

Case Report

Tumor-to-Tumor Metastasis in Synchronous Primary Kidney and Colon Tumors

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Abstract

Background: Synchronous tumors are defined as two or more distinct and malignant tumors excluding the possibility of one being a metastasis of the other. The development of tumor metastasis from another synchronous primary malignancy is rare. The incidence of synchronous neoplasms of the colon and kidney is rare. Renal cell carcinoma exhibits characteristic features making it suitable for harboring metastases.

Case presentation: We report a unique case of a 49-year-old male with no previous history of cancer that was found to have synchronous rectal adenocarcinoma and left kidney renal cell carcinoma. Additionally, metastasis from colon adenocarcinoma to RCC was identified. Distinguishing double primary neoplasms and metastases in synchronous primary tumors has significant implications with respect to patient prognosis and recommendations for therapy.

Keywords: Primary Colon Tumor; Primary Kidney Tumor; TTM : Tumor-to-Tumor Metastasis
Tumor-to-Tumor Metastasis

Abbreviations

AJCC	:	American Joint Committee on Cancer
CRC	:	Colorectal Cancer
CT	:	Computed Tomography
H.E.	:	Hematoxylin-eosin
MSI	:	Microsatellite Instability
NAACCR	:	North American Association of Central Cancer Registries
PET	:	Positron Emission Tomography
RCC	:	Renal Cell Carcinoma

Introduction

Synchronous multiple primary tumors are relatively rare. It has been hypothesized that concurrent tumors can arise from tissues with similar embryological origin when they are simultaneously affected by environmental factors. Accumulated data show an infrequent yet strong association of the urogenital and gastrointestinal tumors as most common pairing of synchronous primary cancers [1,2]. Tumor-To-Tumor Metastasis (TTM) is an uncommon phenomenon explained as a metastasis in a histologically separate tumor [3,4]. We present a case of clinically and pathologically documented synchronous double malignant tumors of the colon and kidney, meanwhile tumor to tumor metastasis from colon to kidney. To the best of our knowledge, no case with such a concurrency has been reported to date in the literature.

Case reports

Case presentation

A 49-year-old male presented with a chief complaint of abdominal pain. Patient reported a recent change in his bowel habit. His medical history was significant for smoking and obesity with no family history of malignancies. He previously underwent sleeve gastrectomy in 2014 and reported 100 lbs. weight loss since then.

Abdominal Computed Tomography (CT) (Figure 1 and 2) showed generalized sigmoid colon wall thickening and luminal narrowing suggestive of the annular constricting lesion and several hepatic lesions concerning for metastatic disease. The CT scan also revealed an exophytic complex mass arising from the upper pole of the left kidney, suggestive of Renal Cell Carcinoma (RCC).

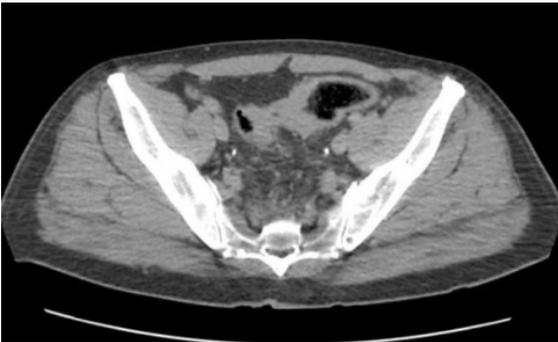


Figure 1: CT scan of the abdomen and pelvis. Annular constricting lesion involving sigmoid colon.



Figure 2: Staging CT shows partially exophytic complex mass in the upper pole of the left kidney, 4.7 cm, suggestive of renal cell carcinoma.

The patient underwent an endoscopic examination and was biopsied for histological definition. Histological diagnosis of the colon biopsy confirmed the presence of tubular adenoma with intramucosal adenocarcinoma. The staging Positron Emission Tomography (PET) scan was consistent with the primary diagnosis. A CT-guided biopsy of the right liver and left kidney was performed. Both Histologic and immunophenotypic profiles (positive for CK20 and CDX2, negative for CK7) of the liver lesion supported a diagnosis of metastatic adenocarcinoma of colon as the primary origin. However, the tumor cells morphology and immunoprofile of the left kidney mass were most compatible with renal cell carcinoma. After careful review of the findings, a multidisciplinary surgical approach was planned. Following neoadjuvant chemotherapy, the patient underwent simultaneous lower anterior resection of the recto sigmoid colon and left radical nephrectomy. He had an uneventful and favorable postoperative course and was transferred back to the oncology division afterward.

