

## CASE REPORT

# Peripheral T-Cell Lymphoma of Urinary Bladder Presenting With Just Irritative Voiding Symptoms

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Peripheral T-cell lymphoma (PTCL) of the urinary bladder is rare. PTCL can either be primary or secondary and is difficult to differentiate from other inflammatory bladder lesions. We report a case of PTCL involving the bladder in a 63-year-old man who complained of dysuria without gross hematuria. In this report, we focus on the cystoscopic and histologic findings of urinary bladder lymphoma and its differential diagnosis.

**Key Words:** Peripheral T-cell lymphoma, Bladder tumor, Dysuria

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## INTRODUCTION

The bladder cancer prevalence is over than 1.6 million patients in the world. The risk of bladder cancer is 1.1% in men and 0.27% in women.<sup>1</sup> About 90% of bladder cancers consist of urothelial cell carcinomas. Histologically, pure urothelial carcinoma accounts for 75% of all bladder cancers. Lymphomas rarely involve the urinary bladder. In the United States, the age-adjusted incidence of primary urinary tract lymphoma was 1 case per 1,000,000 people in a year, with T-cell lymphomas accounting for only 0.5% of cases.<sup>2</sup>

The most common presentations of bladder cancer are hematuria (microscopic or gross) and voiding symptoms. Hematuria and irritative voiding symptoms like dysuria are the frequent common in inflammatory diseases and bladder lymphomas. Therefore, it is difficult to differentiate these diseases from bladder tumor by clinical presentation alone. In such cases, cystoscopic findings of urothelial carcinoma usually appear

as papillary lesions, which is often very helpful in the differential diagnosis. However, cystoscopic and histologic findings of bladder lymphoma can be very similar to those of inflammatory diseases; therefore, caution should be taken.

This report describes a very rare case of PTCL that invaded the urinary bladder.

## CASE REPORT

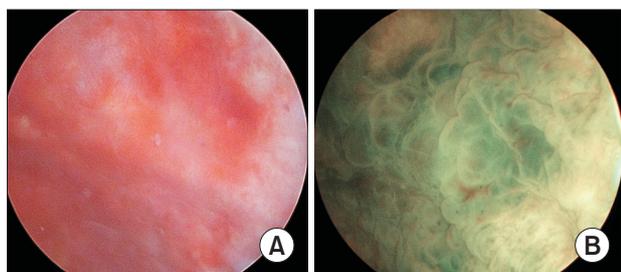
A 63-year-old man was referred to Keimyung University Dongsan Medical Center, Daegu, Korea, in May 2020 with a 4-week history of irritative voiding symptoms without gross hematuria. International Prostate Symptom Score was 26 (obstructive 16, irritative 10). Physical examination revealed not specific conditions. Routine hematological and biochemical tests were normal. Prostate-specific antigen level was 2.4 ng/mL. At transrectal ultrasound finding, total prostate volume was 32 g. Before the onset of symptoms, he was in good health. White light cystoscopy revealed diffuse



hyperemic edematous mucosal changes in the right dome area. Narrow-band imaging cystoscopy also showed hyperemic and red-pedunculated mucosa (Fig. 1). Atypical cells were detected on the first urine cytology. Computed tomography (CT) revealed a diffusely thickened right urinary bladder wall with inner layer enhancement and 2 pancreatic lesions with low attenuation (Fig. 2). Positron emission tomography/CT revealed 2 hypermetabolic mass lesions in the pancreatic head and tail. Transurethral resection of the bladder lesion was performed. Histopathological examination showed monotonous small lymphocytic infiltrates in the mucosa and lamina propria. Lymphoid cells were negative for CD20 and positive for CD3 and CD8. T-cell receptor gamma gene rearrangement showed an obvious T-cell clonal peak (Fig. 3). Therefore, the tumor

