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ARTICLE

The intersection of histologies: navigating the complexity of a renal collision tumor

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Renal cell carcinoma is a heterogeneous group of renal tumors characterized by several histological subtypes. Herein, we discuss an unusual case of a 55-year-old male who presented as a consultation to our urology clinic with an incidentally found renal mass. After shared decision making patient proceeded with a Robotic Assisted Laparoscopy (RAL) left sided partial nephrectomy. Final pathology confirmed the presence of high nuclear grade mixed clear cell and papillary renal cell carcinoma (RCC) of the left kidney (pT3aN0M0). This case elucidates a very rare incidence of a patient seen to have a collision tumor, and furthermore demonstrates guideline-based treatment.

Key Words: renal cell carcinoma, collision tumor, mixed renal carcinoma, renal cyst, Bosniak III

Introduction

Renal cell carcinoma (RCC) is the most common type of urogenital cancer with a mortality rate of 30%–40%.[1] RCCs are responsible for 80%–85% of all primary renal carcinomas and predominately include clear cell RCC (70%), papillary RCC (10%–15%), and chromophobe RCC (5%).[2,3] Although they have traditionally been divided into these categories, renal neoplasms with overlapping histologies, such as tumors with mixed clear and papillary cell features, are increasingly being seen,[4] however, collision tumors remain rare. Mixed and collision tumors can pose a diagnostic challenge with important therapeutic implications to be aware of in order to provide appropriate management. Here we present a case of a patient found to have two distinct adjacent carcinomas within the same renal mass-clear cell and papillary RCC, consistent with a collision tumor. The occurrence of a high-grade clear cell and papillary RCC collision tumor is a rare and noteworthy clinical entity. To date, only limited cases of such a unique histological combination have been reported in the literature, underscoring the exceptional nature of this presentation.

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Case Presentation

Our patient initially presented as a 55-year-old male with a past medical history of nicotine dependence, hypertension, chronic obstructive pulmonary disease, alcohol dependence, and dysphagia. Family medical history included father with prostate cancer and paternal grandfather with history of leukemia. The renal mass was discovered incidentally during an examination of his distal esophageal stricture using a chest CT scan. Initial CT abdomen pelvis noted the left-sided renal mass to measure 2.8 cm. Patient elected to follow up with repeat CT scan which was then obtained a few months later demonstrating growth of the left renal mass to 3 cm and now with a multiloculated cystic mass in the right kidney measuring 8.7 × 6.6 cm. The patient then failed to establish care with urology but did follow up with his primary care physician two years after his mass was initially found and MRI was obtained. MRI kidney mass with and without contrast again

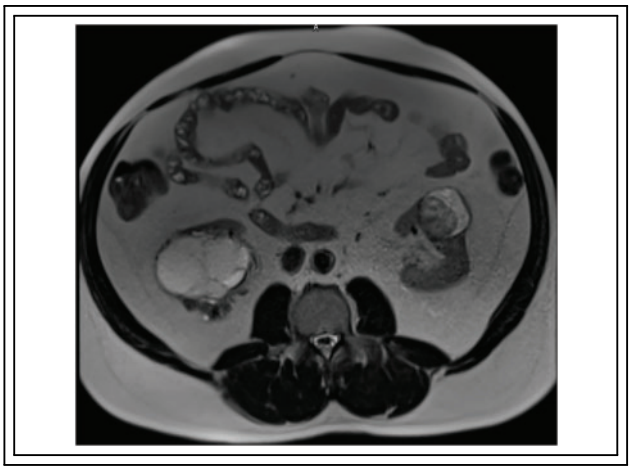

FIGURE 1. MRI demonstrating right large multiloculated cyst measuring 8.5 × 7.2 cm with mild enhancement of the septations (Bosniak III). Heterogeneous mixed cystic and solid mass in the anterior mid left kidney measuring 4.5 cm

noted a heterogenous mixed cystic and solid mass in the anterior aspect of the mid left kidney, however it now measured 4.5 cm. Furthermore, the large multiloculated cystic mass with enhancing septations in the right kidney now measured 8.5 × 7.2 cm in size classifying it as a Bosniak III lesion (Figure 1). He was then referred to the urologic oncology clinic again. On evaluation at our clinic he denied any gross hematuria.

