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CASE REPORT Open Access

Metastatic colorectal adenocarcinoma in a 76-year old male: a pitfall in the diagnosis for unclassified renal cell carcinoma

Dafne C. Andrade[1*], Sheila F. Faraj[2], Leopoldo Alves Ribeiro Filho[3] and Romulo L. Mattedi[2]

Abstract

Background: The kidney is the most common site of metastatic disease to the urinary tract. However, tumor characteristics are commonly deceptive, and the diagnosis of metastatic disease to the kidney may be challenging.

Case presentation: A 76- year old male was submitted to a total left nephrectomy with splenectomy due to pyonephrosis. At gross examination, the kidney presented a distorted anatomy, with firm parenchyma and an extensively necrotic lesion occupying the renal pyelo-calix and ureter. The spleen had a white pericapsular lesion measuring 1.2 cm. Histologic sections demonstrated a high grade solid carcinoma with rare areas of tubular differentiation. The tumor was highly infiltrative, with invasion of the renal sinus, perirenal fat and spleen. Considering the tumor location, high grade and infiltrative growth pattern, the diagnostic hypothesis of collecting duct carcinoma and urothelial carcinoma were drawn and investigated. Furthermore, a suspicion of metastatic disease was raised after a thorough investigation of the patient's chart, which revealed a previous history of colorectal carcinoma 4 years earlier. Immunohistochemical studies demonstrated expression of CK20 and CDX-2 and negativity for CK7, CK5, PAX-8, Vimentin, CD117, GATA3 and p63; therefore, the patient was diagnosed with a poorly differentiated metastatic colorectal adenocarcinoma.

Conclusion: A high degree of suspicion is necessary for the diagnosis of metastatic disease to the kidney, which should ruled out before the final diagnosis of an unclassified renal cell carcinoma. A careful examination of the patient's history and adequate communication with the attending physician is recommended for the correct diagnosis of these cases.

Keywords: Colon, Kidney, Metastasis, Unclassified renal cell carcinoma

Background

The diagnosis of metastatic tumors to the kidney is challenging. Limited information exist on the prevalence of secondary tumors to the kidney, with a high variability according to the applied diagnostic method (Bates & Baithun, 2002; Gattuso et al., 1999). Furthermore, metastatic tumors may mimic primary kidney carcinomas in clinical presentation, imaging and histological studies (Wu et al., 2015). An adequate history is paramount to yield the hypothesis of metastatic disease, as the development of metastasis can occur several years after the diagnosis of the primary tumor (Wu et al., 2015). Therefore, a high degree of suspicion is required for the diagnosis of secondary tumors of the kidney. Here, we present a case of colorectal adenocarcinoma metastasis to the kidney.

Case presentation

A 76- year old male with history of recurrent urinary infections and loss of renal function over the course of 4 years was admitted for a total nephrectomy after a clinical diagnosis of pyonephrosis secondary to chronic ureteral obstruction. The patient had undergone a nephrostomy one year earlier after failed attempts of ureteral stenting. Imaging studies demonstrated a diffusely enlarged left kidney with hypoconcentration of contrast solution, as well as a moderate dilation and irregular thickening of the collecting system (Fig. 1). The patient was submitted to a radical left nephrectomy. During the

* Correspondence: andradedafne@yahoo.com.br
[1]Department of Pathology, University of São Paulo, Av. Dr. Arnaldo, 455-Cerqueira César, São Paulo, SP 01246-903, Brazil
Full list of author information is available at the end of the article

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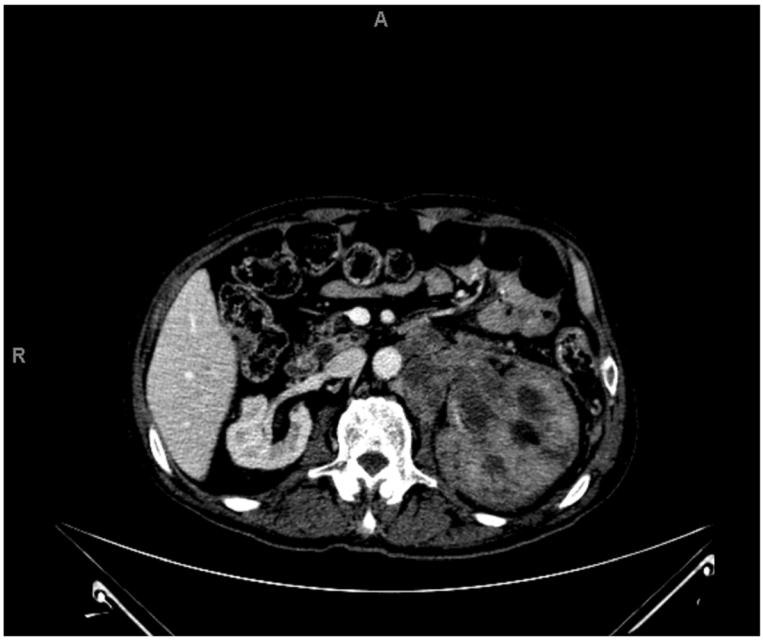

