

# World Journal of *Clinical Cases*

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## Synchronous renal pelvis carcinoma associated with small lymphocytic lymphoma: A case report

Han-Jin Yang, Xiao Huang

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### Abstract

#### BACKGROUND

Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) is often associated with an increased risk of developing subsequent neoplasms of epithelial and mesenchymal origin. Coincidence of CLL/SLL and urothelial carcinoma (UC) is very rare. Herein, we report a case of synchronous renal pelvis carcinoma with SLL.

#### CASE SUMMARY

A 78-year-old man presented with the complaint of terminal painless gross hematuria for the past 2 mo. On physical examination, enlarged lymph nodes were palpable in the cervical and axillary regions. The patient's peripheral blood film was normal. He had a significant smoking history for the past 50 years. Cystoscopy revealed bleeding in the left upper urinary tract. Abdominal computed tomography imaging demonstrated a left renal pelvis tumor. The patient underwent laparoscopic radical nephroureterectomy. Histopathology revealed left renal pelvis high-grade invasive papillary UC and SLL involving the kidney and bone marrow. Renal pelvis lymphatic tissue and lymphocytes were positive for CD5, CD20, and CD23. In addition, the following results were obtained: CD3 (-), Ki-67 (30%+), Bcl-2 (+), Bcl-6 (+), CD10 (-), and CD79a (+). Moreover, no UC metastasis was observed in the lymph nodes.

#### CONCLUSION

This is the first case of coincident CLL/SLL and upper tract UC in the literature. Cancer patients with lymphadenopathies should always be investigated to rule out the possibility of synchronous or metachronous malignancy.

**Key Words:** Synchronous malignancy; Coincidence; Upper tract urothelial carcinomas;

Small lymphocytic lymphoma

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**Core Tip:** Coincidence of chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) and urothelial carcinoma (UC) is very rare. We report a case of synchronous renal pelvis carcinoma with SLL. This is the first case of coincident CLL/SLL and upper tract UC in the literature. Cancer patients should always be investigated to rule out the possibility of a synchronous or metachronous malignancy.

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## INTRODUCTION

Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) is often associated with an increased risk of developing subsequent neoplasms of epithelial and mesenchymal origin[1,2]. Coincidence of CLL/SLL and urothelial carcinoma (UC) is very rare. Only five cases of coincident CLL/SLL and bladder cancer have been reported[2-5]. Upper tract UCs (UTUCs) are uncommon, accounting for only 5%-10% of UCs worldwide[6]. Here, we present a case of synchronous CLL/SLL and renal pelvis carcinoma diagnosed in laparoscopic radical nephroureterectomy specimens. To our knowledge, this is the first case of coincident CLL/SLL and UTUC in the literature.

## CASE PRESENTATION

### Chief complaints

A 78-year-old male farmer presented with the complaint of terminal painless gross hematuria without frequency or urgency during micturition for the past 2 mo.

### History of present illness

No history of present illness.

### History of past illness

The patient's medical history was significant for hypertension for 10 years, and his blood pressure was well controlled with levotidine amlodipine and timisartan tablets. He also had a significant history of smoking for the past 50 years.

### Personal and family history

No familial history of cancer and other illness.

### Physical examination

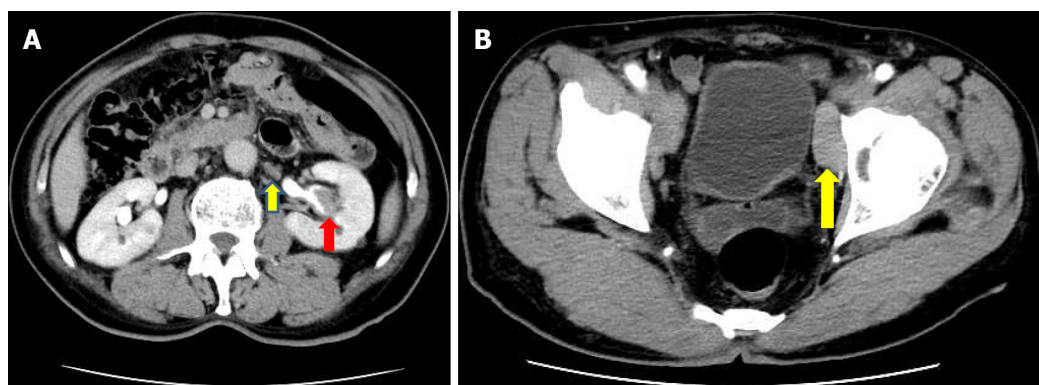
Enlarged lymph nodes were palpable in the cervical and axillary regions.