Gross Pathology

Both radical nephrectomy and sigmoid colon specimens were obtained by our department of pathology for histopathological examination. The radical nephrectomy specimen composed of left kidney, ureter stump and perinephric tissue. Grossly a well-circumscribed, solitary mass (3.5 x 2.5 x 2.5 cm) involving the upper pole of the left kidney was recognized. The tumor was tan-yellow with focal areas of hemorrhage. The renal sinus or the Gerota's fascia was not involved by the tumor. A gray flat lesion (5 x 4.5 x 4 cm) with velvety granular surface adjacent to a polyp (2 x 1.5 x 0.7 cm) was identified in the colon. Macroscopically the tumor seemed to extend through the colonic wall.

Microscopic Features

The microscopic features are illustrated in (Figure 3). All tissue samples were routinely fixed in 10% formalin and embedded in paraffin. Hematoxylin-Eosin (H.E.) and immunohistochemical stains were performed. Microscopic examination of the colon revealed a tumor invading through the muscularis propria, consisting of poorly differentiated glands surrounded by desmoplastic reaction. The carcinomatous glands were lined by tall columnar cells and their lamina showed frequent dirty necrosis. The tumor cells expressed CK20 and CDX2 in accordance with the diagnosis of colorectal adenocarcinoma.

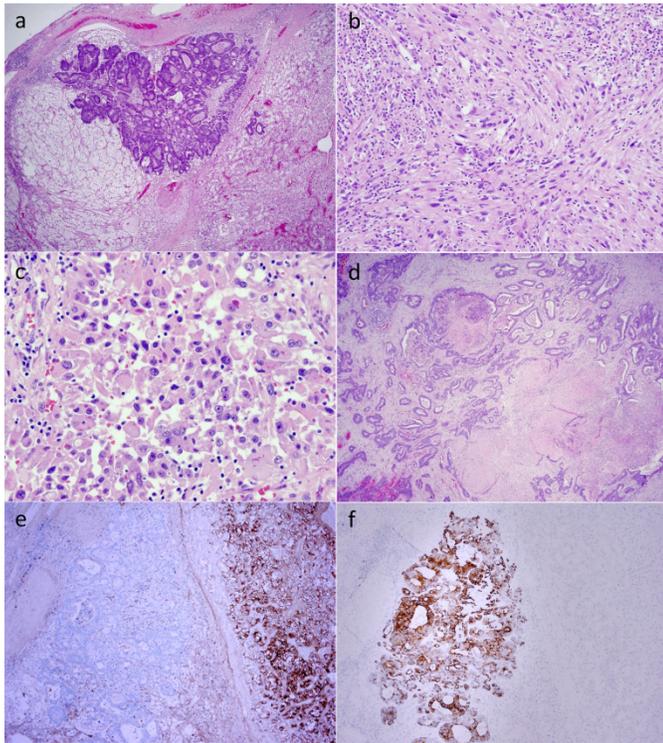


Figure 3: **a:** Clear cell renal cell carcinoma containing metastatic deposit of colorectal carcinoma (H.E. x 20), **b:** Renal Cell Carcinoma with sarcomatoid features (H.E. x 100), **c:** Renal Cell Carcinoma with rhabdoid features (H.E. x 200), **d:** Tumor histology of poorly differentiated adenocarcinoma of colon (H.E. x 200), **e:** Positive immunoreactivity for RCC by clear cell carcinoma nests (x 40), **f:** The colon adenocarcinoma is strongly positive for CK20 while the renal cell carcinoma is negative. (x 40).

Metastatic carcinoma involving five of twelve resected peri-colonic lymph nodes was noted, giving a final American Joint Committee on Cancer (AJCC) tumor stage of T3 N2a M1b. Histological analysis of the left kidney revealed a renal cell carcinoma, with compact alveolar architecture and sharply outlined boundaries. The nests were composed of neoplastic cells with abundant clear cytoplasm and high nuclear grade. Several areas of atypical spindle cells having marked nuclear pleomorphism as well as rhomboid differentiation were identified. To our surprise, a morphologically distinct area was found mostly circumscribed by the RCC, showing glandular structure similar to the colorectal carcinoma. Immunohistochemical staining was performed. The clear cell component exhibited vimentin, RCC and PAX8 and was focally positive for CD10. The metastatic component was positive for CK20 and CDX2 and negative for RCC, PAX-8 and vimentin. These findings strongly evinced a colonic origin for metastatic tumor. A diagnosis of clear cell renal cell carcinoma, histologic grade of four with both sarcomatoid and rhabdoid features was then established. Also tumor revealed features compatible with tumor to

tumor metastasis of rectal adenocarcinoma to renal cell carcinoma. The following genetic studies were done: K-RAS, N-RAS, and BRAF mutation, EGFR amplifications and microsatellite instability tests were performed, but all were found to be negative.

Conclusions

This is the first reported case of coinciding synchronous malignant tumors of the colon and kidney with tumor-to-tumor metastasis from the colon to the kidney.