Fig. 1 Abdominal CT showing a diffusely enlarged left kidney with hypoconcentration of contrast solution, as well as a moderate dilation and irregular thickening of the collecting system

surgical procedure, it was decided to also perform a splenectomy due to adherences with the upper pole of the kidney.

At gross examination, the kidney, ureter and perirenal fat weighted 800.9 g and measured 16.5 × 11.3 × 9.2 cm (Fig. 2). The kidney presented a distorted anatomy, with a tan and granular lesion with extensive necrosis and poorly defined limits occupying the renal pyelo-calix, medulla and ureter with an extension of 9.8 × 5.2 cm. The mucosal surface of the renal pelvis was also irregular and presented micronodular lesions measuring up to 0.3 cm. The parenchyma was firm and exhibited a grayish coloration with loss of the corticomedullary junction and had multiple adherences with the renal capsule. The ureter was dilated (1.0 cm in diameter) and had thickened walls with a friable aspect. The spleen weighted 139.7 g and had a white and firm pericapsular lesion measuring 1.2 cm.

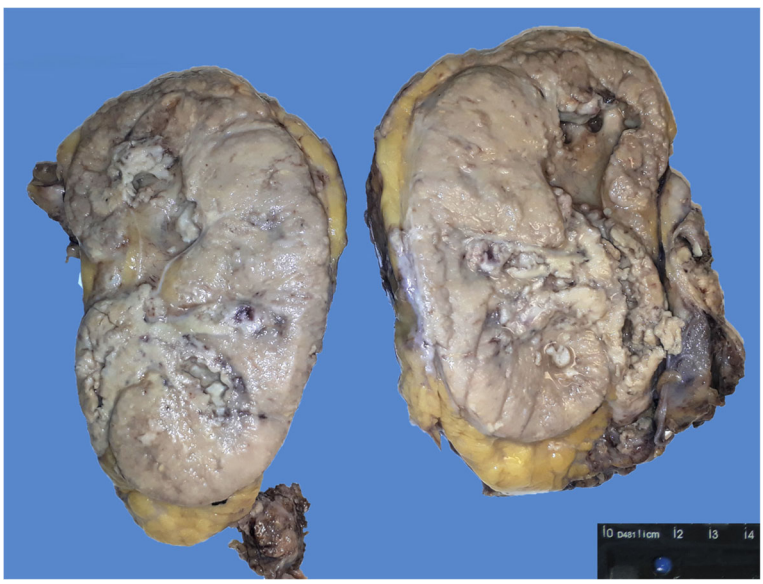

Fig. 2 Gross image of the resected kidney, demonstrating a distorted renal parenchyma with a friable lesion in the pyelo-calix, medulla and ureter

Histologic sections demonstrated a high grade solid carcinoma with rare areas of tubular differentiation with intraluminal eosinophilic secretion. The tumor was infiltrative throughout the renal parenchyma, with some preserved tubules and glomeruli, and presented tumoral necrosis in 40% of the lesion, as well as multiple foci of angiolymphatic and perineural invasion. However, a desmoplastic reaction was not prominent, as expected in some primary renal carcinomas. The renal sinus was involved by the tumor and there was direct tumor extension into the perirenal fat and spleen (Fig. 3).