### Laboratory examinations

The patient's urinalysis results were positive for red blood cells (+++). The peripheral blood parameters were normal: White blood cell count ( $6.6 \times 10^9/L$ ), neutrophil percentage (54.9%), lymphocyte percentage (25.9%), hemoglobin (129 g/L), and platelet count ( $169 \times 10^9/L$ ).

### Imaging examinations

Cystoscopy revealed that the urinary tract bleeding originated from the left upper urinary tract. Abdominal computed tomography imaging demonstrated a tumor mass of approximately 2.7 cm × 1.5 cm × 1 cm in the central part of the left renal pelvis cavity (Figure 1A). Multiple enlarged lymph nodes were noted in the retroperitoneal and pelvic walls (Figure 1). Bone and chest radiographs were negative for metastases.



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**Figure 1** Multiple enlarged lymph nodes were noted in the retroperitoneal and pelvic walls. A: Abdominal computed tomography imaging demonstrated a tumor mass of approximately 2.7 cm × 1.5 cm × 1 cm in the central part of the left renal pelvis cavity; B: Multiple enlarged lymph nodes were noted in the retroperitoneal and pelvic walls.

## FINAL DIAGNOSIS

UTUC of the left renal pelvis with possible lymphatic metastasis.

### Pathological examinations

A 2.7 cm × 1.5 cm × 1.0 cm tumor was found in the renal pelvis in an isolated kidney specimen. The resected specimen was fixed in 10% neutral buffered formalin. Routine H&E staining was performed for histological examination. Immunohistochemistry was conducted on the formalin-fixed, paraffinembedded tissue sections. Light microscopic examination confirmed the diagnosis of UTUC of the renal pelvis urothelium extending into the lamina propria (Figure 2). A large amount of diffuse small lymphocytic infiltration was observed along the periphery of the tumor mucosa. The lymphocytes were well differentiated and were of the same type (Figure 3). Immunohistochemistry studies revealed that the urothelial tumor cells were positive for P63 (Figure 4A). Retroperitoneal renal pedicle enlarged lymph nodes showed diffuse architectural effacement due to the proliferation of small lymphocytes with variably prominent scattered proliferation centers composed of prolymphocytes and paraimmunoblasts, and were positive for CD5, CD20, and CD23. No UC metastases were observed in the lymph nodes. Renal pelvis lymphatic tissue and lymphocytes were positive for CD5, CD20, and CD23 (Figure 4). In addition, the following results were obtained: CD3 (-), Ki-67 (30%+), Bcl-2 (+), Bcl-6 (+), CD10 (-), CD79a (+), CD43 (+), CyclinD1 (-), CD21 (-), MUM1 (partial +), CD138 (-), Kappa K (-), Lambda λ (-), and CD30 (-). The final diagnosis was left renal pelvis high-grade invasive papillary UC and left retroperitoneal SLL with left kidney involvement (Figures 2 and 3).

### Hematological examinations

After an additional diagnosis of CLL/SLL was made, the patient underwent a retrospective examination for a complete hematology evaluation. Enlarged lymph nodes were detected in the bilateral cervical, axillary, and inguinal regions by ultrasound, with a maximal lymph node size of 2.8 cm × 1.4 cm. Enlarged lymph nodes were also detected around the pancreas with a maximal lymph node size of 3.6 cm × 3.2 cm at the pancreatic tail. The patient's peripheral blood parameters were normal after surgery. Bone marrow aspiration results showed hypocellular hematopoietic tissue with trilineage growth inhibition. Focal aggregation of the same type of small lymphocytes was observed between the bone trabeculas. The bone marrow fibrosis (MF) grading in the silver-stained bone marrow biopsy sections suggested MF-1. Immunohistochemistry studies showed that the small lymphocytes were positive for CD5, CD19, CD20, and CD23. These results confirmed the diagnosis of CLL/SLL with bone marrow involvement.

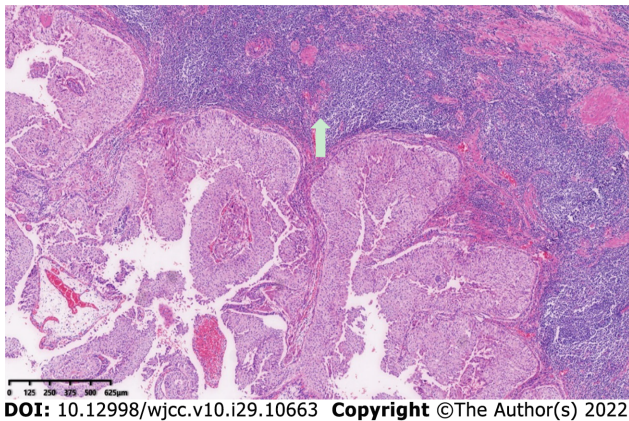
## TREATMENT

The patient underwent laparoscopic radical nephroureterectomy under general anesthesia.

