitis is a rare condition. In present case and the two previously reported cases of *C. albicans* peritonitis, all patients received concurrent antibacterial therapy after surgery. However, our case differed in the type of surgery, which was a urethrostomy. The other two cases underwent exploratory laparotomies (19,22), which is related to certain disruptions of the intestinal mucosal barrier. In the current case, the patient's abdominal cavity was intact during surgery. Therefore, the administration of broad spectrum antimicrobials is suspected to be a risk factor. The urethrostomy may also have altered the urinary system to contribute to a *C. albicans* infection.

The most common cause of septic peritonitis is the leakage of gastrointestinal contents, which was observed in 21 of 28 (75%) dogs (4). In humans, the main cause of *Candida* peritonitis is gastrointestinal perforation in more than 50% of cases, regardless of the outcome (4). In our case, there were multiple administrations of nonsteroidal anti-inflammatory drugs (NSAIDs) after urethrostomy without gastrointestinal protectants by the referring veterinarian. These factors may have contributed to the observed macrocytic normochromic anemia. There were no observable gastrointestinal signs, such as melena or hematochezia, except vomiting after hospitalization. However, melena was observed by the owner before admission to our hospital. Some patients with gastrointestinal hemorrhage do not present hematemesis, melena, or hematochezia (6). Moreover, borderline low normoalbuminuria and dehydration support the possibility of gastrointestinal hemorrhage caused by perforation. In a recent study, *C. albicans* colonization and its risk factors were investigated. In three interventional groups of guinea pigs, one group received only NSAIDs, and one group received pathogenic *C. albicans* to induce gastrointestinal colonization and inflammation. The third group received NSAIDs and was subsequently colonized with pathogenic *C. albicans.* The most severe necroinflammatory lesions were observed in the group that received both NSAIDs and *C. albicans* (17). The interaction between NSAIDs and *C. albicans* in the same organism may have clinical relevance because the use of these anti-inflammatory drugs has increased and is associated with both gastric and enteral severe toxicity (18). In our case, bleeding from GI perforation, bleeding from the urethrostomy and the use of NSAIDs may have contributed to the anemia (HCT 12.2%). However, further diagnostic tests, such as an endoscopic examination to find the bleeding lesion, were not performed because after whole blood transfusion on the day of admission, GI signs were resolved and the hematocrit level increased continuously.

In humans, the mortality of *Candida* peritonitis is 52%, and the mortality of postsurgical candidiasis has been reported at up to 63% (4,22). Despite high mortality rates, implementation of *Candida* spp. infection treatment is contentious in humans (16). Several criteria and predictive mortality risk factors have been reported. In humans, the isolation of *Candida* spp. in peritoneal specimens of nosocomial peritonitis (16), acute physiology and chronic health evaluation II scores, respiratory failure, upper gastrointestinal tract origin peritonitis, results of direct examination of peritoneal fluids, total parenteral nutrition, surgery upon ICU admission, multifocal colonization, and the presence of severe sepsis are proven risk factors of mortality (13). Although implementation of *Candida* infection treatment is debatable in human medicine, the consideration of these mortality risk factors may help to determine the appropriate use of antifungal treatment.

*Candida* peritonitis treatment options, which summarize the current knowledge on the treatment of multiple forms of candidiasis from the Infectious Diseases Society of America (IDSA), are intravenous amphotericin B or oral or intravenous fluconazole (23). Fluconazole has a lower frequency of adverse effects compared to amphotericin B (9). Fluconazole is a fungistatic triazole compound. Triazole-derivative agents, such as imidazoles, presumably act by altering the cellular membranes of susceptible fungi, thereby increasing membrane permeability and allowing leakage of cellular contents and impairing uptake of purine and pyrimidine precursors (24). Fluconazole has a low protein binding efficiency, is widely distributed throughout the body, and penetrates well into the CSF, eye, and peritoneal fluid. The required duration of therapy for all forms of *Candida* peritonitis is not well defined in humans (23). In general, 2-3 weeks of therapy is required (23). In this case, the patient also receives antifungal therapy for up to 3 weeks after clinical signs are presented.

## Conclusion

*Candida* peritonitis in dogs is rare. There are several risk factors causing *Candida* infections. If certain risk factors are suspected in a case, *Candida* infection should be considered, especially if risk factors such as concurrent antibacterial therapy, the use of NSAIDs, and gastrointestinal leakage are present. The diagnosis of *Candida* peritonitis is made by microscopic examination of peritoneal fluids. Microbial culture tests should follow this examination. Clear guidelines for antifungal therapy have not been established in veterinary medicine. Considering the high mortality of *Candida* peritonitis, the administration of fluconazole, which has several advantages, including relative safety, intravenous administration, and penetration into the peritoneal cavity, is preferable in circumstances with mortality risk factors based on clinical and laboratory findings. In our case, early diagnosis and adequate treatment of *Candida* peritonitis yielded a good outcome.

## Acknowledgements

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# 요도루조성술 후에 개에서 발생한 *Candida albicans* 복막염

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**요 약** : 중성화한 수컷 7년 령의 Maltese가 요도결석으로 인한 요도루조성술 후에 3일 동안 지속된 빈혈 증상으로 충남대학교 동물병원에 진료 의뢰되었다. 수혈 후 복수 소견을 발견 하였다. 복수 검사 결과 *Candida albicans* 이 검출되었다. *Candida albicans* 에 의한 복막염으로 진단하여 항진균제로 fluconazole을 정맥 주사 하였다. 임상증상이 호전된 후 경구제로 전환 하였으며 진료 의뢰 후 37일후에 완전히 회복이 되었다. *Candida albicans* 복막염을 조기에 진단하고 치료를 하여 좋은 예후를 보인 증례였다.

**주요어** : *Candida albicans*, fluconazole, 개, 복막염.