Considering the tumor location centered in the pyelocalix system and medulla, histological high grade and infiltrative growth pattern, the diagnostic hypothesis of collecting duct carcinoma and urothelial carcinoma were drawn and investigated. The medical history of the patient was also thoroughly reviewed, and it was revealed that the patient had a previous history of colorectal adenocarcinoma four years earlier, thereby raising the suspicion of metastatic disease. The tumor originally invaded the colonic muscularis propria, had no lymph node metastasis, was microsatellite stable and wildtype for KRAS and NRAS. Metastatic disease to the liver, peritoneum and pre-sacral lymph node had already been diagnosed one year after the primary site diagnosis, and the patient was then submitted to chemotherapy based on oxaliplatin and 5-fluorouracil. Immunohistochemical studies were performed in light of the clinical data and demonstrated positive expression for CK20 and CDX-2 and negativity for CK7, CK5, PAX-8, vimentin, CD117, GATA3 and p63; therefore, the patient was diagnosed with a poorly differentiated metastatic colorectal adenocarcinoma to both left kidney and spleen (Fig. 4).

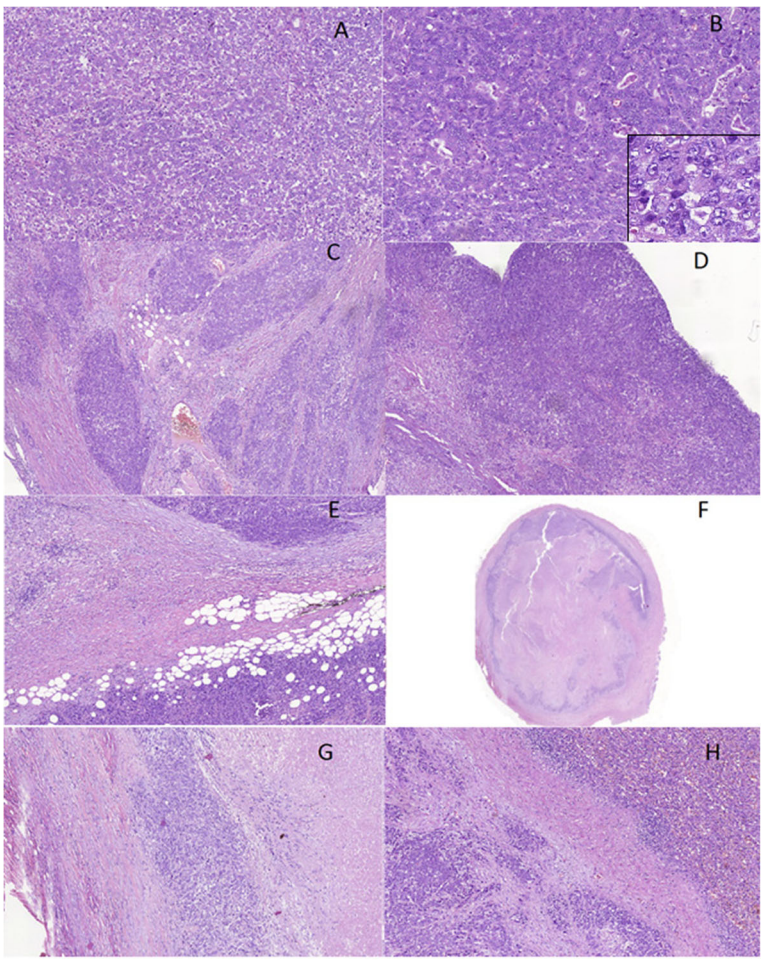

Fig. 3 **a**. Infiltration of the renal parenchyma by a solid high grade adenocarcinoma; **b**. Rare tubular structures with eosinophilic secretions (inlet: high power view of the glandular structures); **c**. Invasion of the renal sinus; **d**. Invasion of the renal pelvis; **e**. Invasion of the perirenal fat; **f**. Panoramic view of the ureter, showing diffuse infiltration by a highly necrotic neoplasm; **g**. High power view of the ureteral wall with infiltration by a high grade adenocarcinoma; **h**. Infiltration of the splenic capsule by high grade adenocarcinoma