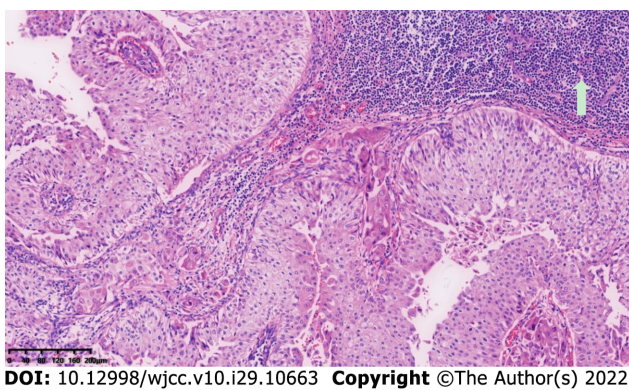
## OUTCOME AND FOLLOW-UP

The patient smoothly recovered from the surgery without any complications and was discharged after 7





**Figure 2** Light microscopic examination confirmed the diagnosis of upper tract urothelial carcinoma of the renal pelvis urothelium extending into the lamina propria. Original magnification: 100 ×; scale bar: 100 μm.



**Figure 3** A large amount of diffuse small lymphocytic infiltration was observed along the periphery of the tumor mucosa. Original magnification: 100 ×; scale bar: 100 μm.

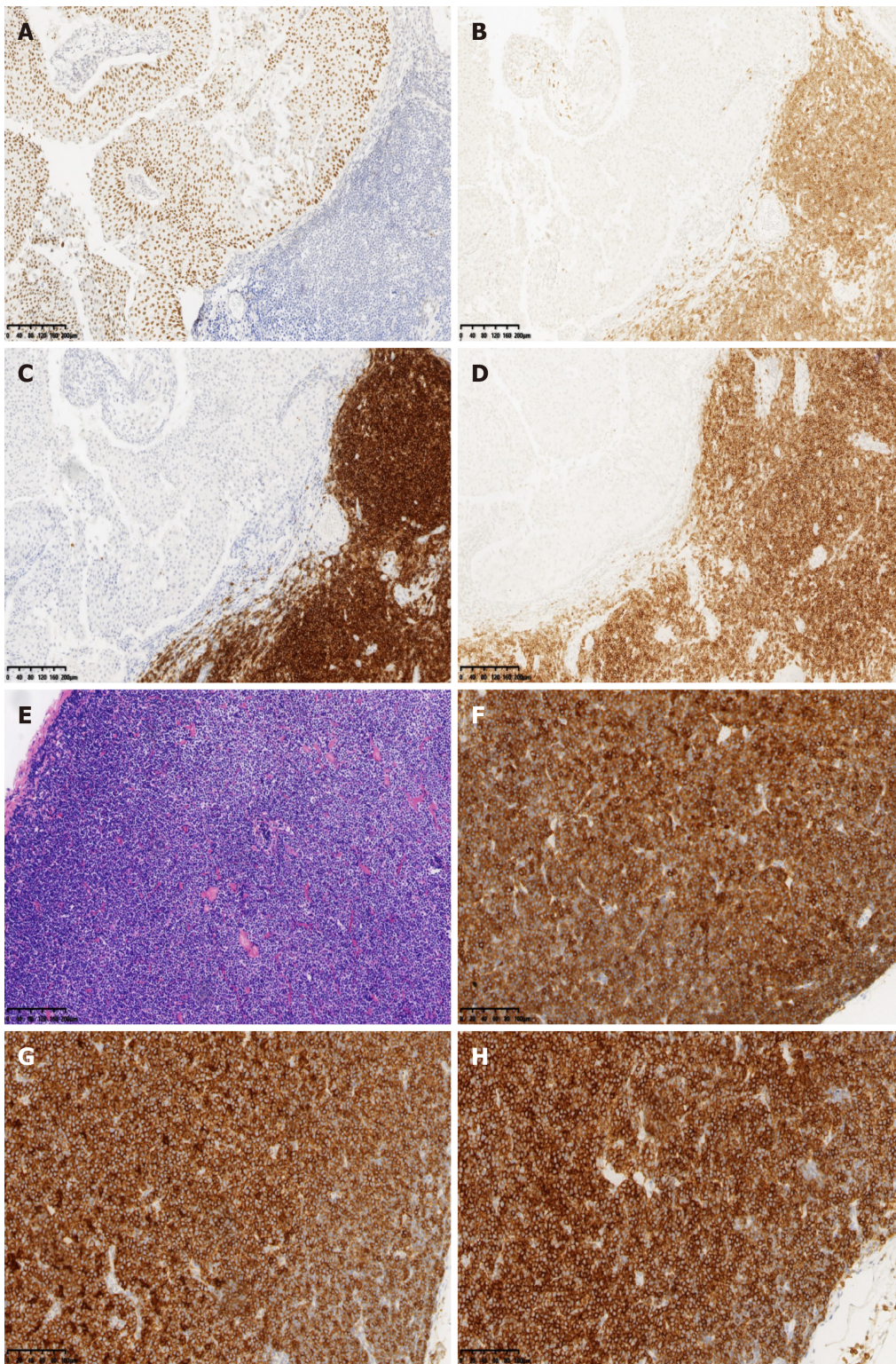
d of hospitalization. His CLL/SLL situation did not require any medication according to the related guidelines from hematology. The patient stopped smoking following the physician's advice. After 2 years of regular follow-up, he was doing well with UTUC and CLL/SLL.