was diagnosed as PTCL. Endoscopic ultrasound-guided fine-needle aspiration was performed on pancreatic head and tail lesions. In addition, T-cell receptor gamma gene rearrangement was performed using urine and pancreatic tissue, and clonal peaks were found at the same location as those in the test results for the bladder tissue. Laboratory examination showed a white blood cell (WBC) count of  $9.14 \times 10^9/L$  (neutrophils 49.7%, lymphocytes 36.7%, monocytes 12.0%, eosinophils 0.9%, and basophils 0.7% of WBC), a hemoglobin level of 15.1 g/L, and a platelet count of  $258 \times 10^9/L$ . There was no evidence of T-cell leukemia or bone marrow involvement in malignant lymphoma.

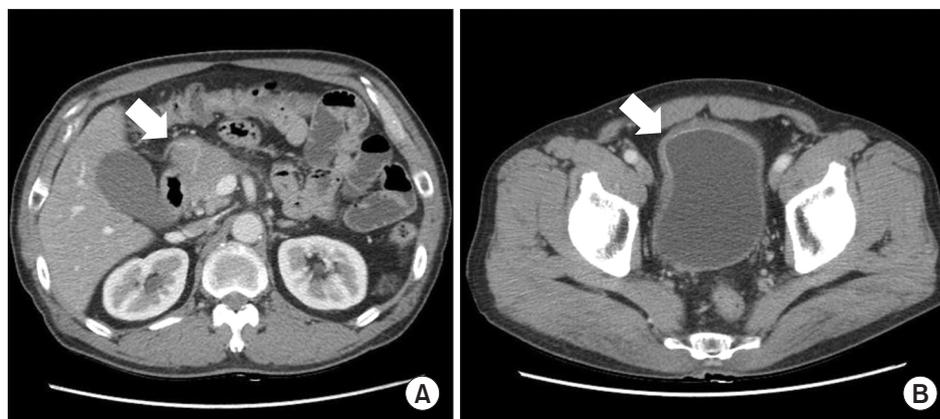
The patient underwent 3 cycles of CHOP (cyclophosphamide, doxorubicin, vincristine, prednisolone), followed by 5 cycles of gemcitabine, dexamethasone, and cisplatin. By the end of the treatment, the sizes of the pancreatic lesions decreased. However, the diffusely thickened bladder wall showed no change. T-cell receptor gamma gene rearrangement performed with urine still showed clonal peaks at the same location as the first tested lesion. The patient died of pancytopenia one year of the diagnosis, despite appropriate treatment.



