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Clear cell papillary renal cell carcinoma: A case report and review of the literature

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Abstract

Clear cell papillary renal cell carcinoma (ccpRCC) was recently established as a distinct type of epithelial neoplasm by the International Society of Urological Pathology Vancouver Classification of Renal Neoplasia. Here, we report a case of partial nephrectomy for a ccpRCC detected during the routine follow-up of a previously treated liposarcoma in a 70-year-old male patient. The patient was referred to the urology department for a right-sided renal mass (size: 2 cm) detected during routine annual imaging follow-up for a malignant right inguinal fibrous histiocytoma and liposarcoma that had been diagnosed 6 and 4 years earlier, respectively, and treated with surgery and adjuvant radiation therapy. Following partial nephrectomy, the renal mass was pathologically diagnosed as ccpRCC, and immunohistochemistry revealed carbonic anhydrase 9 (CA9) expression. No recurrences or metastases were detected on follow-up imaging for 6 months. This is the first report of partial nephrectomy for incidentally discovered CA9-positive ccpRCC.

Key words: Clear cell; Papillary; Renal cell carcinoma; Partial nephrectomy; Carbonic anhydrase 9; Case report

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Core tip: Clear cell papillary renal cell carcinoma (ccpRCC) was recently established as a distinct type of epithelial neoplasm. Here, we report a case of partial nephrectomy for a ccpRCC detected during the routine follow-up a previously treated liposarcoma in a 70-year-old male patient. The patient received partial nephrectomy, the renal mass was pathologically diagnosed as ccpRCC, and immunohistochemistry revealed carbonic anhydrase 9 (CA9) expression. No recurrences or metastases were detected on follow-up imaging for 6 mo. This is the first report of partial nephrectomy for incidentally discovered CA9-positive ccpRCC.

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INTRODUCTION

Clear cell papillary renal cell carcinoma (ccpRCC), which is also known as clear cell tubulopapillary renal cell carcinoma, is a rare type of malignant renal tumor that differs markedly from other malignant tumor subtypes in terms of visual, microscopic, and immunohistochemical characteristics^[1-4]. Cytopathologically, ccpRCC comprises epithelial cells with clear cytoplasm in both tubular and papillary arrangements, and thus exhibits characteristics of both clear cell renal cell carcinoma (ccRCC) and papillary renal cell carcinoma (pRCC). These clear tumor cells harbor a linear array of low-grade nuclei distal from the basement membrane and develop a range of tubular, papillary, and cystic structures. By contrast, atypical and mitotic cells, vascular invasion, necrosis, hyaline globules, foamy macrophages, and pleomorphism are rarely observed.

Although Tickoo *et al*^[5] first identified ccpRCC in the context of end-stage kidney disease in 2006, this entity mainly occurs in normal kidneys and is rare in patients with end-stage or cystic kidney disease^[1,2,6]. Recently, the International Society of Urological Pathology (ISUP) Vancouver Classification of Renal Neoplasia^[7,8] recognized ccpRCC as a distinct epithelial tumor that could be distinguished from ccRCC and pRCC by genetic differences in the *von Hippel-Lindau (VHL)* tumor suppressor gene mutation and 3p loss status and the extreme rarity of gains in chromosomes 7 and 17 or the loss of chromosome Y, despite significant morphological, immunohistochemical, and genetic similarities among the three tumors^[9]. Here, we report a case in which partial nephrectomy was used to treat a ccpRCC that was incidentally diagnosed during a recent imaging follow-up in a patient with a history of previously treated liposarcoma and malignant fibrous histiocytoma.

CASE REPORT

A 17-year-old man was referred to department of urology after a routine computed tomography (CT) scan detected a right-sided enhancing mid-pole renal mass measuring 2.3 cm (Figure 1). He was previously treated for a right-sided inguinal lymph nodal malignant fibrous histiocytoma and right-sided pelvic high-grade pleomorphic and spindle cell sarcoma 6 and 3 years earlier, respectively, *via* surgical excision in the orthopedic department and radiation therapy (adjuvant dose of 60 Gy/30 fractions to the pelvis) in the radiology department. He had no other underlying diseases such as hypertension or diabetes. The follow-up of the patient included biannual pelvic magnetic resonance imaging (MRI) and chest CT and annual positron emission tomography (PET)-CT. No signs of recurrence or metastasis were identified until the currently described renal mass (Figure 1).

