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Editorial Board Member of *World Journal of Clinical Cases*, Ashraf F Hefny, MD, MSc, Associate Professor, Surgeon, Department of Surgery, College of Medicine and Health Sciences, UAE University, Al Ain 00000, United Arab Emirates. ahefny@uaeu.ac.ae

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Coexistence of urinary tuberculosis and urothelial carcinoma: A case report

Yu-Chi Tsai, Chiao-Ching Li, Bing-Tau Chen, Chien-Yao Wang

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Yu-Chi Tsai, Chien-Yao Wang, Division of Infectious Diseases, Department of Internal Medicine, Kaohsiung Armed Forces General Hospital, Kaohsiung 802301, Taiwan

Yu-Chi Tsai, Division of Infectious Diseases and Tropical Medicine, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei 114202, Taiwan

Chiao-Ching Li, Division of Urology, Department of Surgery, Pingtung branch, Kaohsiung Armed Forces General Hospital, Pingtung 900048, Taiwan

Chiao-Ching Li, Bing-Tau Chen, Division of Urology, Department of Surgery, Kaohsiung Armed Forces General Hospital, Kaohsiung 802301, Taiwan

Chiao-Ching Li, Division of Urology, Department of Surgery, Tri-Service General Hospital, National Defense Medical Center, Taipei 114202, Taiwan

Bing-Tau Chen, Division of Urology, Department of Surgery, Kaohsiung Veterans General Hospital, Kaohsiung Veterans General Hospital, Kaohsiung 813414, Taiwan

Corresponding author: Chien-Yao Wang, MD, Doctor, Division of Infectious Diseases, Department of Internal Medicine, Kaohsiung Armed Forces General Hospital, No. 2, Zhongzheng 1st Road, Lingya District, Kaohsiung 802301, Taiwan. atsb1234@msn.com

Abstract

BACKGROUND

Taiwan has a high prevalence of tuberculosis and urothelial carcinoma. However, the simultaneous occurrence of both disorders in one patient is uncommon. Tuberculosis and urothelial carcinoma share some common risk factors and could demonstrate overlapping clinical manifestations.

CASE SUMMARY

Herein, we report the case of a patient who presented with fever, persistent hematuria, and pyuria. Chest computed tomography scans revealed a bilateral upper lobes cavitory lesion with fibrosis. Severe hydronephrosis of the right kidney and renal stones and cysts in the left kidney were observed. Initial microbiological testing was negative; however, a polymerase chain reaction assay of the urine confirmed a urinary tuberculosis infection. The patient was started on an anti-tuberculosis regimen. Ureteroscopy performed to resolve obstructive nephropathy revealed the incidental finding of a left middle-third ureteral tumor.

Examination after biopsy and transurethral resection of the bladder tumor indicated urothelial carcinoma. The patient underwent laparoscopic nephroureterectomy, with bladder cuff excision for the right kidney and ureter, and holmium laser ablation of the ureteral lesion to preserve the left kidney and ureter. He has remained stable after the procedures.

CONCLUSION

Although establishing a causal relationship between tuberculosis and cancer is difficult, medical personnel should consider their correlation.

Key Words: Urinary tuberculosis; Urothelial carcinoma; Fever; Hematuria; Taiwan; Case report

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Core Tip: We have reported the case of a patient who presented with fever, persistent hematuria, and pyuria and was diagnosed with both urinary tuberculosis and urothelial carcinoma. Tuberculosis and urothelial carcinoma have some common risk factors such as smoking, alcohol consumption, chronic diseases, and malnutrition. Although it is difficult to establish a causal relationship between these two diseases, clinical medical personnel should consider the correlation between the two diseases.

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INTRODUCTION

Taiwan has a high prevalence of tuberculosis and urothelial carcinoma. However, the simultaneous occurrence of these disorders is uncommon in the same patient. The concurrent development of both of these diseases in the same patient could be explained by the following mechanisms: Local long-term inflammatory response, leading to the destruction of the host protective barrier, resulting in the invasion of microorganisms or cancer cells[1]. In addition, the inflammatory response damages immune cells and weakens the host's immunity.

Tuberculosis and urothelial carcinoma have some common risk factors, such as smoking, alcohol consumption, chronic diseases, and malnutrition. Although it is difficult to establish a causal relationship between these two diseases, clinical medical personnel should consider the correlation between the two. Herein, we report the case of a patient who presented with fever, persistent hematuria, and pyuria and was diagnosed with both urinary tuberculosis and urothelial carcinoma.