After shared decision making, the patient elected to proceed with robotic assisted laparoscopy left sided partial nephrectomy via a transperitoneal approach. The patient tolerated the procedure well however discharged home on postoperative day five due to postoperative ileus. Final pathology was consistent with stage 3 (pT3aN0M0) clear cell (80%) and papillary (20%) renal cell carcinoma with G4. Microscopically, it was noted that there were two distinct carcinomas adjacent to one another with RCC patchy positive both tumors (Figure 2). As a result of his rare and aggressive tumor pathology his case was presented to the multidisciplinary urologic tumor board. Patient is currently to begin treatment with adjuvant pembrolizumab with surveillance CT chest abdomen pelvis 5 months post-operatively.

Discussion

In all patient encounters the cornerstone of treatment is counseling and this case began as would all new patients presenting with renal masses, a consideration of the mass and anatomy in coordination with patient co-morbidities and preferences after counseling. When considering surgical approaches for RCC, the RENAL nephrotomy score is highly useful. The RENAL nephrotomy score assigns numerical values to renal masses and attributes complexity grades and likelihood percentages of major complications based on the tumor radius, percentage endophytic vs. exophytic, nearness to the collecting system or sinus, anterior vs. posterior location, location relative to the polar lines, and whether the tumor has a hilar location abutting the vein or artery.[5] With our patient's left RCC having a score of 9a (intermediate risk with 11.1% liklihood of major complications), a shared decision was made that partial nephrectomy would be most appropriate to preserve renal function.

Counseling also included a discussion of the contralateral Bosniak III large multiloculated cystic mass measuring at 8.5 cm. The Bosniak scoring system is used to categorize renal cysts based on imaging characteristics and predict the likelihood of malignancy, guiding the need for follow up or treatment. While the lesion's complexity underscored the need for careful monitoring, emerging evidence suggests these lesions can often be managed with active surveillance due to their relatively low metastatic potential. One specific study, with a mean follow-up of 74.5 months, showed that no Bosniak III cysts were formally upgraded to Bosniak IV.[6] The only patient who developed metastasis while on active surveillance experienced progression after 12 years, despite an initial diagnosis of a Bosniak IV cyst.[6] This further emphasizes the favorable natural history of complex renal cysts. This context informed the decision-making process, balancing the treatment of the left RCC with ongoing observation of the contralateral lesion.

Our patient's renal tumor ultimately demonstrated two distinct carcinomas adjacent to one another, consistent with a collision tumor. A collision tumor is defined by the coexistence of two adjacent but histologically distinct malignant tumors in the same organ without histological admixture.[7] While this phenomenon has been described in various organs, kidney collision tumors have been previously described, albeit with rarity.[8] In our case, a collision tumor with two distinct RCC subtypes, clear and papillary, is a rare finding.[9]

Different theories exist regarding the histopathogenesis of renal collision tumors. The cell proliferation theory details that while both clear cell and papillary RCCs originate from the renal parenchyma, they stem from distinct cell types, and