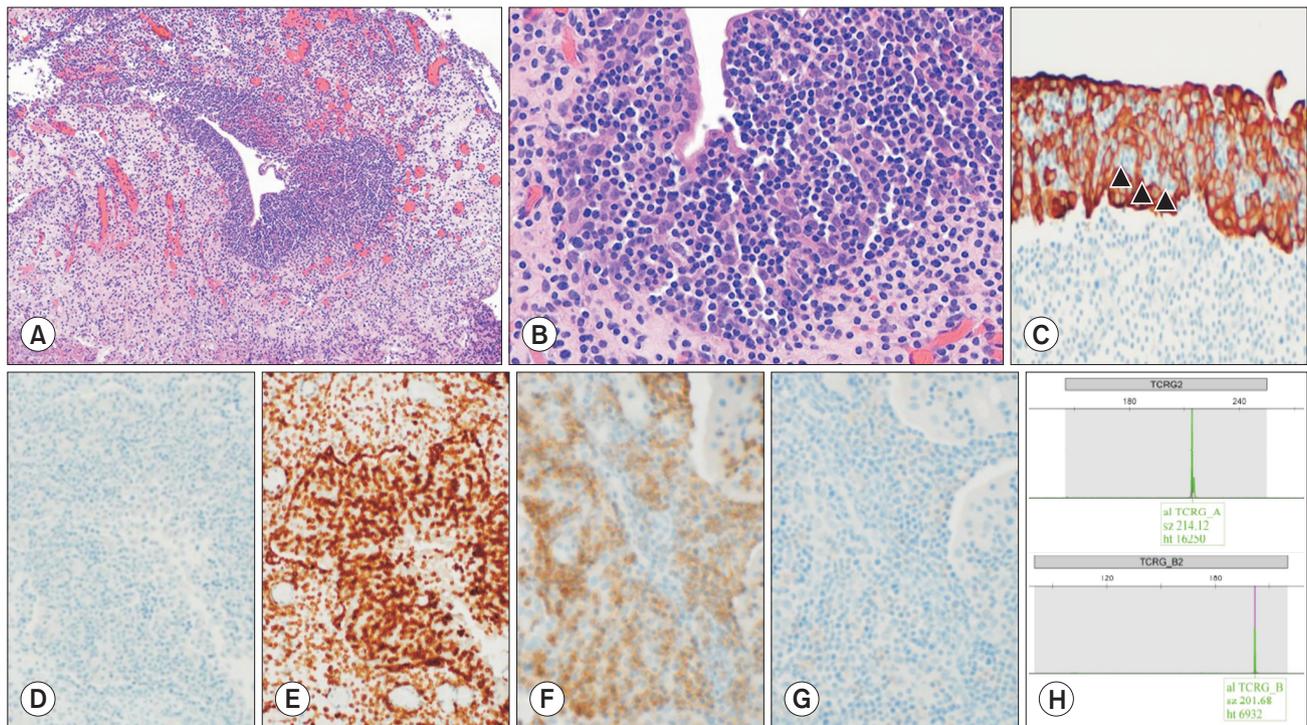
**Fig. 1.** (A) White light cystoscopy revealed diffuse hyperemic edematous mucosal changes in the right dome area. (B) Narrow-band imaging cystoscopy also showed hyperemic and red-pedunculated mucosa.

## DISCUSSION

Malignant lymphoma of the urinary bladder was a



**Fig. 2.** Computed tomography (CT) images at diagnosis. (A) CT showed a 2 foci of low attenuating lesions in the pancreas head/neck and body (arrow). (B) CT revealed a diffusely thickened right urinary bladder wall with inner layer enhancement (arrow).



**Fig. 3.** (A) The bladder mucosa shows lymphocytic infiltrate at the lamina propria (H&E,  $\times 40$ ). (B) The lymphoid cells are small and extensively infiltrate the mucosal epithelium (H&E,  $\times 200$ ). (C) Immunohistochemical stain for cytokeratin highlights extensive lymphoepithelial-lesion-like feature (arrowheads) (cytokeratin,  $\times 200$ ). The lymphoid cells were negative for CD20 (D) and positive for CD3 (E) and CD8 (F). (G) The tumor cells are negative for CD4. (H) T-cell receptor gamma gene rearrangement showed an obvious T-cell clonality peak at 214 base pair and 202 base pair of TCRG\_A and TCRG\_B.

very rare disease that can developed either primary or secondary. Primary lymphomas of the urinary bladder are rare. It is accounting for just 0.2% of extranodal lymphomas. However, secondary invasion of the bladder by systemic lymphoma is relatively common. Diffuse large B-cell lymphoma (DLBCL) and marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALToma), which are reported as the most common bladder lymphomas, are both B-cell lymphomas. Lontos et al.<sup>2</sup> reviewed 1,264 patients with urinary bladder lymphoma. Histologically, the urinary tract lymphoma was DLBCL (51.9%), followed by MALToma (12.5%), and follicular lymphoma (9.4%). Contrary to most reports, present case was diagnosed with PTCL, which is a type of T-cell lymphoma. In Korea, PTCL accounts for 3.2% of all malignant lymphomas and only 1.9% of extranodal

lymphomas.<sup>3</sup> In present case, lymphoma was found in the bladder and the pancreas; therefore, it was not appropriate to consider it primary lymphoma. This is thought to be regarded as a systemic lymphoma that also occurred in the urinary bladder and pancreas.

