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Renal pelvis sarcomatoid carcinoma with renal vein tumor thrombus: A case report and literature review

Renal pelvis sarcomatoid carcinoma

Abstract

BACKGROUND

Renal pelvis sarcomatoid carcinoma (RPSC) is a rare and aggressive malignancy whose diagnosis is difficult because radiological imaging results can lead to misclassification as a more common type of renal tumor. In addition, clinical management of patients with RPSC is difficult because of the limited efficacy of available treatments. In this study, we present a comprehensive description of a patient who presented with RPSC and a simultaneous renal vein tumor thrombus.

CASE SUMMARY

During April, 2020, a 64-year-old female presented with an isolated episode of hematuria accompanied by abdominal pain. Computed tomography (CT) and magnetic resonance imaging (MRI) showed a lesion in the right renal pelvis. We therefore performed a radical nephrectomy of the right kidney. The subsequent histopathological and immunological results verified the diagnosis of RPSC. Despite administration of 6 cycles of a gemcitabine-cisplatin regimen, the patient's condition progressively deteriorated, and she died about 15 mo after the nephrectomy.

CONCLUSION

We performed a comprehensive analysis of a patient with RPSC that included CT, MRI, immunohistochemistry, and genetic testing. The insights from our detailed analysis of this patient and our concomitant review of the literature may assist clinicians in their diagnosis and treatment of RPSC.

Key Words: Sarcomatoid carcinoma; Renal pelvis; Gene analysis; Literature review; Case report.

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Core Tip: Renal pelvis sarcomatoid carcinoma is an extremely rare tumor that is associated with a high mortality rate. We present a rare case of right renal pelvis sarcomatoid carcinoma with renal vein tumor thrombus, in which diagnosis was based on evidence from radiology, pathology, and analysis of tumor mutations. The specific genetic mutations in this patient's tumor may provide insights into the invasive phenotype and pathogenesis of this cancer.

INTRODUCTION

Renal pelvis sarcomatoid carcinoma (RPSC) is a rare type of urinary tract malignancy[1]. This cancer has a low incidence, and it accounts for only about 0.3% of all urothelial carcinomas[2]. Since the initial description of this tumor by Fauci and colleagues in 1961, there have been fewer than 30 reported cases[3]. There are similar predisposing factors for RPSC and squamous cell carcinoma, including tobacco consumption, persistent irritation, chronic inflammation, and nephrolithiasis[4]. Surgery is the most efficacious and widely adopted treatment for patients with RPSC[5], and the major approaches are nephroureterectomy or nephrectomy. An accurate diagnosis of

RPSC requires a comprehensive clinical assessment with histological and immunohistochemical analyses of the tumor[6].

Herein we present a patient with RPSC and describe the results from imaging, histochemistry, and genetics. We also provide a comprehensive review of the literature on this topic to consolidate all previous clinical findings on this cancer.

CASE PRESENTATION

Chief complaints

A 64-year-old female (weight: 60 kg, height: 165 cm) who presented in April, 2020 was assessed for a recent isolated episode of hematuria that was accompanied by abdominal pain.

History of present illness

During the past five months, the patient reported a decrease in body weight of about 5 kg.

History of past illness

The patient had a medical history of renal stones in both kidneys. Additionally, she received pharmaceutical management for hypertension for many years, and intermittently utilized nifedipine.

Personal and family history

The patient had no specific personal or family history of illnesses.

Physical examination

Upon admission, the patient's body temperature was 36.5°C, heart rate was 75 beats per min, respiratory rate was 19 breaths per min, blood pressure was 145/90 mmHg, and oxygen saturation (while breathing ambient air) was 99%. She also had mild tenderness in the right lumbar and abdominal regions.

Laboratory examinations

A urinalysis indicated the red blood cell count was 581.5/μL and the round epithelial cell count was 2.4/μL. An exfoliative cytology test indicated no atypical epithelial cells.

Imaging examinations

A conventional abdominal computed tomography (CT) scan (**Figure 2**) demonstrated irregular enlargement of the right kidney, indicative of a space-occupying lesion. A subsequent enhanced magnetic resonance imaging (MRI) result using the gadolinium-based contrast agent (**Figure 3**) revealed a distinctive clumpy abnormal signal in the right renal pelvis, with dimensions of 7.9 × 6.4 × 7.4 cm (**Figure 4**). The tumor had uniformly low signal intensity in the T1-weighted phase, and slightly elevated mixed signal intensity in the T2-weighted phase. We also identified multiple enlarged lymph nodes in the retroperitoneal region, raising a concern of metastasis. After nephrectomy, immunohistochemical analysis of tumor samples indicated positive staining for Ki-67 (70%), CKpan, 34β12, p63, GATA3, and vimentin, but negative staining for CK7 and PAX8 (**Figure 5**). There was also evidence from the MRI of cancerous infiltration in the renal sinus, renal parenchyma, and vasculature, and a cancerous thrombus in the right renal vein.

A genetic analysis of the tumor tissue showed mutations in the *ELF*, *LTK*, *NOTCH2*, *REL*, and *ZFHX3* genes (**Table 1**). However, there were no mutations in genes that have known relationships with hereditary tumors. Furthermore, the gene analysis yielded no specific drug targets that could be used for pharmacological intervention.

FINAL DIAGNOSIS

A postoperative pathological assessment confirmed that the tumor was RPSC, and had dimensions of 9.0 × 8.0 × 5.5 cm. Based on standard staging criteria, we classified the tumor as T3N1Mx.