CASE PRESENTATION

Chief complaints

A 70-year-old man was transferred to our hospital for further management of intermittent fever, chills, and fatigue lasting for 10 d.

History of present illness

The patient experienced intermittent symptoms accompanied by severe night sweats. His body temperature was 38.5 °C, and his fever temporarily subsided after taking oral acetaminophen. He denied respiratory symptoms, such as cough, sore throat, or runny nose, and did not experience any gastrointestinal symptoms such as vomiting or diarrhea. Although the patient did not report urinary symptoms such as blood in urine, urgency, difficulty or pain during urination, or frequent voiding, he did report persistent bilateral lower back pain in the past 10 d. The patient had previously been diagnosed with lumbar herniated intervertebral disc disorder and had been undergoing rehabilitation therapy. As he believed that his current back pain was not significantly different from his previous pain, he did not pay particular attention to it.

History of past illness

The patient had developed anorexia, with a weight loss of 5.6 kg during the past year. Moreover, he had third-fourth lumbar herniated intervertebral disc disorder which had been treated with physical

rehabilitation therapy since the age of 63. He did not have any systemic disorders, such as diabetes mellitus or liver cirrhosis.

Personal and family history

The patient disclosed a smoking history of 31 pack-years and reported infrequent alcohol consumption. He worked as a bus driver and had been experiencing fatigue prior to this visit. The patient denied any recent travel history or engagement in unsafe sexual activities or drug abuse. Furthermore, he had no history of prescription medication use or underlying medical conditions.

Physical examination

During the physical examination, dull percussions were noted bilaterally in the upper back, along with the presence of rhonchi in the same region. Despite these findings, the patient did not exhibit any signs of respiratory distress. His vital signs were within normal limits, with a temperature of 36.5 °C, blood pressure of 144/87 mmHg, heart rate of 102 beats per minute, and respiratory rate of 18 breaths per minute. The patient did not display any pain or discomfort upon percussion of the bilateral kidney areas. No discharge was observed around the urethra, and there were no suspicious lumps, rashes, or wounds in the perineal or other areas of the body.

Laboratory examinations

The patient's hemogram revealed leukocytosis with neutrophil predominance. The blood electrolytes, glucose levels, and hepatic function were all within normal ranges. His serum urea nitrogen and creatinine levels were elevated. The urinal analysis found microscopic hematuria and pyuria. Detailed laboratory test results are presented in [Table 1](#).

Imaging examinations

Chest radiography revealed patchy consolidation with fibrosis in both upper lungs ([Figure 1](#)).

MULTIDISCIPLINARY EXPERT CONSULTATION

The patient was admitted to our ward for further management of the bilateral upper lung lesions observed on chest radiography.

Initially, the patient was prescribed intravenous ceftriaxone 2 g per day after blood and sputum cultures had been obtained. On day 3 of admission, the empiric antibiotics were escalated to intravenous piperacillin/tazobactam 2.25 g every 6 h for broad-spectrum coverage as the patient was experiencing persistent fever and worsening conditions. Additionally, testing for lung lesions was performed. Chest computed tomography (CT) scans revealed fibrotic lesions surrounded by parenchymal fibrosis, calcified granuloma, calcification atelectasis, and bronchiectasis over the bilateral upper and right lower lobes. Severe hydronephrosis of the right kidney was further observed. Sequential CT scans of the abdomen revealed an upper-third ureteral stone complicated by severe hydronephrosis of the right kidney. Moreover, renal stones and cysts were observed in the left kidney with hemorrhagic changes ([Figure 2](#)).

Owing to the lack of an initial adequate microbiological clue, repeated sputum cultures and rapid serology tests, including pneumococcus urine antigen and Cryptococcus antigen serum test, were performed. However, they all demonstrated negative results. Four acid-fast stain sputum smear sets and the final tuberculosis culture results were also all negative. Sputum fungus culture yielded negative results as well.

A urologist was consulted for renal function deterioration and persistent turbid urine passage by the patient. On admission day 5, a decompressive percutaneous nephrostomy (PCN) was performed on the right kidney to correct the worsening infection and collect adequate microbiological evidence. Urine culture and cytology samples from the right kidney were collected, and acid-fast staining of the urine demonstrated positive results.