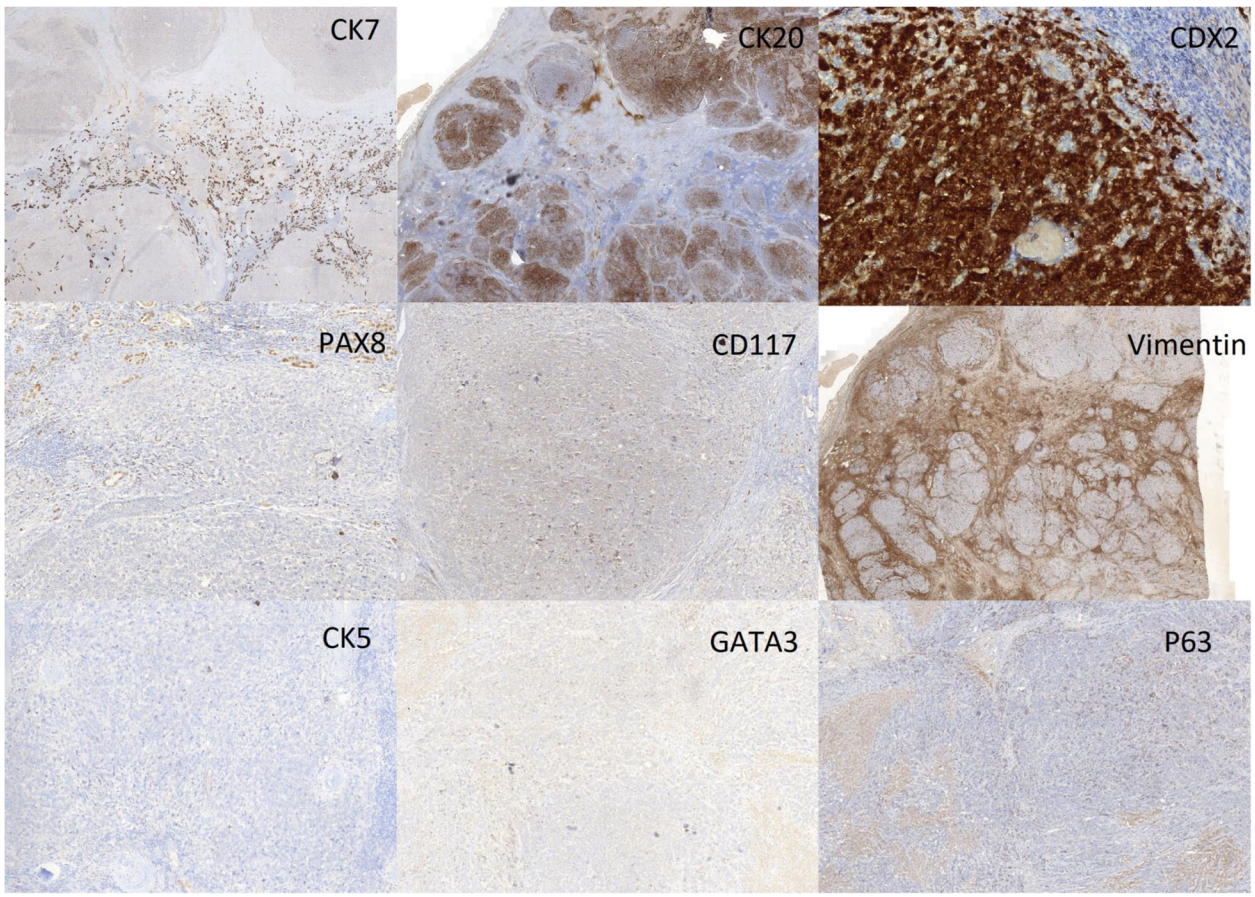

Fig. 4 Immunohistochemical studies performed in the reported case, demonstrating strong positivity for CK20 and CDX2 and negativity for CK7, CK5, p63, GATA3, PAX8, vimentin and CD117

Discussion and conclusions

The kidney is the most common site of metastasis in the genitourinary tract (Morichetti et al., 2009). The prevalence of secondary tumors involving the kidney varies greatly between different studies depending on the applied diagnostic method. Gattuso et al., (1999) found that 11% of renal masses investigated with fine needle aspiration were metastasis from other primary sites (Gattuso et al., 1999). The frequency of secondary tumors was lower (3%) when investigated with surgical pathology specimens (Bates & Baithun, 2002; Aleong et al., 2000) and higher (up to 30%) in autopsy studies (Aleong et al., 2000). The lung is the most common source. Other primary sites are also reported, including breast, female genital tract, and thyroid. Colorectal adenocarcinoma accounts for 4.6 to 10.6% of metastatic tumor to the kidney.