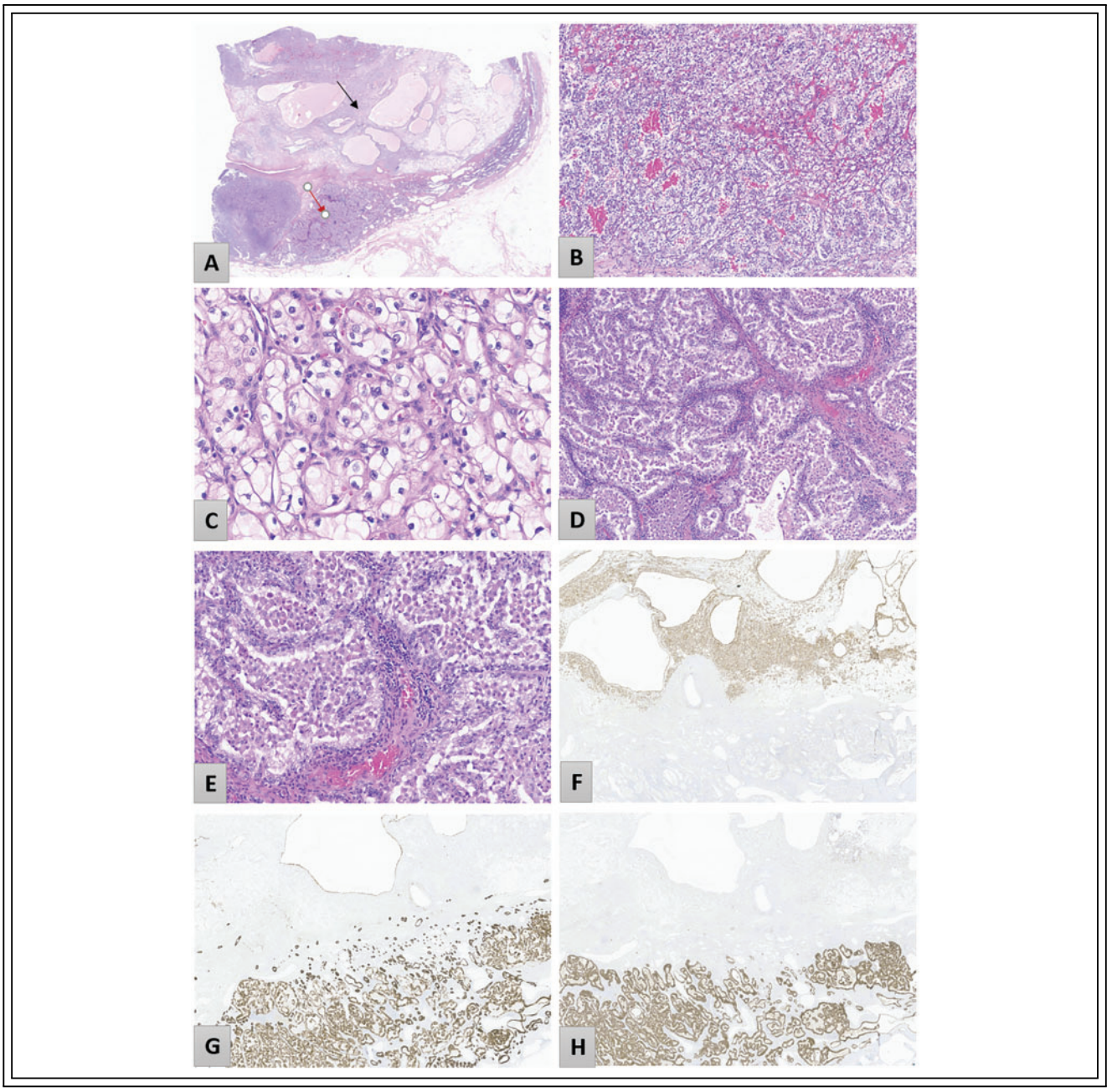

FIGURE 2. The histopathological findings of the nephrectomy specimen showed two adjacent carcinomas, with the black arrow indicating clear cell renal cell carcinoma (CCRCC) and the red arrow indicating papillary renal cell carcinoma (PRCC) (A, hematoxylin and eosin, ×20 magnification). Microscopic findings CCRCC exhibited clear to eosinophilic cells arranged in nests, micro-/macrocysts, or solid sheets, surrounded by intricate, branching fibrovascular septation (B and C, hematoxylin and eosin, ×100 and ×400 magnification). Microscopic findings of PRCC revealed a prominent papillary architecture with abundant foamy macrophages in the central fibrovascular cores (D and E, hematoxylin and eosin, ×100 and ×400 magnification). Immunohistochemical staining for CA 9 in CCRCC demonstrated strong membranous positivity, while PRCC showed negativity (F, ×200 magnification). CK7 and AMACR immunostaining showed diffuse cytoplasmic positivity in PRCC and negativity in CCRCC (G and H, ×200 magnification)

the occurrence of a collision tumor is attributed to the simultaneous presence of these different forms of cell proliferation and differentiation.[10] An alternative theory revolves around the cancer stem cell concept, suggesting that the emergence of collision tumors might be linked to the capacity of cancer stem cells to differentiate into various tumor cell lines within the same organ or anatomical site.[11] Both theories could serve as plausible explanations for the occurrence of collision tumors.