A polymerase chain reaction assay of the urine confirmed a urinary tuberculosis infection on admission day 12. The patient was initiated on empirical anti-tuberculosis regimen (isoniazid, rifampin, pyrazinamide, and ethambutol).

Ureteroscopy was performed to resolve obstructive nephropathy on admission day 15. However, during the procedure, a cauliflower-like lesion was incidentally observed over the right posterior and right lateral wall junction of the urinary bladder. A left middle-third ureter tumor was also incidentally diagnosed during the same procedure ([Figure 3](#)). After discussion with the family, a biopsy of the left ureteral tumor with double-J catheterization was performed.

Histological examination of the specimen obtained from the left middle third ureter revealed high-grade papillary pattern urothelial carcinoma with lamina propria invasion (cT1). Immunohistochemical staining was positive for CK7, CK20, and Ki67. Urothelial carcinoma of the urinary bladder was identified based on pathological evidence after transurethral resection of the bladder tumor.

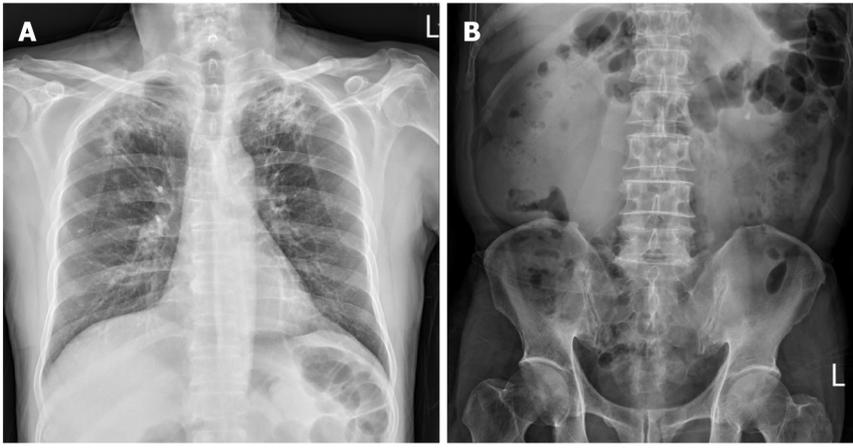
Table 1 Laboratory test results

Variable	Reference range	Illness day 10, on presentation	Illness day 30, on discharge
Hemoglobin (g/dL)	12–15.5	14.9	12.4
Hematocrit (%)	34.9–44.5	43.3	37.2
White-cell count (per mm ³)	4000–11000	12710	14960
Differential count (%)			
Neutrophils	40–70	83.0	86.1
Lymphocytes	22–44	7.9	6.8
Monocytes	4–11	8.4	5.8
Basophils	0–3	0.4	0.5
Eosinophils	0–8	0.3	0.8
Platelet count (×10 ³ per mm ³)	135–400	253	304
Red-cell count (×10 ⁶ per mm ³)	3.90–5.03	4.71	4.12
Mean corpuscular volume (fL)	80.0–100.0	91.9	90.3
C-reactive protein (mg/dL)	< 1	16.11	7.69
Sodium (mmol/L)	136–145	132	135
Potassium (mmol/L)	3.5–5.2	3.9	4.0
Urea nitrogen (mg/dL)	8–25	20	20
Creatinine (mg/dL)	0.60–1.50	2.1	1.4
Estimated glomerular filtration rate (ml/min/1.73 m ²)	> 60	33.4	53.3
Glucose (mg/dL)	70–110		
Aspartate aminotransferase (U/L)	≤ 33	26	15
Alanine aminotransferase (U/L)	10–49	24	32
Total bilirubin (mg/dL)	0.3–1.2	0.79	0.68
Glycated Hemoglobin (%)	< 5.8	5.7	
Specimen			
Anti-human immunodeficiency virus test	Negative	Negative	
Aspergillus antigen (serum)	Negative	Negative	
Cryptococcus antigen (serum)	Negative	Negative	
Pneumococcus antigen (urine)	Negative	Negative	
Blood culture	Negative	Negative	
Sputum culture	Negative	Negative	
Sputum acid fasting smear	Negative	Negative	
Urine acid fasting smear	Negative	Positive	Negative
Urine polymerase chain reaction assay	Negative	Positive; <i>Mycobacterium tuberculosis</i>	

An integrated tumor study was conducted for comprehensive disease staging. Through a dynamic renal function scan, it was discovered that the renal function of the left kidney was intact. Meanwhile, the right kidney was non-functioning.

