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<Case Report>

Candida glabrata infection of urinary bladder in a Chinchilla Persian cat

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Abstract: A 5-year-old castrated male Chinchilla Persian cat weighing 4.84 kg was referred for hematuria. The cat had a history of urethrostomy and bacterial cystitis. In urine culture, *Candida glabrata* was cultured on Sabouraud dextrose agar. Based on these results, the cat was diagnosed with Candida cystitis. Subsequently, oral administration of fluconazole was initiated. Urine culture was negative at 31 days after administration. This case describes the diagnosis and treatment of *Candida glabrata* infection of urinary bladder in a cat with a history of urethrostomy.

Keywords: *Candida glabrata,* cat, hematuria, urinary bladder

Candida spp. is composed of more than 150 species of budding yeasts [3]. *Candida* spp. is ubiquitously found on many plants and normal flora of dogs and cats [7]. However, pathogenic *Candida* spp. infections can occur under immune compromised condition [6].

The most common disease-causing *Candida* spp. in dogs and cats is *Candida* (*C.*) *albicans*. However, several reports have demonstrated an increase of non-*C. albicans* species isolated from both healthy and ill animals [1, 6, 10, 13]. In cats, *Candida* spp. infection most commonly results in cutaneous or lower urinary tract infection. Gastrointestinal, ocular, and systemic infections occur less frequently [3].

The term feline lower urinary tract disease (FLUTD) is used to describe the group of clinical signs related to problems in voiding urine [8]. Clinical signs include hematuria, pollakiuria, stranguria, periuria, and urethral obstruction [5]. The most common cause of FLUTD is feline idiopathic cystitis (FIC). A study reported that 8% of 77 cats were due to bacterial infection [5], suggesting infection is relatively uncommon in cats with LUTD. Less than 1% of urinary tract infections in cats are due to *Candida* spp. infections [11]. *C. glabrata* is an extremely rare causative agent. Although there are a few case reports of *C. glabrata* infection of urinary tract in cats, no report has described infection in cats under normal immune status. Herein, we describe the diagnosis and treatment of *C. glabrata* infection of urinary bladder in a cat having a history of urethrostomy due to obstructive FLUTD.

A 5-year-old castrated male Chinchilla Persian cat weighing 4.84 kg was presented with hematuria. The patient was referred for intermittent hematuria with a history of urethrostomy and bacterial cystitis. At presentation, physical examination and results of blood analyses were non-remarkable. Abdominal ultrasonography revealed thickening and irregular margin of urinary bladder wall, and sediments showing hyperechoic and non-shadowing echogenicity of bladder lumen were suspected to mobile blood clots (Fig. 1). Urine was reddish brown in color. Urine specific gravity (1.049) was normal. There was no causative agent on microscopic examination of urine. Based on the previous history of bacte-

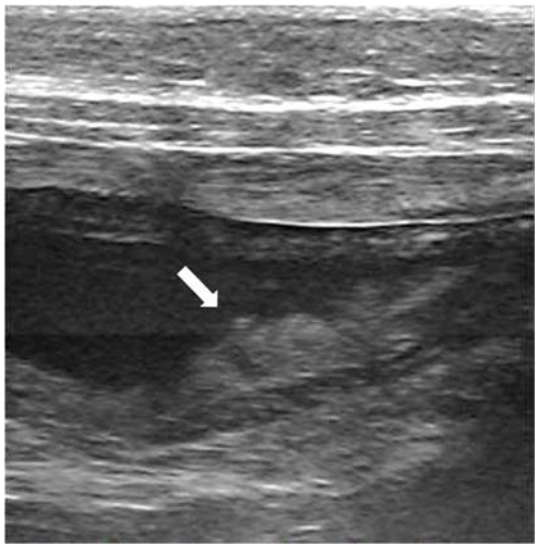

Fig. 1. An ultrasonographic image obtained from a Chinchilla Persian cat with *Candida* cystitis. Thickening and irregular margin of urinary bladder are observed. Mobile blood clots (arrow) within urinary bladder are suspected.

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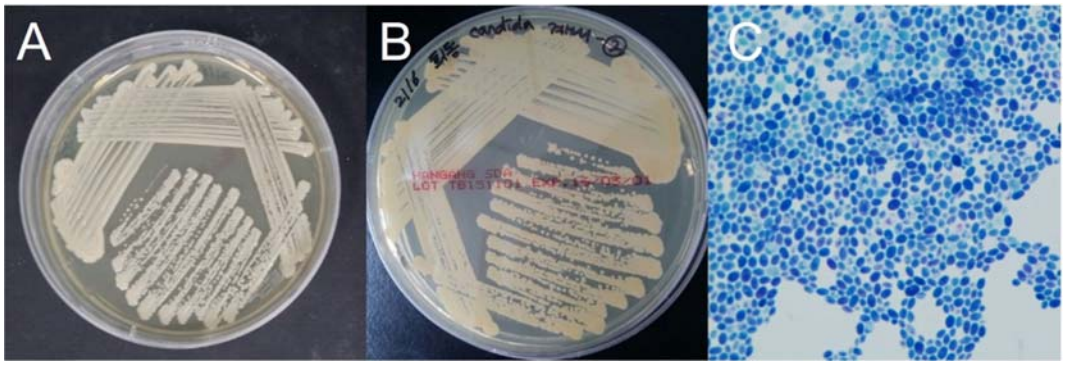

Fig. 2. Culture of *Candida* (*C.*) *glabrata* on Sabouraud dextrose agar (A and B). *C. glabrata is* observed with characterization of cream color and small round blastoconidia. Microscopically, *C. glabrata* is observed using Diff-Quik stain (C).