When analyzing the main subtypes of RCCs, typical immunohistochemical staining profiles can assist in classification. Clear cell RCC is usually positive for vimentin, keratin, EMA, CD10, Pax 2, RCC marker, and CAIX and negative for kidney-specific cadherin and parvalbumin.[12] Whereas Papillary RCC type 1 is positive for vimentin, broad-spectrum keratins, CK7, AMACR (P504s), and RCC marker, and negative for CD117, kidney-specific cadherin, and parvalbumin.[12] Papillary RCC type 2 has variable staining patterns, consistent with the fact that this is likely a heterogenous category rather than a distinct entity.[12] In our patient, the immunohistochemical stains showed that CK7 and P504s were positive in the papillary RCC, CA-IX was positive in the clear cell RCC, while CD10, RCC, EMA, PAX8, and Vimentin were all positive in both tumors. The diagnosis of renal collision tumor of clear and papillary type RCC was confirmed based on microscopic morphological features and immunohistochemistry. While papillary and clear cell collision renal cell carcinoma collision renal tumors are reported, this is the first case series we have seen in the literature.

Based on the National Comprehensive Cancer Network (NCCN) Guidelines, stage 3 kidney cancer should be treated with a partial nephrectomy, if clinically indicated, and administered pembrolizumab as adjuvant treatment if the mass had clear cell histology.[13] Our patient had 80% clear cell RCC, with most of the tumor having a high nuclear histological grade of G4. With the high risk of recurrence, pembrolizumab is recommended as an adjuvant treatment. The patient underwent a RAL left sided partial nephrectomy and is now currently being treated with pembrolizumab.

This case highlights the importance of appropriate workup, as the patient had a large multiloculated cystic mass measuring approximately 8.5 cm in the right kidney. Septations throughout the lesion appeared to demonstrate enhancement and was classified as a Bosniak III lesion. The Bosniak renal cyst classification system was first introduced based on CT scan findings, and while other imaging techniques like ultrasound and magnetic resonance imaging (MRI) are commonly employed for assessing renal masses, CT scan (with and without contrast enhancement) remains the foremost diagnostic method.[14] Specifically, it aids in predicting the likelihood of malignancy and indicates the need for either follow-up or treatment.

The Bosniak system comprises four categories based on triphasic CT findings, delineating cysts from simple to complex. For our case, a Bosniak III lesion manifests with irregularities and thickening of the wall, along with wall nodularity. Additionally, they might exhibit contrast-enhanced septa, typically multiple, which are often irregular, thickened, and/or calcified.[15] An average of 54% of these cysts are believed to be malignant, with larger lesions having a higher likelihood of malignancy compared to smaller ones.[15] While the recommended primary treatment for these lesions is surgical excision, there is a growing body of evidence suggesting their relatively low metastatic potential and an associated excellent prognosis.[14,15] Due to their relatively indolent behavior, emerging evidence indicates that these lesions, particularly those classified as Bosniak III, can be effectively monitored through active surveillance.[15] The significance of pivotal trials such as Keynote-564 is exemplified in showcasing the application of adjuvant therapy. This involves the exploration of how the approach is implemented, including the workup process and its application to uncommon pathologies resulting from the surgical excision of masses. The principles derived from Keynote trials guide real-world patient encounters.

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Author Contributions

Tatiana Henriksson: manuscript author, data collection, submission of manuscript and revisions;

Katharina Mitchell: manuscript editing, assistance with ascertainment of supporting studies; Reima El Naili: pathology review and preparation of pathologic images; Ali Hajiran: attending surgeon involved, review of manuscript, ascertainment of MRI imaging. All authors reviewed the results and approved the final version of the manuscript.

Availability of Data and Materials

The data that support the findings of this case report are available from the corresponding author, Tatiana Henriksson, upon reasonable request.

Ethics Approval

Ethical review and approval were not required for this study as it did not involve human or animal subjects.

Conflicts of Interest

The authors declare no conflicts of interest to report regarding the present study.

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