



Oncology

Upper tract urothelial carcinoma accompanied by hyperthermia: A case report

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ABSTRACT

Upper tract urothelial carcinoma (UTUC) is a relatively rare malignant neoplasm of the urinary system. Due to its highly aggressiveness, the tumor has already undergone invasive growth when most UTUC patients are diagnosed. In addition, the most common cause of fever in cancer patients is infection, and cancer patients with neoplastic fever are relatively rare. We reported a 58-year-old man with invasive high-grade UTUC accompanied by hyperthermia.

1. Introduction

Upper tract urothelial carcinoma (UTUC) is a relatively rare malignant neoplasm, accounting for approximately 5%–10% of uroepithelial carcinomas.¹ Due to the lack of typical clinical symptoms and specific diagnostic methods in the early stages, approximately 60% of UTUCs have already undergone invasive growth by the time of diagnosis. The diagnosis and treatment of invasive high-grade UTUC, which is highly malignant, more invasive and has a poorer prognosis, has been being a hot topic of discussion in clinical practice.

Fever is one of the common clinical symptoms in cancer patients. Meanwhile, infection, tumor itself and radiotherapy all can cause fever in cancer patients. Among them, infection is the most common cause of fever in cancer patients, and about 27% of cancer patients have neoplastic fever.² However, neoplastic fever is not easily differentiated from infectious fever, making it easy to be misdiagnosed.

2. Case presentation

A 58-year-old man with no known medical history was evaluated in our hospital because of a 1-year history of intermittent hematuria and a half-year history of left waist and back pain on March 22, 2022. After admission to our hospital, physical examinations showed that there was percussion pain in the left renal region. The urine exfoliative cytology revealed: more migrating epithelial cells and neutrophils were seen and

no cancer cells were detected. Auxiliary examinations revealed the followings (Fig. 1). Computed tomography (CT) revealed that the left renal pelvis and the upper pole of the kidney were occupied and a node in the left adrenal gland was present (Fig. 2). Magnetic resonance imaging (MRI) findings were as follows. The left kidney was obviously enlarged in size, and there was a large mass at the middle and upper part of the left kidney (with limited diffusion), accompanied by multiple lymph nodes next to the abdominal aorta. The left adrenal gland had an orbicular abnormal signal, seemed to be enhanced in the shape of a ring, which was considered to be metastatic tumor. Cystoscopy showed no abnormality.

The patient developed fever on the 6th day after admission, with a maximum temperature of 39.0 °C on that day. Subsequently, the patient had recurrent intermittent fever for more than 10 days, mostly accompanied by chills. The maximum temperature is 40.0 °C, peaked 1–2 times per day, which often occurs in the late afternoon or at night. But blood and urine cultures did not reveal pathogenic bacteria. The patient was treated with cefozoxime and piperacillin tazobactam as anti-infective treatment, and there was no significant relief in the fever symptom.

After exclusion of contraindications to surgery, the patient underwent bladder infusion of 1 g of gemcitabine with preservation and subsequent robotic-assisted laparoscopic left nephroureterectomy under general anesthesia on April 4, 2022. The left kidney, left adrenal gland and left ureter were completely resected during the operation. The patient's temperature gradually returned to normal within one day after

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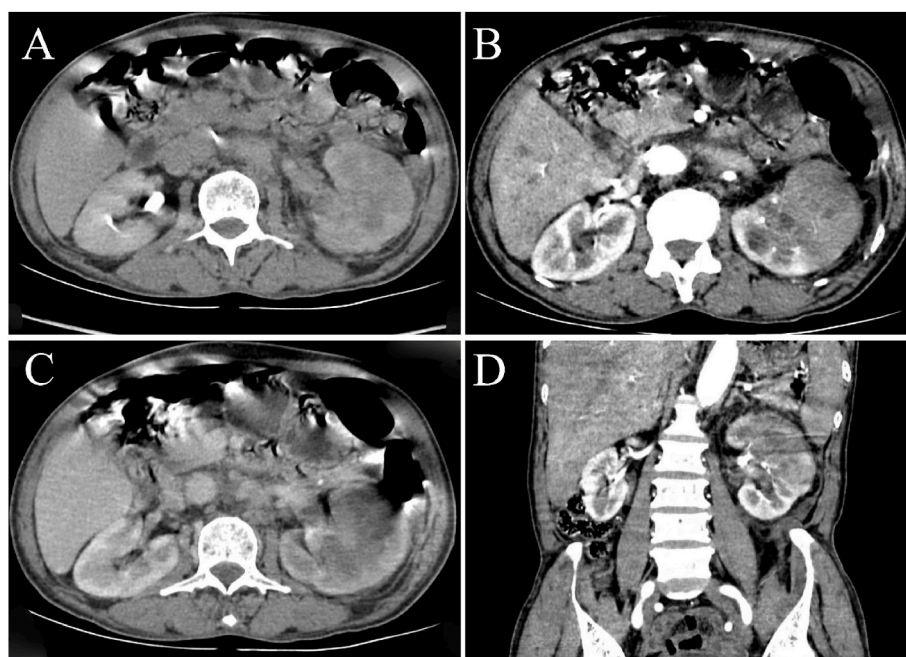


Fig. 1. The left renal pelvis and the upper pole of the kidney were occupied, which were mostly considered that the renal pelvis cancer invaded the renal parenchyma, with peri-abdominal aortic lymph nodules. A node in the left adrenal gland was present, and it should be identified whether it was an adenoma or a metastasis tumor, while the latter was more likely to be the case. (A) Arterial phase (B) Venous phase (C) Delay phase (D) Three dimensional reconstruction of arterial phase.