Metastasis to the kidney usually occur in the setting of widespread disease (Morichetti et al., 2009), but the clinical presentation may be similar to that of primary tumors, including presenting symptoms such as flank pain, hematuria and weight loss (Zhou et al., 2016; Goyal et al., 2011; Grise et al., 1987). Secondary tumors of the kidney can also mimic primary carcinomas both in imaging studies and gross examination. Although autopsy-based studies had previously reported that secondary renal tumors were commonly multiple and bilateral (Aleong et al., 2000), recent evidence with surgical pathology specimens has indicated that the detection of a single renal mass is not a reliable marker of primary disease. Indeed, a series of 43 secondary tumors to the kidney found that, although most tumors presented as a solid renal mass on imaging studies, only 30% were multiple and 23% presented bilaterally (Wu et al., 2015). Similarly, in a series of 151 patients, 77.5% of the metastatic tumors to the kidney were solitary lesions (Zhou et al., 2016). Nevertheless, the detection of a single mass is still a confounding factor for the diagnosis of metastatic disease to the kidney. (Wu et al. 2015) found that a diagnosis of primary disease was favored in 35% of the cases with

metastatic disease based on clinical and radiological data (Wu et al., 2015).

Another confounding factor for the diagnosis of metastatic disease to the kidney is the time period between the diagnosis of the primary tumor and the metastasis. A median time interval of 3.1 years between the diagnosis of the primary site and the metastasis has been reported, but a longer time interval (> 10 years) was found in 19% of the cases (Wu et al., 2015). The longer time interval between primary tumor and metastasis, in turn, tends to limit the information provided to the surgical pathologist (Wu et al., 2015). Since an adequate history is the most important factor to create the suspicion of metastatic disease, this prolonged interval may misguide the diagnostic workup for a renal mass. It is important to note, however, that metastatic tumors may also be diagnosed simultaneously with the primary tumor or, more rarely, before the diagnosis of the primary site (Wu et al., 2015). Among the reports in the literature of colorectal adenocarcinomas with renal metastasis, most cases presented as recurrences of a primary tumor within a time frame of months up to 8 years after primary diagnosis, and after adjuvant chemotherapy (Dagnoni et al., 2011; Waleczek et al., 2005; Dulskas et al., 2015; Adamy et al., 2011; Choyke et al., 1987). (Aksu et al. 2003) reported one case of colorectal adenocarcinoma which presented simultaneously with a renal metastasis (Aksu et al., 2003). In most of the aforementioned cases, however, the patient died in the setting of widespread disease within months of the diagnosis of renal metastasis. In our case, also, the patient had a primary diagnosis of colorectal adenocarcinoma 4 years earlier, which was not reported at first by the attending physician and delayed the diagnosis of metastatic adenocarcinoma.

The evaluation of surgical specimens has demonstrated that metastatic tumors to the kidney commonly present as a locally invasive disease, with extension into the perirenal fat or renal sinus (Wu et al., 2015). Furthermore, although histological sections of secondary renal tumors may resemble features of the primary site, a significant proportion of the cases may present as high grade tumors. In this situation, the differential diagnoses include high grade renal cell carcinomas or urothelial carcinomas, similarly to what was considered in the case reported herein. Therefore, immunohistochemical studies are commonly needed to confirm the metastatic nature of the tumor as well as the primary site. Diligent review of the patient's history and imaging studies is also highly recommended to guide the diagnostic workup. However, when adequate clinical data is not available after active pursuit, a broad immunohistochemical panel may help to assess the possibility of metastatic disease.

In conclusion, metastatic tumors to the kidney are uncommon and may mimic primary lesions in clinical, gross and histological findings. The possibility of a secondary tumor in the kidney should be investigated further with immunohistochemical studies and careful review of the patient records in any case with morphological findings that are not compatible with the most prevalent kidney neoplasms.

Abbreviations

CDX2: Caudal type homeobox transcription factor 2; CK: Cytokeratin; PAX 8: Paired box 8

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DCA, RM and SF participated in data collection and processing. DCA wrote the first draft and RM and SF reviewed the paper for intellectual content. All authors read and approved the final manuscript.

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Author details

[1]Department of Pathology, University of São Paulo, Av. Dr. Arnaldo, 455-Cerqueira César, São Paulo, SP 01246-903, Brazil. [2]Department of Pathology, Instituto do Câncer do Estado de São Paulo, São Paulo, Brazil. [3]Division of Urology, University of São Paulo, São Paulo, Brazil.

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