Although a small number, there are some reports with PTCL at urinary bladder. Wang et al.<sup>4</sup> reported 45-year-old man who had primary T-cell lymphoma of the urinary bladder. Also, Mourad et al.<sup>5</sup> reported 52-year-old man. In these 2 cases, presented symptoms were gross hematuria, dysuria, and suprapubic pain. Because had hematuria, they could an early investigation included CT scan and the results were good after CHOP treatment. But present case complained only irritative voiding symptoms. Therefore, absence of hematuria was one cause of delay in treatment, as a result, the

prognosis was poor.

Cystitis developed from chronic inflammation of bladder was considered a cause of bladder lymphoma. Approximately 20% of patients come with this history. There is no organized lymphoid tissue in the urinary tract, however, lymphoid tissue may originate from lymphocytes that have been drawn into the area due to a recurrent infection.<sup>6</sup> Raderer et al.<sup>7</sup> support this hypothesis. Particularly MALT-associated lymphomas, the regression of some lymphomas was developed after the use of antibiotics. On the other hands, most common type of bladder lymphoma was MALT-associated lymphoma, which is usually associated with bacterial infections.<sup>7</sup> Morita et al.<sup>8</sup> explained that chronic bladder inflammation due to repeated infections results in an accumulation of extranodal lymphoid tissue. In addition, the symptoms of bladder lymphoma clinically presented urinary frequency, hematuria, and suprapubic pain, which similarly overlap with symptoms of bacterial cystitis. Reddish erosive mucosa covering the entire bladder on cystoscopy is similarly observed in both bladder lymphoma and cystitis. Our patient visited the clinic with irritative voiding symptoms, and cystoscopic findings also showed similar signs to inflammatory disease. CT did not show significant lymph node enlargement but revealed severe diffuse wall thickening compared to usual cystitis. Therefore, although very rare, lymphomas should also be included in the list of impressions when evaluating patients with irritable voiding symptoms.

The currently recommended treatment strategy for PTCLs derives mostly from B-cell lymphoma treatment strategies, with the recommended use of an aggressive approach with anthracycline-based polychemotherapy (CHOP or CHOEP). Even if associated with unsatisfactory results, CHOP chemotherapy should still be considered as the reference therapy. On the other hands, several new drugs were under evaluation in clinical trials.

CD30 monoclonal antibody was improvements in progression-free survival and overall survival.<sup>9</sup>

In terms of prognosis, extranodal lymphoma has worse prognosis compared than nodal disease. Castillo et al.<sup>10</sup> reported that gastrointestinal, pulmonary, liver, and pancreatic DLBCL have worse prognosis than nodal DLBCL. Also, urinary tract DLBCL is associated with worse cancer-specific survival than primary nodal DLBCL.<sup>2</sup> Lontos et al.<sup>2</sup> reported, the patients' overall survival and cancer-specific survival at 5 years were 49% and 58%, respectively. In the rituximab-CHOP era, the 5-year overall survival rate and progression-free survival rate of DLBCL are improved by approximately 65% and 60%, respectively. However, PTCL is more aggressive than DLBCL, with lower 5-year overall survival and disease-free survival rates was just 20%–30%. Like that, in this report, the patient died just one year after diagnosis, despite appropriate treatment. PTCL of the urinary bladder is rare. Therefore, further research on treatment is required.

PTCL of the urinary bladder is a rare phenomenon that can occur either in primary or secondary form and is difficult to differentiate from other inflammatory bladder lesions. Moreover, it has been shown to have a poor prognosis. Consequently, from a clinical aspect, when a patient does not show improvement in the symptoms after receiving the appropriate treatment for inflammatory disease, the clinician must check for the possibility of bladder lymphoma. Careful follow-up with cystoscopy and CT image may be helpful to diagnose this rare disease.

## NOTES

- Conflicts of Interest: No potential conflict of interest relevant to this article was reported.
- Funding: This study received no specific grant from any funding agency in the public, commercial,

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