Case Report

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# 간세포암 환자에서 발생한 가피성 방광염과 신우요관염

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# Encrusted Cystitis and Pyeloureteritis in Patient with Hepatocellular Carcinoma

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Encrusted cystitis and pyeloureteritis are rare chronic infectious conditions characterized by mucosal inflammation and encrustations of the urinary tract. It is caused by fastidious growing urea splitting microorganisms, mainly *Corynebacterium*. Herein, we report an unusual case of an 80-year-old man with encrusted cystitis and pyeloureteritis who was previously treated with transcatheteral arterial chemoembolization for hepatocellular carcinoma. Abdomino-pelvic computerized tomography showed a bilateral hydronephrosis with calcifications of renal pelvis, ureter, and bladder. Cystoscopy showed calcified bladder mucosa with necrosis and bleeding. After transurethral removal of calcified plaques, the patient was treated with antibiotic and oral urine acidification. One-month follow-up cystoscopy showed that inflammation was improved and calcification was significantly reduced.

**Keywords:** Bacteria; Urinary calculi; Urinary tract infections

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Infections in immunocompromised hosts have been an important clinical problem. Patients with hepatocellular carcinoma are at a high risk of infection due to cancer itself, diagnostic procedures, therapeutic intervention, and hematologic complications after chemotherapy. The respiratory tract and urinary tract were the most common sites of infection, being involved in 50% and 28% of cases after diagnosis of hepatocellular carcinoma, respectively.[1]

Encrusted cystitis and pyeloureteritis (EC/PU) are rare chronic infection and inflammation of upper urinary tract and/or the bladder mucosa, induced by urea-splitting bacterial infection belonging to *Corynebacterium* and *Proteus*.[2] Calcified plaques in bladder mucosa accompanied with inflammation and ulcerations characterize pathologically EC/PU.[3] The clinical manifestations are nonspecific and can be minimal for a prolonged period. Unfortunately, the diagnosis can be easily missed because *Corynebacterium* grows fastidiously in common culture medium. Herein, we

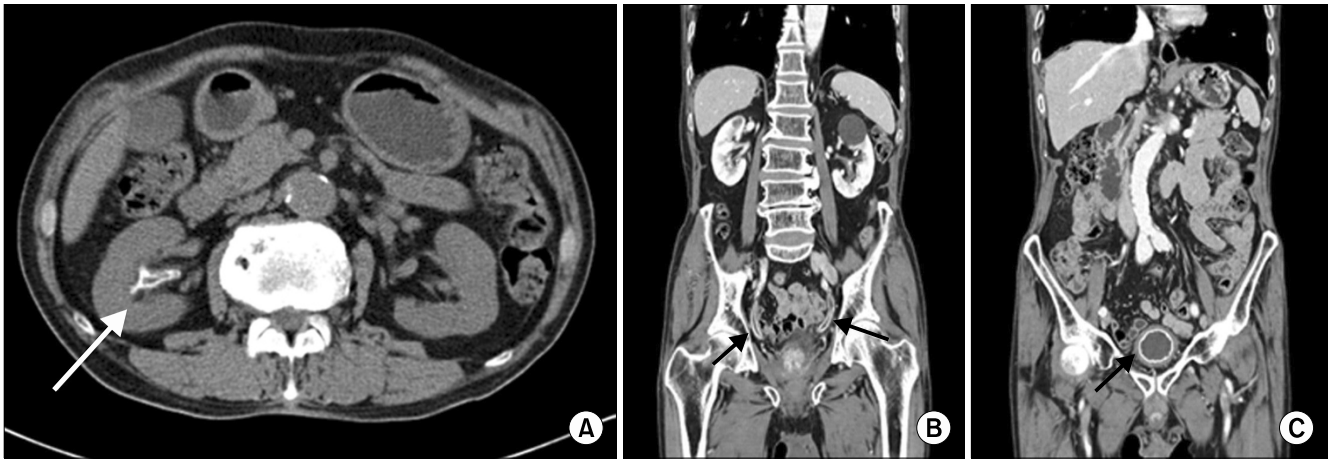


**Fig. 1.** Abdomino-pelvic computed tomography (CT) images. (A) Non-contrast enhanced CT shows bilateral mild hydronephrosis with calcifications of the right renal pelvis (arrow). Enhanced CT shows calcification of ureter (B, arrows) and urinary bladder (C, arrow).