Following a full metastatic work-up, the patient underwent open right-sided partial nephrectomy. Subsequent pathology revealed a tumor measuring 1.7 cm × 1.4 cm × 1.0 cm with a capsule abutting, leading to a diagnosis of a grade 2 ccpRCC without necrosis and a final pathologic stage of T1aN × M0 (Figure 2). The patient was routinely followed at the urology outpatient clinic without any further adjuvant plan for 9 mo postoperatively.

DISCUSSION

According to the ISUP (ISUP) Vancouver Classification 2012, ccpRCC, which has also been described as clear cell tubulopapillary RCC or renal angio adenomatous tumor (RAT), is a recently recognized type of indolent epithelial tumor of the renal cortex, with a prevalence rate of 1%-4% among all resected asymptomatic renal tumors^[7,10]. These tumors exhibit no age or sex prevalence, and no cases of local or nodal recurrence or distant metastasis have been reported^[11,12]. However, despite the generally asymptomatic nature of ccpRCC, some patients, including the subject of this case, complain of abdominal or flank pain. Although these tumors may occur in patients with end-stage renal disease or von Hippel-Lindau (VHL) syndrome, most

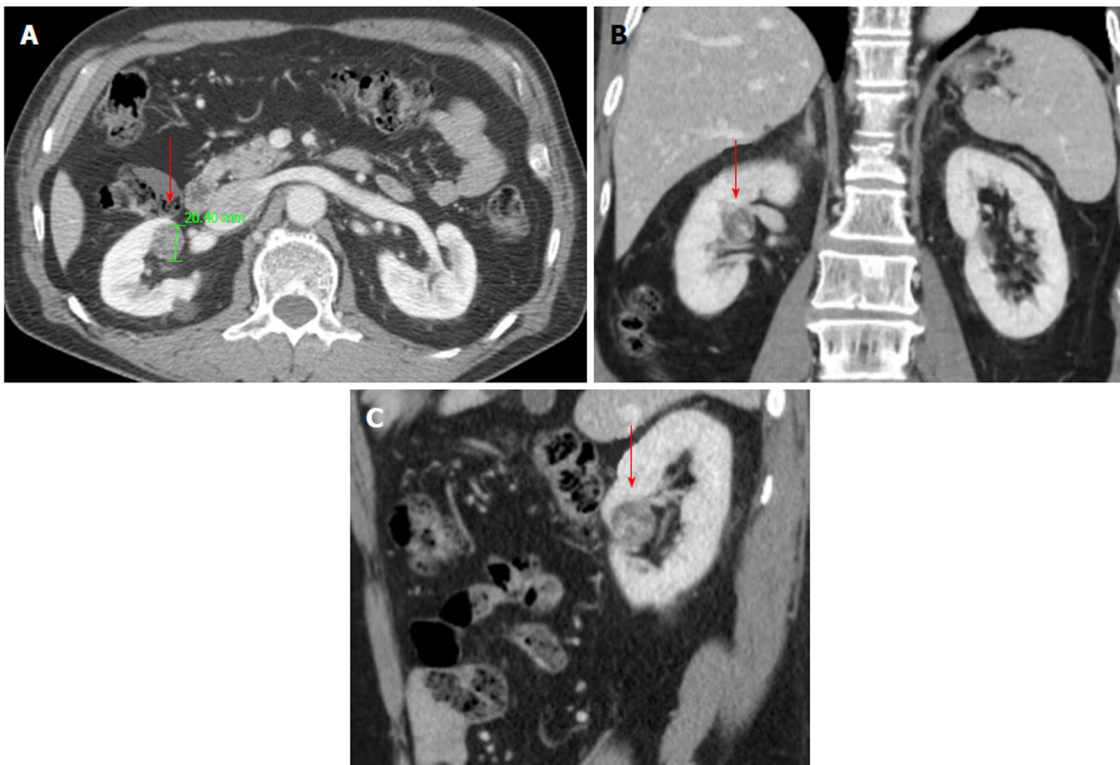


Figure 1 Computed tomography findings of clear cell papillary renal cell carcinoma. A 2-cm mass with an area of irregular enhancement is visible in the right kidney. A: Axial view; B: Coronal view; C: Sagittal view.

affect normal kidneys^[1,2]. The finding that most ccpRCCs are diagnosed as stage 1 (excepting two stage 2 cases)^[2,4,9,11] led to the designation of “low malignant potential” in the recent ISUP classification^[12].