Discussion

Coexistence of two or more primary neoplasms in the same patient is an unusual but well documented occurrence. The North American Association of Central Cancer Registries (NAACCR) classifies double primary malignancies into two categories. Synchronous malignancies are secondary tumors occurring either simultaneously or within 2 months of the first malignancy. However, metachronous malignancies are secondary tumors that develop at least 2 months after the first malignancy [5]. The current criteria by Warren and Gates are used to identify synchronous tumors: each tumor must be malignant, each must be distinct, and the possibility that one is a metastasis of the other must be excluded [6]. Colorectal cancer (CRC) is the fourth common cancer in the United States [7]. It has been suggested that patients with CRC have increased risk for developing a second cancer [8]. In comparison to CRC, Renal cell carcinoma occurs less frequently with an incidence of 61,816 new cases per year [7]. The risk of multiple primary cancers is higher in patients with kidney and renal pelvis cancers [9]. In particular, RCC has been the focus of many studies within the past decade since it is associated with other primary malignancies including breast, genitourinary, colorectal cancers and non-Hodgkin's lymphoma [10-12].

Although these tumors are individually common, the incidence of synchronous neoplasms of the colon and kidney is rare [12]. Capra et al. [13] reported synchronous RCC in 0.4% of patients with primary colorectal carcinoma. This concurrency is reported 0.5 % by O'Boyle and Kemeny, [14] and 4.85% by Halak et al. [12]. However, autopsy series do not distinguish between synchronous and metachronous tumors. Calderwood et al reported higher risk of renal parenchymal tumors in patients diagnosed with CRC before age of 60 years [2]. Although the etiology of synchronous primary malignancies is not fully understood, the results of this cohort analysis supported possible shared environmental and genetic risk factors between CRC and urologic cancers. Any benign or malignant tumor can be a recipient of metastasis. While slowly increasing, it is still uncommon to have metastasis from tumor-to-tumor. Renal cell carcinoma is the most common recipient for tumor-to-tumor metastasis [10,15]. Among the donor tumors, lung cancer is the most frequent primary, followed by breast cancer [16,17]. The higher stage of the primary

non-renal malignancies is correlated with the higher rate of metastasis to kidney [18,19].

Renal metastasis from the primary colon adenocarcinoma is rare [20]. It only accounts for less than 3% of all secondary renal neoplasm's based on historical postmortem analysis [16]. A recent study at MD Anderson revealed that primary colorectal tumors comprise 10.6% of metastatic tumors to the kidney [20]. To the best of our knowledge, no case with a concurrency of these synchronous tumors with tumor-to-tumor metastasis at the time of diagnosis has been reported to date in the literature. We used the keywords "tumor-to-tumor metastasis" and "synchronous tumors" in PubMed to perform an English literature review of combined and separate publications of these entities, to date no case has been reported. Tumor-to-tumor metastasis must be differentiated from a collision tumor. In the literature, the two terms have frequently been used interchangeably. Collision tumor is defined as two adjacent but histologically distinct tumors in the same organ without any histological intermixing [21,22]. Campbell et al established the following criteria for the diagnosis of TTM:

1) At least two primary tumors must be present; 2) The recipient tumor must be a true neoplasm; 3) The metastasis has to demonstrate real growth in the recipient tumor, not simply contiguous invasion or non-adherent tumor emboli; 4) Metastases into lymphoid tissue involved by hematopoietic neoplasms do not count [23,24]. Our case met all of the above criteria and considered a true TTM.

There has been much debate about why certain tumors are more likely to be donors or recipients. The "seed and soil" theory by Paget's, proposes that metastatic tumor cells (seeds) have better development in a more favorable biochemical microenvironment (soil) [25]. The "mechanical" theory suggests that due to high blood flow, highly vascular architecture, and anatomical location, the recipient tumors could be prone to metastases [26]. Individual characteristics of these tumors have been described by several hypotheses. Indolent nature of RCC, its rich vascularity and high glycogen/lipid content provides a proper environment for tumor growth and it would explain why renal carcinoma is the most frequently described recipient for TTM3, [15,27,28]. The colon is drained by the portal venous system, thus CRC spreads through the lymphatic and venous systems to local or distant organs. Although the liver is by far the most common involved organ, CRC can metastasize to the brain, spleen and kidney [17].

Both tumor-to-tumor metastasis and synchronous primary tumors are infrequent phenomena; Recognition of these incidents is important to avoid an incorrect diagnosis as well as to provide an appropriate management. In the present case, both colon and renal tumors were identified concurrently. Renal biopsy was done to determine the treatment plan. Simultaneous hand-assisted laparoscopic removal of both primary tumors was performed. With

improvements in medical imaging, early diagnosis of the silent RCC is possible during discovering another cancer. Coexistence of renal mass in a patient with non-renal malignancy is more likely to be an incidental primary renal tumor [18], however high degree of suspicion should be employed to exclude metastasis. Additional studies are needed to further improve our understanding of both synchronous tumors and TTM in order to achieve the most optimal management for these patients.

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Conflict of interest

All authors declare that they have no conflict of interest.

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