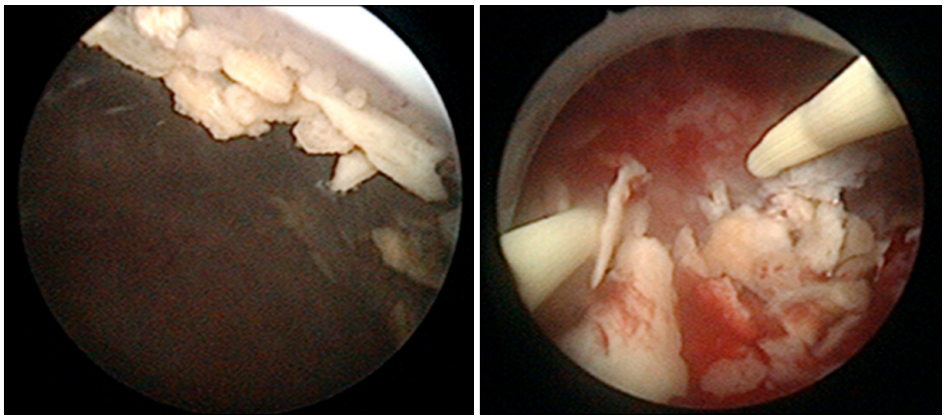

**Fig. 2.** Cystoscopy shows encrusted bladder mucosa with severe inflammation, necrosis and bleeding.

report a case of EC/PU which was occurred in patient who was previously treated with transcatheteral arterial chemoembolization for hepatocellular carcinoma.

## CASE REPORT

An 80-year-old man was referred to another urologic clinic because of urinary frequency, dysuria, and lower abdominal discomfort. He had undergone a transurethral removal of bladder stone 5 years ago. He had been treated with transcatheteral arterial chemoembolization for hepatocellular carcinoma two times. He was treated with oral ciprofloxacin and non-steroidal anti-inflammatory drug for 4 weeks in another urologic clinic. However, his urinary symptoms including dysuria, frequency, and hematuria were not improved. Therefore, he wanted to refer to our urology department for further treatment. Hematologic examination revealed that a white blood cell count was 10,170/μl, and serum creatinine level was 1.52 mg/dl. Urinalysis showed pyuria and microscopic hematuria with alkaline urine (pH 8.0). However, urine culture grew no microorganism in common culture media. Abdomino-pelvic computerized tomography showed a bilateral hydronephorosis with calcifications of renal calyx, ureter and bladder (Fig. 1). Cystoscopy revealed the calcified, edematous bladder mucosa with necrosis and bleeding. After admission, he received fluid and intravenous vancomycin. We didn't perform percutaneous nephrostomy because of mild hydronephrosis and nearly normal renal function. He underwent transurethral removal of calcified plaques with spinal anesthesia (Fig. 2). After operation, intravenous antibiotic treatment was continued for 14 days and urine acidification was started. Although oral urine acidification is not sufficient, oral vitamin C was given because of absence of percutaneous nephrostomy. He was discharged without deterioration of renal function, bacteriuria, and bladder

calculi. At 1 month follow-up cystoscopy, inflammation was improved and calcification was significantly reduced. His urinary symptoms were improved and urine pH decreased to 7.0.