TREATMENT

Following thorough preoperative evaluation, the patient underwent right renal nephrectomy. Two months later, the patient opted for conventional systemic chemotherapy. This treatment commenced in July, 2020, and consisted of 6 cycles (21 days per cycle) of gemcitabine-cisplatin (GC).

OUTCOME AND FOLLOW-UP

The patient experienced a favorable postoperative recovery and was discharged after 6 days. However, the subsequent GC chemotherapy was ineffective and the patient died about 15 mo after the surgery.

DISCUSSION

Upper-tract urothelial cancer (UTUC) is the most prevalent malignancy affecting the renal pelvis, but only accounts for 5 to 10% of all urothelial cancers. Squamous cell carcinoma and adenocarcinoma are the second and third most common types of renal pelvis malignancies[8]. RPSC is a very rare and aggressive type of urothelial carcinoma, and there have only been descriptions of fewer than 30 cases (**Table 2**). A retrospective analysis of these previous cases indicated the onset of RPSC typically occurs in patients more than 50-years-old, and the sex ratio is about 4 or 5 males to 12 females[2](**Table 2**). The apparent risk factors for RPSC are tobacco smoking, previous genital tract irradiation, inflammation, and nephrolithiasis[9]. Our 64-year-old female patient had no history of smoking or genital tract irradiation, but she did have a history of nephrolithiasis. Renal stones can possibly lead to provocation of squamous cell carcinoma in the renal pelvis[10], so we hypothesize that renal stones could have contributed to the progression of RPSC in our patient. The origin of RPSC remains controversial. The monoclonal theory posits that carcinomatous and sarcomatous tumor cells arise from pluripotent stem cells, whereas the multiclonal theory proposes that sarcomatoid carcinoma is a 'collision tumor' that results from derivatives of distinct epithelial and mesenchymal stem cells[11].

The clinical manifestations of RPSC are variable. Previous studies reported that hematuria was the most frequently reported symptom. Localized or non-specific pain was the second most prevalent symptom[5], and this can escalate to severe pain. In rare cases, the presence of a renal pelvis abscess could indicate RPSC[6,12]. These patients also frequently experience initial symptoms indicative of an inflammatory infection. In situations where RPSC coincides with a renal abscess, the abscess frequently obscures the symptoms of the tumor, leading to a delayed or missed diagnosis.

Imaging examinations are crucial for the preoperative assessment of tumors in the renal pelvis. CT and MRI scans can be used to determine tumor size, metastasis, and the presence of a tumor thrombus (**Figure 2** and **3**). mild to moderate heterogeneous enhancement when using a contrast agent, distinguishing RPSC from other renal pelvis tumors remains challenging. The immunohistochemistry results therefore play an indispensable role in the diagnosis of RPSC. The sarcomatoid component of RPSC can coexist with other tumor types, including adenocarcinoma, small cell carcinoma, or squamous cell carcinoma. Hematoxylin and eosin (H&E) staining yields similar cellular morphologies for carcinosarcoma and sarcomatoid carcinoma (**Figure 4**), but RPSC has positive staining for Ki-67 (70%), CKpan, 34β12, p63, GATA3, and vimentin, but negative staining for PAX8 and CK7.

We also performed a comprehensive analysis of genetic alterations in the tumor of our patient, and identified mutations in the *ELF*, *LTK*, *NOTCH2*, *REL*, and *ZFHX3* genes (**Table 1**). The *ELF3* gene is a member of the E26 transformation-specific (ETS) family of transcription factors, is located on chromosome 1q32.1, and encodes a protein of 371 amino acids[13]. Previous studies have implicated *ELF3* in various diseases, including cancers of the bladder, ovary, biliary tract, stomach, cervix, breast, prostate, lung, liver, and colon[14]. Studies of mutations in the *ELF3* gene demonstrated this gene functions as a tumor suppressor in certain cancers, although increased *ELF3* expression also occurs in other cancers[15]. *NOTCH2* is a member of the Notch receptor family that is overexpressed in many cancers and is linked with distinctive oncogenic mechanisms[16].

LTK is in the anaplastic lymphoma kinase (*ALK*)/*LTK* subfamily, and increased expression of *LTK* is associated with metastasis in certain cancers[17].

Although our genetic testing confirmed that RPSC has a highly invasive and metastatic phenotype, the lack of effective targeted therapies accounts for the grim prognosis for most patients with this cancer. Only a limited number of these patients achieve survival beyond two years[1]. The unique characteristics of this tumor are likely responsible for the ineffectiveness of conventional chemotherapy and radiotherapy regimens. Surgical excision is the preferred initial method for treating RPSC[6], and subsequent radiotherapy can enhance local control when combined with cisplatin-based chemotherapy[18]. However, cisplatin-based chemotherapy is unfeasible in some patients due to a low estimated glomerular filtration rate (eGFR) and diminished renal function after nephrectomy[19]. Previous research has indicated heightened expression of the epidermal growth factor receptor (EGFR) on the surface of RPSC cells[20], so therapeutic strategies that target EGFR may have some potential. Other research found that RPSC cells had high expression of PDL1, suggesting that immunotherapy may be beneficial[21]. Our patient only survived 15 mo after surgery, despite your use of GC-based chemotherapy. We hope that future studies can identify more effective treatments that can prolong the survival times of these patients.

CONCLUSION

Given the rarity of RPSC, diagnosis is difficult and there are inadequate available treatments. In this study, we presented a new case of RPSC and conducted a comprehensive review of the most recent literature. We also performed immunohistochemical and genetic analyses of our patient. The indicators described herein may be useful in guiding future clinical interventions for treatment of patients with RPSC.

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