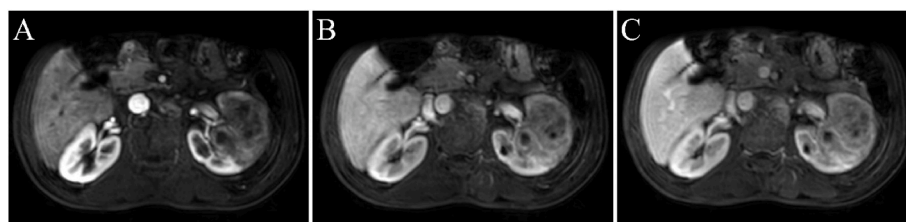


Fig. 2. The left kidney was obviously enlarged in size, and there was a large mass at the middle and upper part of the left kidney (with limited diffusion), accompanied by multiple lymph nodes next to the abdominal aorta. It was considered to be a renal malignant tumor invading the left renal pelvis, resulting in left renal dilation with hydronephrosis. The left adrenal gland had an orbicular abnormal signal, seemed to be enhanced in the shape of a ring, which was considered to be metastatic tumor. There were small cysts in both kidneys. (A) Cortical phase (B) Medullary phase (C) Excretory phase.

the operation, and he did not develop fever again until he was discharged from the hospital.

Postoperative pathological examination were as follows (Fig. 3). The gross specimen showed that the kidney was 13 x 8 x 5 cm in size, the ureter was 16 cm in length and 0.5 cm in diameter, and a grayish-white mass measuring approximately 8 x 6 x 6 cm was seen on the section of kidney, with unclear borders, grayish-white, medium-textured surface and a small amount of perirenal adipose tissue (Fig. 4). And under the microscope, it showed that kidney was invasive high-grade uroepithelial carcinoma.

The patient received 4 cycles of gemcitabine plus cisplatin (GC) chemotherapy after surgery. However, the patient's condition gradually worsened during the 4th cycle of chemotherapy. Based on previous gene sequencing of tumor tissue sections which showed TERT and HRAS mutations in the patient, we suggested that the patient be treated with immunotherapy, but the patient and his family refused further treatment and asked to be discharged from the hospital. The patient died 5 months after surgery.

3. Discussion

UTUC includes renal pelvic cancer and ureteral cancer. Renal pelvic cancer originates from the epithelium of the renal pelvis or renal calyx

and has a low incidence, accounting for about 10%–15% of all renal tumors. 90% of renal pelvic cancers are migratory cell carcinomas, the clinical manifestations of which include macroscopic or microscopic hematuria, dull pain in the lower back or acute renal colic caused by obstruction.³ In this case, the patient had painless, intermittent gross hematuria as the first symptom, and the renal pelvis cancer had already invading the renal parenchyma and surrounding tissues at the time of diagnosis.

The most common cause of fever in cancer patients is infection, and cancer patients with neoplastic fever are relatively rare. The level of neoplastic fever is usually between 37.5 °C and 38 °C, which belongs to the range of low fever. However, the patient in this case had a temperature of 40 °C, belonging to the range of hyperthermia. Therefore, we initially suspected that his fever was caused by infection. But laboratory tests and imaging examinations revealed that he lacked evidence of specific infection, and his fever was not relieved significantly after antibiotic treatment. After excluding the possibility of infection, his fever was considered to be neoplastic fever. No infection was found on the his postoperative specimen, and his postoperative temperature returned to normal level and remained in the normal range. Thus, the diagnosis of neoplastic fever was further supported.

Based on the current study,⁴ surgical treatment with adjuvant chemotherapy or immunotherapy is a more therapeutic option for