## DISCUSSION

Patients with cancer compromise a heterogeneous group with regard to risk factors, predisposing to infectious complications. As examples, hematological malignancies may result in global leucopenia or a reduction in functional myeloid and lymphoid cells. Solid tumors can also increase the risk of infectious complications based on anatomical location. As examples, obstructive hepatobiliary and pancreatic tumors can lead to cholangitis. Malnutrition and general debilitation associated with advanced cancer also increase the risk of infections.[4] Cytotoxic regimens increase the risk of infectious complications in two ways. First is the leucopenia related to chemotherapy- and radiation-induced bone marrow suppression. Second is the mucosal toxicity that predisposes to infection by gastrointestinal flora. The risk of infectious complications is directly related to the intensity and duration of neutropenia.[5]

EC/PU is a rare chronic infectious and inflammatory condition characterized by calcific deposits on or encrustation of the urothelium. Urea-splitting bacteria, *Corynebacterium urealyticum* and *Proteus*, is causative microorganism in EC/PU.[2] *Corynebacterium* is a Gram-positive, slow-growing microorganism that is multi-resistant against antibiotics. It is often isolated from the skin or groin of elderly patients (up to 37%), especially those having received broad-spectrum antibiotics, but only 60% of them develop an infection.[6] It can adhere strongly to urothelium and penetrated into the mucosa. Corynebacterium infection causes continuous increase in the urinary pH, above 7.5, which plays a key role in the pathogenesis of encrustation on urothelium. The mineral compounds are responsible for encrustation along the infected urothelium and debris/stone formation.[7]

Clinical manifestations of EC/PU are nonspecific and can be minimal for a prolonged period. Patients with this disease usually have hematuria and deteriorating renal function. Other features that have reported at presentation are fluid overload, pyuria, suprapubic pain, passage of debris, stone, and fever. Predisposing factors for EC/PU include old age, long-period hospitalization with broad spectrum antibiotic therapy, immunosuppression, renal transplantation, cancer or systemic diseases, underlying urological disease, manipulations of the urinary tract.[6,8] Diagnosis should be considered in patients with predisposing factors, alkaline urine, and calcification of urinary tract. When EC/PU is clinically suspected, imaging is a major part of the diagnosis. Direct visualization on imaging of encrusted plaque should be confirmed. Sometimes the presence of calcification in the bladder area on plain abdominal X-ray is not so extensive and is often neglected. Computed tomography (CT) appears to be the optimal technique to diagnose EC/PU.[9]

Vitamin C (ascorbic acid) is an essential micronutrient involved in many biologic and biochemical functions, acting as an electron donor or reducing agent in chemical reaction. The growth of uropathogens was markedly reduced by the addition of nitrite to acidified urine. This inhibition was enhanced by ascorbic acid.[10] Although is has been suggested that vitamin C has some effect on urinary acidification, reducing the urinary pH, the role of vitamin C as a urinary acidifier is still controversial.

In this case, the diagnosis was suggested on clinical manifestations, urine pH, CT findings and cystoscopy. Although the urine culture was negative, diagnosis of EC/PU can be suspected on the basis of sterile pyuria, alkaline urine pH, calcifications of renal pelvis, ureter, and urinary bladder on CT, and direct visualization of calcification of urinary mucosa on cystoscopy. We assumed that negative urine culture was caused by previous antibiotics use in another hospital and fastidiously growing of *Corynebacterium* in common culture media. It is an unusual case that encrustations are occurred in both of upper urinary tract and bladder. Patient was treated with transcatheteral arterial chemoembolization for hepatocellular carcinoma. Caner itself is a predisposing factor in EC/PU. We believe that the transcatheteral arterial chemoembolization could have helped the organism tract up the collecting system.

EC/PU is a rare disease in urinary tract, but potential emerging complication such as postrenal failure. Especially, it can be occurred in old age, malignancy, prolonged antibiotics use, and previous intervention of urinary tract. It is important to recognize that calcifications are urothelial in nature and are not due to renal or ureteral stone. A high level of suspicion in appropriate clinical setting and characteristic imaging features enables early diagnosis and treatment of this disease.

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## CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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