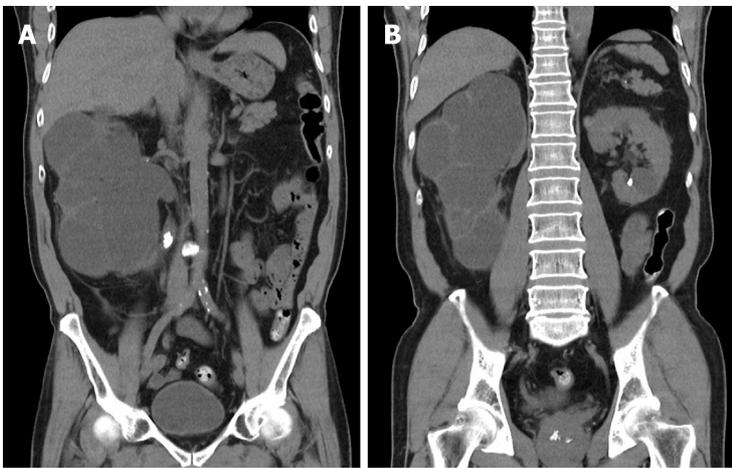
FINAL DIAGNOSIS

Based on clinical manifestations, laboratory examinations, imaging examination, and pathological biopsy, the patient was finally diagnosed with coexisting urinary tuberculosis and urothelial carcinoma.



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Figure 1 Chest and abdominal radiograph. A: Chest radiograph reveals the presence of a bilateral upper-lobe cavitory lesion with fibrosis; B: Abdominal radiograph reveals a renal stone in the left kidney.



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Figure 2 Computed tomography scans. A: Computed tomography (CT) scans of the abdomen demonstrate severe hydronephrosis of the right kidney with a paper-thin cortex. Upper-third ureteral stone is noted; B: CT scans of the same area revealed a left renal stone with a cyst.

TREATMENT

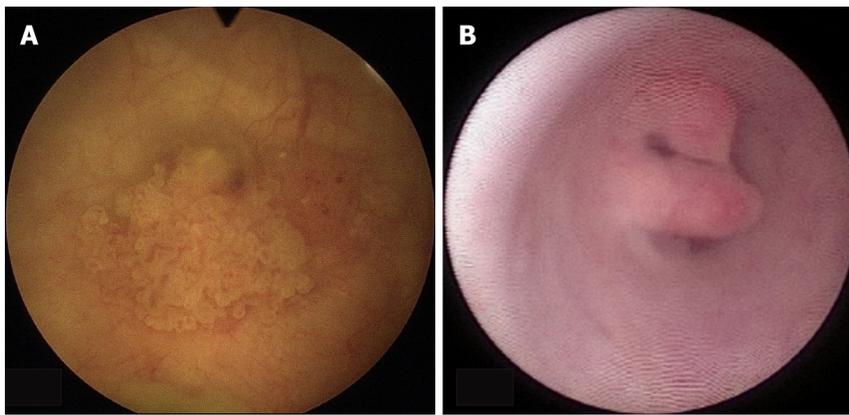
After discussion, the surgeon decided to perform laparoscopic nephroureterectomy, with bladder cuff excision for the right kidney and ureter, and to preserve the left kidney and ureter with holmium laser ablation of the ureteral lesion on admission day 25. There were no surgery-related complications. The patient was discharged on admission day 30.

OUTCOME AND FOLLOW-UP

The initial anti-tuberculosis regimen consisted of four drugs (isoniazid, rifampin, pyrazinamide, and ethambutol) for 2 mo, followed by isoniazid and rifampin for 4 mo owing to susceptibility to the first-line therapy. One month after antibiotic treatment commencement, the patient's urine culture demonstrated no growth of the tuberculosis species. Although the patient's renal function did not fully recover, it also did not deteriorate to the extent of requiring dialysis. The patient continued regular follow-ups at our clinic.