rial cystitis, the cat was administered with antibiotic drug, amoxicillin-clavulanic acid (Amocla tab, 25 mg/kg, per orally [PO], twice a day [bid]; Kuhnil Pharmaceutical, Korea) and H_2 receptor antagonist, ranitidine (Ranitidine HCl tab, 3.5 mg/kg, PO, bid; Wooridul Pharmaceutical, Korea) for 3 days. However, 3 days after initiating the administration, clinical sign of hematuria was not resolved, and the urine culture at presentation was negative for bacterial growth, but fungal infection was identified. A definitive diagnosis of fungal infection was made by identifying organisms in urine sample. The urine sample was centrifuged at 400 × g for 20 min and sediment was inoculated on sabouraud dextrose agar. The agar plates were incubated at 37°C under aerobic condition in 5% to 7% carbon dioxide for 2 weeks. Fungi were identified with a commercial test kit and stain. *C. glabrata* was identified by using an API 20C AUX commercial kit (bioMérieux, France). Based on results of this kit, biochemical reactions indicating *C. glabrata* infection were found, including fermentation and assimilation of glucose and trehalose [6]. From fungal culture, growth of *C. glabrata* was macroscopically observed with characteristics of cream color and small round blastoconidia (1 to 4 mm) (Fig. 2A and B). Microscopically, budding and no-hyphae formation were observed using Diff-Quik stain (Fig. 2C). With a diagnosis of *C. glabrata* infection, antibacterial drug was replaced with antifungal drug, fluconazole (Furacan, 5 mg/kg, PO, bid; Myungmoon Pharm, Korea).

Administration of H_2 receptor antagonist was maintained. All these drugs were prescribed for 30 days. At 31th day after the administration, re-examination revealed no clinical sign. Repeated urine culture result was negative for fungal growth.

This report describes a case of *C. glabrata* infection of urinary bladder in a Chinchilla Persian cat having a history of urethrostomy. According to previous studies, urinary tract infections caused by *Candida* spp. account for less than 1% of all urinary tract diseases in cats [11]. *C. albicans* is the most common infectious agent causing *Candida* spp. urinary tract infection. However, infection caused by *C. glabrata* is very rare. In this case, we considered several possibilities causing this infection including weakened urothelial barrier, use of silicone or latex material and urethrostomy.

Cats with candida urinary tract infection including *C. glabrata* show typical clinical signs of lower urinary tract infection, with hematuria in 50% of cases [3, 9]. Clinical signs of hematuria might be due to injury of bladder mucosa. In cats and humans, normal bladder layers consist of glycosaminoglycan (GAG) layer, urothelium, and muscular layer [8]. The term urothelium has been used to describe the epithelia covering the mucosal surface of most urinary tract [5]. GAG layer components and cell-to-cell adhesion molecules in the urothelium may function as a barrier [7]. This barrier might have been weakened by previous bacterial cystitis, subsequently allowing the invasion of *C. glabrata.*

In addition to defected barrier function, there are two widely cited potential virulence factors that contribute to the pathogenicity of *C. glabrata* [14]. The two factors are adhesion coded by epithelial adhesion (EPA) genes and microbial biofilms [14]. Adherence is critical to successful infection. It might be facilitated by exposing receptors to which *Candida* spp. can bind [4]. In the infectious process, the invasion of tissue commences when burrowing of hyphae begins through layers of cells [4]. However, *C. glabrata* does not develop hyphae except under extreme *in vitro* cultural condition. A major contributor of virulence and adherence to host cell is EPA1 gene [2]. Moreover, it has been reported that nicotinic acid deficiency is associated with adherence of *C. glabrata* [4]. Privation of nicotinic acid has been shown to signal the expression of a lectin encoded by the yeast's EPA1 gene, thus enhancing its adherence to bladder mucosal cell [10]. Because several articles such as cat toy and sand catcher are made of silicone or latex material, persistent existence of pathogen on silicon or latex with low nicotinic acid might play major roles in *C. glabrata* infection [4]. Furthermore, microbial biofilm may help facilitate fungal pathogen by evading host defense mechanisms, resisting fungal treatment, and withstanding competitive pressure from other organisms [15].

C. glabrata can enter the urinary tract by ascending from the perineum (retrograde infection) or by hematogenously seeding the kidney and "spilling over" into the urine (ante-

grade infection) [4]. In the present case, *C. glabrata* infection might be retrograde infection because no systemic sign compatible with antegrade infection was revealed. Permanent urethral opening after perineal urethrostomy might have contributed to *C. glabrata* infection. However, there are few reports of urethrostomy as a predisposing factor in *Candida* spp. Infection [9, 13]. Several factors associated with perineal urethrostomy may predispose to ascending bacterial urinary tract infection [12]. These factors include decreased length of urethra, loss of penile urethral mucosal defense mechanisms, increased diameter of external urethral orifice, impaired striated urethralis muscle function, and decreased intraluminal pressure [12]. However, these factors are limited to bacterial urinary tract infections. Further studies are needed to determine whether aforementioned factors caused by urethrostomy might influence fungal infection of urinary tract.

Clinicians often overlook the possibility of *C. glabrata* infection because the pathogen is very rarely observed. Nevertheless, *C. glabrata* may remain in silicon or latex material and become pathogenic. Retroinfection can occur in cats whose urinary bladder has been weakened by recurrent urinary tract infections. Therefore, *C. glabrata* infection should be considered as a differential diagnosis in patients with clinical symptoms indicating urinary tract infection.

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