Imaging studies of ccpRCC indicate hypodense areas with cystic changes or cyst formation on CT and areas of isointensity and hypointensity on T1- and T2-weighted MRI, respectively^[13]. ccpRCC frequently appears as a well-defined, well-encapsulated tumor with cystic changes or the formation of cysts^[11,12] filled with serosanguinous fluid or colloid-like regions^[9]. Morphologically, ccpRCC appears to be an intermediate between ccRCC and pRCC, with low nuclear grading, tubular and papillary arrangement of clear epithelial cells, a predominantly linear nuclear alignment distal from the basement membrane, and a distinctive immunohistochemical profile similar to that of RAT. Multifocality and bilaterality are rarely reported^[8,10]. Macroscopically, the cut surface is whitish-tan, with variable surface coloration. Microscopically, most ccpRCCs are small and lack necrosis or invasion of the lymphatic vasculature and renal sinus, but are well-circumscribed and encapsulated with common cystic changes. Proteineous secretions are often observed within the lumina or acini of tubules^[3]. Although foamy macrophages, psammoma bodies, and hemosiderin deposits are rarely observed^[14], fibrous stroma is common^[1] and usually indicates the association of a smooth muscle metaplasia with the tumor capsule^[11]. Some previously diagnosed renal angiomyoadenomatous tumors with a predominantly smooth muscle histology have since been recognized as examples of ccpRCC.

Immunohistochemically, ccpRCC is positive for cytokeratin (CK)-7, CA-9, high-molecular-weight CK, Pax2 and Pax8, and 34 β E12 and negative for CD10 and alpha-methylacyl-CoA racemase^[7,8,10]. Concurrent strong, diffuse CK-7 expression and a cup-shaped CA-9 expression pattern is usually considered an immunohistochemical hallmark of ccpRCC; this pattern corresponds with the shape of the neoplastic cell, which is typically cuboidal to low columnar, with round and generally uniform nuclei and inconspicuous linearly arranged nucleoli distal from the basal membrane.

Genetic analysis can be used to further differentiate ccpRCC from ccRCC and pRCC, and comparative genomic hybridization can differentiate sporadic ccpRCC from cases associated with end-stage renal disease. Although *VHL* mutation is a hallmark of ccRCC, mutations in this gene have been described in 15%-30% of ccpRCC cases. Furthermore, pRCC exhibits a loss of heterogeneity, although this is not accompanied by mutation or promoter methylation. Rather than *VHL* alterations, pRCC is known to harbor trisomies of chromosomes 7 and 17 and losses of Y, whereas ccpRCC does not exhibit these changes^[15]. ccpRCC may occur in normal kidney, non-

