Full of twists and turns: Collecting duct carcinoma presenting as persistent cough

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ABSTRACT

We report a case of collecting duct carcinoma (CDC) in a 60-year-old man who presented with persistent cough, low back pain, and weight loss. Contrast-enhanced CT of chest and abdomen revealed a mass in the medulla of the middle and upper parts of the right kidney, with spread into perirenal tissue, vascular invasion, and distant metastasis. First renal biopsy only showed inflammation. Repeat biopsy and histopathological examination and immunohistochemistry confirmed CDC. The patient died 2 months after diagnosis despite interventional therapy, chemotherapy, and targeted therapy. This case is being reported because of its rarity and unusual presentation.

1. Introduction

Collecting duct carcinoma (CDC) is a rare and highly malignant tumor originating from the renal distal tubular epithelial cells. The incidence rate is only 1%. The median age at onset is 55 years, and median survival after diagnosis is only 30 months. It was first reported by Mancilla-Jimenez et al. in 1976; since then there have only been a few individual case reports.

2. Case presentation

A 60-year-old man presented after appendectomy more than 20 years with persistent cough, right low back pain and weight loss (10 kg in 20 days). Laboratory tests showed elevated white blood cell and neutrophil counts, urine white blood cell count of 32/μL. Contrast-enhanced computed tomography (CT) of chest and abdomen showed a 6.6 cm × 6.1 cm hypovascular mass in the medulla of the middle and upper part of the right kidney, infiltrating into the perirenal fat space and fascia (Fig. 1A–C). Tumor thrombus were seen in the right renal vein, inferior vena cava and pulmonary artery (Fig. 1D). There were also multiple lesions in the lungs and liver, along with multiple enlarged lymph nodes in the right reniportal, retroperitoneal and mediastinal regions (Fig. 2A-C). Computed tomography angiography (CTA) showed that the renal mass was supplied by the right renal artery (Fig. 2D).

Hematoxylin–eosin (HE) staining and immunohistochemistry of kidney biopsy specimen suggested a diagnosis of chronic pyelonephritis with interstitial hyperplasia, but the clinical manifestations and imaging findings were highly suggestive of malignant tumor. Repeat biopsy and immunohistochemistry showed the tumor to be positive for CK19, CK7, GATA-3 and PAX-8, negative for vimentin, TTF-1, CD117 and villin. The morphology preservation of the renal pelvis and positive expression of PAX8 precluded the possibility of urothelial carcinoma. The final pathological diagnosis was CDC (Fig. 3).

The patient was treated with perfusion chemotherapy, carrelizumab immunotherapy and sorafenib targeted therapy. One month later, repeat CT showed that the lesions in the right kidney, lungs and liver had enlarged. Ten days later, the patient died of suddenly respiratory failure.

3. Discussion

CDC is believed to originate from the distal part of the collecting duct in the renal medulla. In 1998, WHO classified CDC as a separate type of renal cell carcinoma. The diagnostic criteria were modified in 2016, defining CDC as a renal cell carcinoma occurring in the renal medulla and progressing into the cortex with obvious fibro-interstitial response. CDC is more common in men than in women (male: female ratio, 3:1 to 2:1) and in African-Americans than in Caucasians. In previous reports, the median age at onset is 55 years; our patient was also within this age range.

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range.

CDC usually present with the non-characteristic symptoms of low back pain, hematuria and renal mass. It readily invades perirenal fascia and adipose tissue, and two-thirds of patients die within 2 years of diagnosis. Metastasis is most commonly to lymph nodes (55%), while hematogenous distant dissemination (33%) occurs most commonly to lung and liver, but also to bone.\(^2\,^3\) Our patient had lymph node involvement, hematogenous metastases and intravascular tumor thrombus at the time of diagnosis and died within 2 months of diagnosis.

CDC is almost always located in the medulla of the middle part of the kidney, with infiltration into surrounding renal parenchyma. Cut section shows a yellowish-brown or grayish-white surface. Under the microscope, there is tubular or tubular-papillary growth with infiltration of ductal structures and interstitial desmoplastic reaction. The karyotype classification is usually Fuhrman grade 3 and 4. Sarcomatoid or rhabdoid differentiation is common.\(^2\) There is neutrophil infiltration in the stroma; therefore, if biopsy didn’t obtain tumor tissue, only inflammatory reaction may be diagnosed, like our first renal biopsy.

CDC cells are usually positive for renal epithelial cell markers (PAX2 and PAX8) and vimentin, high molecular weight keratins (CK19, 2, 3

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Fig. 1. Contrast-enhanced CT scan and renal artery CTA
A. Corticomedullary phase shows a right renal pelvis and calyceal mass, unobvious enhancement, and enlarged right reniportal and retroperitoneal lymph nodes. B. Nephrographic phase shows a right renal pelvis and calyceal mass and mild enhancement. C. Excretory phase shows a right renal pelvis and calyceal mass and mild continuous enhancement. D. Pulmonary artery filling defect.

Fig. 2. Contrast-enhanced CT.
A&B. Enlarged lung metastasis at follow-up 1 month after treatment. C. Enlarged liver metastasis at follow-up 1 month after treatment. D. Blood supply to the mass is from the right renal artery.
CK34βE12, and CK7. In our patient, immunohistochemistry was negative for vimentin. Chromosomal aberrations and deletions are common in CDC, 1Q, 6P, 8P, 9P, 21q and Y chromosomes are often deleted. However, the molecular mechanism of CDC is complex, no specific molecular detection index has been identified to date. INI1-deficient carcinoma and FH-deficient RCC are also positive for PAX8 expression, but INI1-deficient carcinoma is rare in people over 40 years; for example, renal medullary carcinoma (RMC) almost affects young African Americans with sickle cell trait or disease, which isn’t consistent with our patient. Although immunohistochemistry of FH and 2SC wasn’t performed, the pathologists failed to find extensive viral inclusion-like macronucleoli with perinucleolar halos, the possibility of FH-deficient RCC was incredibly ruled out.

CT is a useful modality for diagnosis of renal tumors. In patients with CDC, enhanced CT shows poor blood supply with patchy areas of cystic necrosis, marginal residual renal tissue with patchy mild enhancement, and unbroken renal cortex with changes like insect bite. There may be mild to moderate delayed enhancement due to the abundant connective tissue. Because CDC has no capsule, the boundary between enhanced and normal renal parenchyma maybe unclear.

Surgery is the treatment of choice but, because of misdiagnosis or metastases, most patients don’t undergo resection. The histological similarities between CDC and urothelial tumor suggest that CDC may be sensitive to chemotherapy and radiation therapy. Peyromaure et al. used cisplatin plus gemcitabine to treat two patients with metastatic CDC and achieved tumor-free survival for 27 months in one patient and 9 months in the other. Sunitinib and sorafenib have been reported to be effective for treatment of metastatic CDC. A prospective phase II trial evaluating the activity and safety of cabozantinib as first-line treatment for metastatic CDC is currently underway at the Fondazione Istituto Nazion Ale Dei Tumori. A multicenter phase II trial of nivolumab in CDC (and other rare tumors) is also currently underway in France.

4. Conclusion

CDC is a highly malignant tumor characterized by rapid progression, early metastasis and poor prognosis. Currently, no effective treatment has been found. Surgery remains the main treatment for CDC. Targeted therapy may be an effective adjuvant treatment after surgery. Researches on molecular genetics can provide evidence for targeted therapy and is expected to improve the survival of patients.

Consent from patient

Obtained.

Declaration of competing interest

The authors have no competing interests to declare.

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