Calculus Pyonephrosis due to *Candida albicans* with Special Reference to Serodiagnostic Parameters

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(Received: February 5, 1992)
(Accepted: March 5, 1992)

Key words: calculus pyonephrosis, *Candida albicans*, serodiagnostic parameters

**Introduction**

Renal candidiasis is uncommonly encountered because there are no universally accepted diagnostic criteria of this disease. The presence of a *Candida* bezoar is considered to distinguish renal candidiasis from benign colonization\(^1,2\), but seems to be of limited value in rapidly diagnosing renal candidiasis. Recently, to make a rapid diagnosis of invasive candidiasis and candidemia, serodiagnostic parameters such as a circulating candidal metabolite\(^3,4\) and antigens\(^4-6\) have been developed to great advantage. However, they have not yet been sufficiently evaluated in renal candidiasis. Herein, we report a case of calculus pyonephrosis due to *Candida albicans* with special reference to serodiagnostic parameters.

**Case Report**

A 76-year-old male, who had undergone subtotal gastrectomy for advanced gastric cancer in July 1989, was referred for fever and severe right flank pain on August 7, 1990. An excretory urogram and an ultrasonogram revealed a right hydronephrosis due to a stone at the right ureteropelvic junction. Routine laboratory tests revealed anemia of 250 × 10⁴/mm³, leukocytosis to 14,800/mm³, and renal insufficiency with a serum creatinine of 2.7 mg/dl. Urine culture yielded *Pseudomonas aeruginosa* with counts of 100,000 colonies per ml and *Candida albicans* with counts of >100,000 colonies per ml. Despite the initiation of antibacterial chemotherapy with aztreonam, no effect on the symptoms or laboratory data was observed, and C-reactive protein rose from 1.0 to 21.5 mg/dl. As calculus pyonephrosis was strongly suspected, emergency percutaneous nephrostomy was performed on August 10. An antegrade pyelogram revealed complete ureter obstruction due to a radiolucent stone, 20 × 9 mm in diameter, and several small filling defects in the renal pelvis (Fig. 1). From the renal pelvis a number of small soft balls with a diameter less than 5 mm were obtained and were microscopically demonstrated to be *Candida* bezoars. Fever and leukocytosis continued for the following 2 days, at which time both renal urine and blood cultures yielded *C. albicans*. Flucytosine was given at a dose of 100 mg/kg per day for 1 week and the 50 mg/kg for another week, leading to normalization of the clinical, laboratory and microbiological findings. Percutaneous pyelolithotripsy was performed a month later with a good result. The stone was composed of uric acid.

Since renal candidiasis was strongly suspected because of the positive candidal urinary culture obtained on August 7, serum levels of serodiagnostic parameters were determined by the following kits:
Fig. 1 Nephrostography demonstrated complete obstruction at the ureteropelvic junction and filling defects due to Candida bezoars in the renal pelvis (arrows).

Fig. 2 Clinical course and serodiagnostic data of the present case

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D-arabinitol/creatinine ratio (umol/mg) 0.6, 1.4, 0.8, 0.6, 0.4, 0.4

Protein antigen (titer) <1:1, 1:4, 1:4, 1:2, <1:1, <1:1

Mannan (ng/ml) <0.5, 0.9, <0.5, <0.5, <0.5, <0.5

Candida albicans Pyonephrosis

Candidal antibody by the indirect haemagglutination test (Candida HA test; Hoffman-La Roche, Basel, Switzerland), D-arabinitol, the main candidal metabolite, by an enzymatic fluorometric assay (LABOFIT™; Nacalai Tesque, Inc., Kyoto, Japan), and Candida protein antigen by a latex agglutination test using the Candida Detection System™ (CAND-TECT™; Ramco Laboratories, Inc., Houston, USA). In addition, the serum level of mannan, the main cell wall component of Candida spp., was measured by the enzyme-linked immunosorbent assay using the biotin-streptavidin procedure. The clinical course and serological data obtained were summarized in Fig. 2. When the patient was admitted, all the parameters were considered normal: an antibody titer of 1:160 (normal ≤1:160), D-arabinitol/creatinine ratio, which was corrected by serum creatinine concentration to eliminate the influence of renal function [8, 9], of 0.6 µmol/mg, a negative titer of Candida protein antigen, and mannan level of less than 0.5 ng/ml. Just before nephrostomy on August 10, the serum D-arabinitol/creatinine ratio was elevated to 1.4 µmol/mg, the
protein antigen altered to 1:4, and the serum mannan level elevated to 0.9 ng/ml. During the treatment with flucytosine after nephrostomy, the D-arabinitol/creatinine ratio, the protein antigen titer, and the mannan level gradually decreased paralleling a decline in the body temperature. On August 18, D-arabinitol/creatinine ratio, the protein antigen titer, and serum mannan concentration returned to normal. However, the antibody titer was remarkably elevated to 1:2,560 at its maximum on August 15 and the titer remained 1:640 until August 31.

Discussion

Infections of the urinary tract due to Candida spp. are becoming an increasingly common complication of modern therapeutics and various debilitating diseases as in our case. Owing to the lack of a consensus regarding reliable diagnostic criteria to differentiate between benign colonization and true infection due to Candida spp., clinically evident renal candidiasis is uncommon, although this condition has been often discovered in patients with risk factors at autopsy. Additionally, despite the establishment of the diagnosis some patients die of the disease because antifungal treatment is begun too late\(^2,10\). Therefore, in order to detect renal candidiasis, rapid and reliable methods are urgently required.

In histologically proven renal candidiasis, an agar gel diffusion precipitin test was reported to be a useful diagnostic aid with a high positive rate\(^11\). In general, however, doubt has been cast on the rapidly diagnostic usefulness of antibody determinations, including precipitin test, for several reasons\(^5,7,12\), e.g. the antibodies are usually present in the sera of healthy humans since almost everyone encounters Candida spp., the tests for antibodies are insufficiently sensitive among immunosuppressed patients, and at least 10 days must elapse before significant changes in levels of the antibody titers are measured.

Recently, several investigators have recommended the determination of a circulating metabolite, D-arabinitol\(^3,4\) and candidal antigens including protein antigen\(^4,6\) and mannan antigen\(^4,5\) for invasive candidiasis and candidemia. However, there have been only a few reports on patients with urinary tract candidiasis. Some studies have documented that D-arabinitol/creatinine ratios are elevated in sera of the animals\(^8\) and patients\(^8,9\) with invasive candidiasis including renal involvement. We also demonstrated that serum D-arabinitol/creatinine ratios in febrile candiduria patients were significantly higher than those of afebrile ones\(^10\). The CAND-TEC system was reported that the debilitated hospital patients with persistent candiduria can be evaluated for candidal antigenemia which can become a prognostic determinant\(^4\). Serum mannan has also been found at a high concentration in the sera of patients with invasive candidiasis and candidemia\(^4,5\).

In the present cases, it is noteworthy that the D-arabinitol/creatinine ratios, the candidal protein antigen titers, and the mannan levels changed almost in parallel with both the clinical and microbiological data. The results strongly suggested that these parameters could be useful for not only rapidly diagnosing but also deciding on effective treatment. However, more experimental and clinical studies are needed.

References

Candida albicans Pyonephrosis

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