DISCUSSION

In Taiwan, the incidence of genitourinary tuberculosis is approximately 0.19 cases per 100000 indi-



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Figure 3 Photograph from ureteroscopy. A: Photograph from ureteroscopy; cauliflower-like lesions over right posterior and right lateral wall junction of the bladder are observed; B: Photograph of the patient's left ureter via ureteroscopy; an intraluminal bulging tumor located at the middle third of the ureteral cavity (approximately 0.8 cm) is observed. Histological examination of the lesion confirms the diagnosis of urothelial carcinoma.

viduals per year, which has been demonstrating a downward trend since 2000[2]. Moreover, Taiwan has a high incidence of upper tract urothelial carcinoma, with 3.14–3.41 cases being diagnosed in approximately 100000 people each year[3]. It is very rare for both of these disorders to coexist in the same patient.

The simultaneous occurrence of both diseases in the same patient may be explained by the fact that tuberculosis may cause a long-term local inflammatory response, which may in turn induce cellular carcinogenesis. This could be further explained by the relationship between pulmonary tuberculosis and lung cancer[4], and ulcerative lesions of intestinal tuberculosis acting as a precursor to intestinal mucosal cancer[5]. Mycobacterium tuberculosis may also promote the development of cancer by inducing a chronic inflammatory state and compromising T cell-mediated immunity[6]. However, tumor cells may also weaken the host's ability to resist the invasion of microorganisms such as mycobacteria by destroying the local infection barrier[7]. These tumor cells can also affect pathogen resistance through systemic immunosuppression[8,9].

Chen *et al*[6] have conducted a retrospective study of 45455 cancer patients and reported that tuberculosis is an independent risk factor for the development of all cancers. Hence, tuberculosis could increase the risk of specific cancers in patients[6]. A retrospective study by Lien *et al*[10] in Taiwan that analyzed national data also reported that urinary tract tuberculosis was associated with the development of urothelial carcinoma[10].

However, cancer has been recognized as a risk factor for active Mycobacterium tuberculosis infection since the 1970s. All types of cancers increase the risk of developing active tuberculosis disease, albeit to varying degrees. This could be due to intrinsic immunosuppression caused by the cancer itself, immunosuppressive effects of chemotherapy, or factors related to the patients themselves. Tuberculosis shares several disease risk factors with cancer, such as smoking[11], alcohol consumption, chronic diseases such as diabetes[3], malnutrition, and low socioeconomic status[12]. A previous study conducted in Taiwan on a large population reported that cancer was an independent risk factor for tuberculosis, with the highest risk observed 1 year before and 1 year after cancer diagnosis[13].

Although the temporal association between cancer and tuberculosis and a potential causal relationship between the two have not been established in the literature, as this may be challenging in clinical practice, clinicians should nonetheless be aware of this relationship[6,9,13].

The diagnosis and identification of a suitable treatment strategy in the present case were challenging, primarily because the patient had persistent pyuria and fever, and microbiological pathogenic evidence was lacking. To improve his condition and obtain relevant samples, we arranged decompressive PCN of the right kidney. Although the urine collected *via* PCN confirmed the tuberculosis infection, this patient already exhibited signs suggestive of urinary tuberculosis, including chest radiography resembling old pulmonary tuberculosis and persistent pyuria despite antibiotic treatment with sterile routine microbial cultures[14]. After several consecutive sets of negative urine cultures, clinicians should perhaps consider urinary tuberculosis as a differential diagnosis.

Surgery is the treatment of choice for early localized urothelial carcinoma. The mainstay of treatment for genitourinary tuberculosis is anti-tuberculosis drugs[15]. Indications for nephrectomy in case of genitourinary tuberculosis combination urothelial carcinoma include a nonfunctioning kidney, extensive disease involving the entire kidney along with hypertension and ureteropelvic junction obstruction, and renal carcinoma[16]. Considering that this patient only had unilateral residual renal function and was worried about the coexistence of potential tumors in the right kidney, he eventually chose the surgical option to remove the non-functional right kidney and is undergoing regular follow-ups to closely monitor the left urinary system that still has renal function.

CONCLUSION

The association between tuberculosis and cancer could be multifaceted. Although the causal relationship between the two has not yet been established, clinicians should be aware of the link between cancer and tuberculosis.

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FOOTNOTES

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Country/Territory of origin: Taiwan

ORCID number: Yu-Chi Tsai [0000-0001-8196-7800](https://orcid.org/0000-0001-8196-7800); Chien-Yao Wang [0000-0002-7583-2173](https://orcid.org/0000-0002-7583-2173).

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