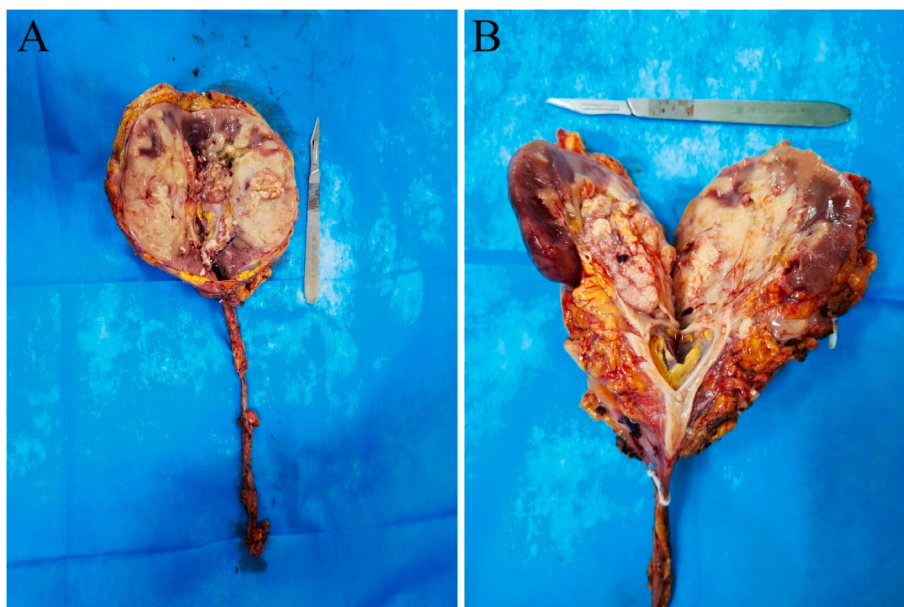


Fig. 3. The gross specimen showed that the kidney was 13 x 8 x 5 cm in size, the ureter was 16 cm in length and 0.5 cm in diameter, and a grayish-white mass measuring approximately 8 x 6 x 6 cm was seen on the section of kidney, with unclear borders, grayish-white, medium-textured surface and a small amount of perirenal adipose tissue.

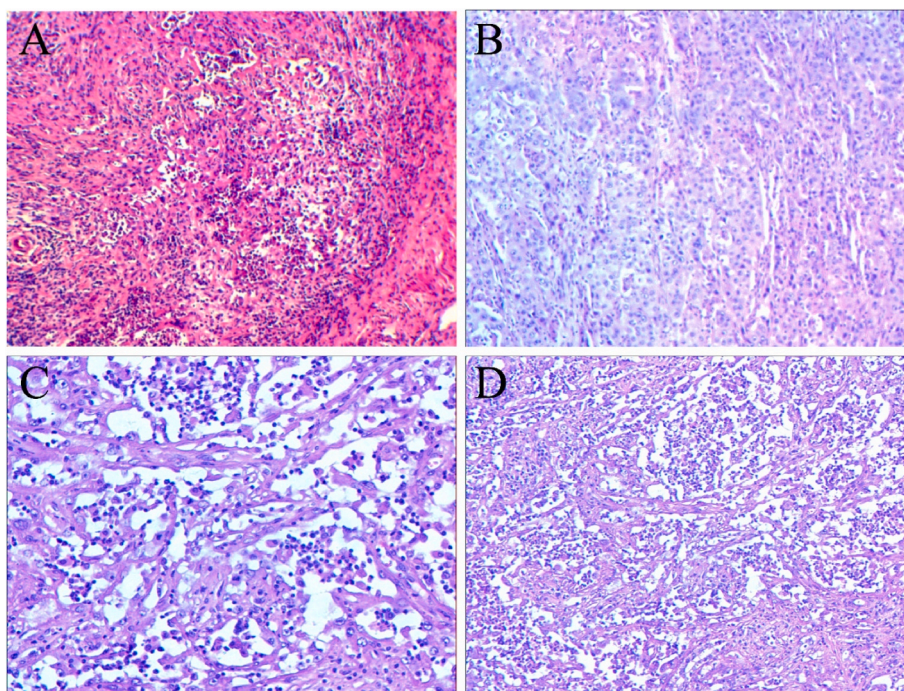


Fig. 4. Under the microscope, it showed that kidney was invasive high-grade uroepithelial carcinoma, which had invaded the renal parenchyma and invaded the renal pelvis, renal sinus fat tissue and renal hilum, and the ureteral margins were not invaded. Adrenal glands were invaded by the carcinoma.

invasive UTUC. But surgery combined with chemotherapy was ineffective for this patient, so therapeutic strategies can be developed from immunotherapy and targeted therapy perspectives. The genetic sequencing of the tumor tissue sections were performed, the results of which showed mutations in the telomerase reverse transcriptase (TERT) and Harvey rat sarcoma viral oncogene homolog (HRAS): TERT c.-124C > T and HRAS p.G13R.

Studies have shown that TERT c.-124C > T is closely associated with the development of uroepithelial carcinoma.⁵ In addition, the distribution of the HRAS is not homogeneous in the whole urogenital pathway,

and is much more abundant at the origin of the renal pelvis and the ureters.⁶

The results of this genetic sequencing provide new ideas for exploring the pathogenesis, early diagnosis, clinical treatment and prognosis of UTUC. Whether the mutations of genes TERT and HRAS have a guiding role in the treatment of UTUC in this patient, who was not treated with immunologic and targeted therapies, remains to be studied in follow-up.

4. Conclusion

Upper tract urothelial carcinoma accompanied by hyperthermia is rare, and the diagnosis and resolution of fever can only be made through surgery when pre- and post-surgical labs show no signs of infection.

CRediT authorship contribution statement

Yijun Cheng: Writing – original draft. **Cong Ma:** Writing – review & editing. **Zonglin Li:** Writing – review & editing. **Jiawei Wu:** Writing – review & editing. **Gongjin Wu:** Writing – review & editing. **Nan Xiao:** Writing – review & editing.

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