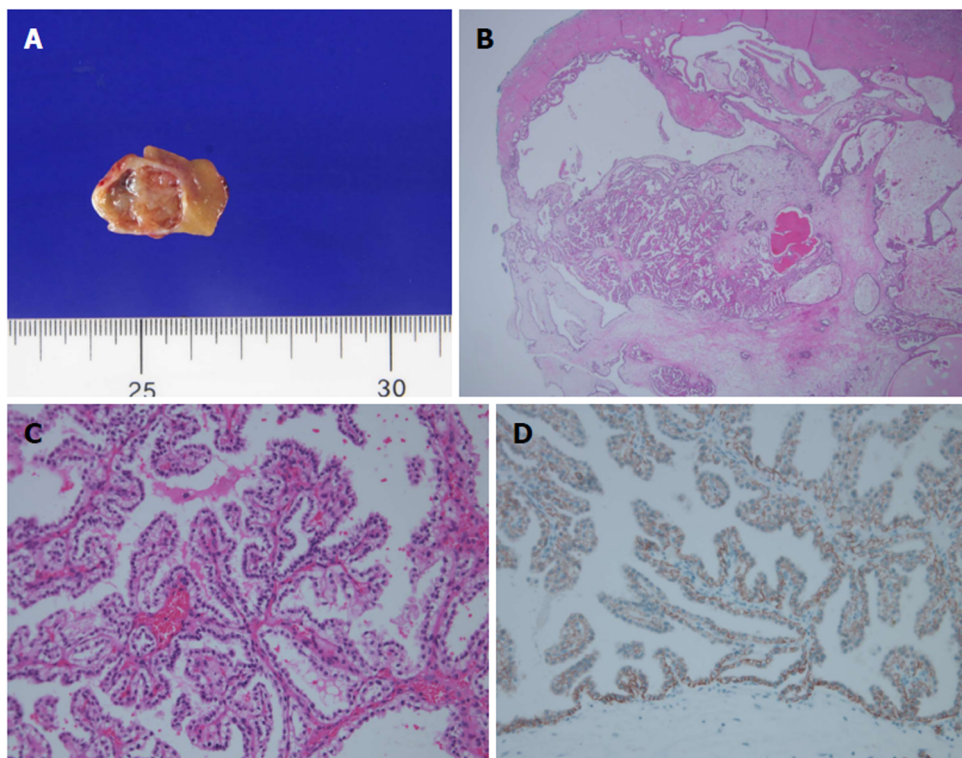


Figure 2 Photomicrographs of clear cell papillary renal cell carcinoma. A: Gross findings; B: H and E: The tumor showed papillary, cystic and tubular patterns in low powered magnification (original magnification $\times 12.5$); C: The tumor is composed of clear cells with uniform nuclei typically showing a linear arrangement away from the basal membrane (original magnification $\times 200$); D: The typical immunohistochemical staining of carbonic anhydrase IX. The staining pattern is a cup-like distribution typical feature of clear cell papillary renal cell carcinoma (original magnification $\times 200$).

cystic end stage renal disease and acquired cystic disease^[3,11,16,17]. Two cases of ccpRCC occurred within 10 years of hemodialysis^[18].

Some cases have been associated with von Hippel-Lindau disease^[19]. The association with other renal cancers such as papillary RCC, clear cell RCC, chromophobe RCC, multilocular cystic RCC, acquired cystic disease-associated RCC and renal oncocytoma have also been reported^[11,16,20].

Total or partial nephrectomy is generally performed when surgical resection is feasible and the tumor is solitary^[1]. Because these tumors are generally indolent, active surveillance with strict follow-up may be possible in selective cases.

In conclusion, this report describes the first case of partial nephrectomy for a ccpRCC that was incidentally diagnosed in an elderly male patient during the imaging follow-up of previously treated tumors. More comprehensive sampling may be warranted to identify the characteristics of ccpRCC with prognostic variables.

ARTICLE HIGHLIGHTS

Case characteristics

The patient was referred to the urology department for a right-sided renal mass (size: 2 cm) detected during routine annual imaging follow-up for a malignant right inguinal fibrous histiocytoma and liposarcoma that had been diagnosed 6 and 4 years earlier, respectively.

Clinical diagnosis

A routine computed tomography (CT) scan detected a right-sided enhancing mid-pole renal mass measuring 2.3.

Differential diagnosis

Immunohistochemistry revealed carbonic anhydrase 9 (CA9) expression could be helpful for differential diagnosis.

Imaging diagnosis

A routine CT scan detected a right-sided enhancing mid-pole renal mass measuring 2.3 cm.

Pathological diagnosis

pathology revealed a tumor measuring 1.7 cm \times 1.4 cm \times 1.0 cm with a capsule abutting, leading

to a diagnosis of a grade 2 ccprCC without necrosis and a final pathologic stage of T1aN × M0.

Treatment

The patient underwent open right-sided partial nephrectomy.

Experiences and lessons

Patients who have previously been treated with tumor need careful follow-up.

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