## DISCUSSION

The occurrence of multiple primary cancers (MPCs) is a very rare situation. They usually grow in elderly people, as the morbidity of malignancies increases with age[1]. Based on the time of diagnosis at each primary site, MPCs are classified into two categories: Synchronous occurrence of more than one tumor or metachronous occurrence of another tumor in a known case of carcinoma. Synchronous malignancy is defined as the occurrence of two tumors within 6 mo[7]. UC coincident with CLL/SLL is very rare with only five cases of bladder cancer reported in the literature[2-5]. The coincidence of CLL/SLL and UTUC is extremely rare. In those reported bladder cancer coincident with CLL/SLL cases, most patients had abnormal peripheral blood smear of leukocytosis with absolute lymphocytosis [2-5]. No lymphadenopathy was noted. This apparent abnormality gave the chance to detect the CLL/SLL at the beginning of diagnosis. In our case, the patient had no peripheral blood abnormality. The only abnormality was multiple enlarged lymph nodes in the retroperitoneal and pelvic walls which implied possible lymphatic metastasis of UTUC. The SLL was found in the renal pedicle lymph nodes and parenchyma of the renal pelvis during the pathological diagnosis procedure after a RUN surgery for renal pelvis carcinoma. The limitation of our case is that we did not perform a biopsy to detect the CLL/SLL before surgery. This is the first case of coincident CLL/SLL and UTUC reported.

The incidence of coincident malignancies in patients with CLL/SLL is increased because of immune dysregulation and consequent treatment[8,9]. Tsimberidou *et al*[10] demonstrated that the frequency of other malignancies in CLL/SLL patients is 2.2 times higher than that in the general population. Breast, brain, skin, and prostate tumors have been reported to be common coincident malignancies of CLL/SLL. However, UC coincident with CLL/SLL is a rare situation[2-5]. The etiology of MPCs is





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**Figure 4** Immunohistochemistry studies revealed that the urothelial tumor cells were positive for P63. A-E: Retroperitoneal renal pedicle enlarged lymph nodes showed diffuse architectural effacement due to the proliferation of small lymphocytes with variably prominent scattered proliferation centers composed of prolymphocytes and paraimmunoblasts, and were positive for CD5, CD20, and CD23; F-H: No urothelial carcinoma metastases were observed in the lymph nodes. Renal pelvis lymphatic tissue and lymphocytes were positive for CD5, CD20, and CD23. Original magnification: 100 ×; scale bar: 100 μm.

complex and includes environmental factors, genetic susceptibility, immunological impairment, previous medical treatment, hormonal factors, and sex[11]. Many kinds of chemical agents including tobacco, aniline dyes, benzidine, aromatic amines, and rubber have been reported to cause bladder cancer[12]. Although the relationship between these two cancers is unclear, one possible explanation involves the glutathione S transferase M1 (GSTM1), which is important for the metabolism of environmental carcinogens, reactive oxygen species, and chemotherapeutic agents. Cigarette smoke carcinogens



inactivate the GSTM1, and the smokers exhibit the GSTM1 null genotype. Increased risk of bladder cancer has been reported in all cigarette smokers with GSTM1 null status[13]. The cause of MPCs in our patient may have been the long-term history of tobacco consumption. Further tests revealed that the patient had both invasive renal pelvis carcinoma and SLL. As a result, this case highlights the importance of lymphocytic infiltration in UC. Patients with cancer should always be investigated to rule out the possibility of a synchronous or metachronous malignancy.

## CONCLUSION

Coincidence of CLL/SLL and UTUCs is an extremely rare situation. In a known case of malignancy, the presence of lymph nodes may indicate metastasis and may be misdiagnosed as advanced stage disease. The possibility of secondary malignancies such as lymphoma should be considered, and biopsy should be performed to confirm the diagnosis and stage the disease.

## FOOTNOTES

**Author contributions:** Yang HJ contributed to data collection, histopathology, and manuscript drafting; Huang X contributed to patient treatment and follow-up, and manuscript writing and revision.

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