



Isolated Kidney Metastases from Rectal Cancer: Report of an Unusual Pattern of Recurrence

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Abstract

Kidney metastases from Rectal Cancer (RC) are quite rare. Only one case has, to the best of our knowledge, been reported. We present the case of a 56-year-old man with lung metastases from a rectal adenocarcinoma diagnosed in October 2015. In June 2018, he developed microhematuria during treatment with regorafenib administered as second-line therapy. The computed tomography scans of the whole body revealed lung disease progression and a solid mass in the cortical site of the left lower kidney. A biopsy was performed and the pathologic examination showed moderately differentiated adenocarcinoma consistent with RC. The tumoral cells stained positively for cytokeratine 20 and CDX2. The administration of third-line chemotherapy plus aflibercept resulted in a dimension reduction of metastases and disappearance of microhematuria. Here we describe the advantages of diagnosing this unusual pattern of metastasization from RC and how it can be explained.

Keywords: Arterial dissemination; Chemotherapy; Kidney metastases; Rectal cancer; Regorafenib

Introduction

Colorectal Cancer (CRC) is the fourth most frequently diagnosed cancer and the second leading cause of cancer death in the United States [1].

Many patients have unresectable disease at diagnosis and will develop metastases over time. Arterial dissemination is more frequent in rectal than in colon cancer as the former is drained from the superior hemorrhoidal veins, but also from the middle and inferior hemorrhoidal veins. Metastatic cells, through the inferior vena cava, may reach the lungs, bones and brain by surmounting the liver filter. This could justify metastasization in atypical sites, such as the kidneys [2]. Although an autopsy study of over 11,000 patients with CRC found kidney metastases in 2.7% of patients, the literature has so far reported just over 15 of these cases from colon cancer and only one case of metastases from Rectal Cancer (RC) [3-5].

Case Presentation

In October 2015, a 56-year-old man came to our hospital following rectorrhage. After sigmoid proctoscopy, an adenocarcinoma of the low rectum was diagnosed. A Computed Tomography (CT) scan of the chest and abdomen revealed a thickening of the rectum walls and multiple bilateral lung metastases. An anterior rectal resection was performed. Microscopically, the histopathological findings of the rectum were consistent with a moderately differentiated, serosa-invading adenocarcinoma (Figure 1a). The Rat Sarcoma virus (RAS) evaluation showed a codon 12 mutation in the Kirsten RAS (KRAS) gene. Chemotherapy consisting of oxaliplatin and capecitabine plus bevacizumab was started in December with partial remission and without reporting significant toxicities. An increase in the number of lung metastases was documented in July 2017. At this point, the patient was enrolled in the phase II STREAM trial (clinicaltrials.gov NCT02619435) with the administration of regorafenib as second-line therapy. Metastases showed cavitation during treatment and the drug was administered for 10 months with moderate toxicity.

In June 2018, after achieving significant disease control over time, a microhematuria was diagnosed and incorrectly suspected as a side effect of regorafenib. The CT scan of the whole body

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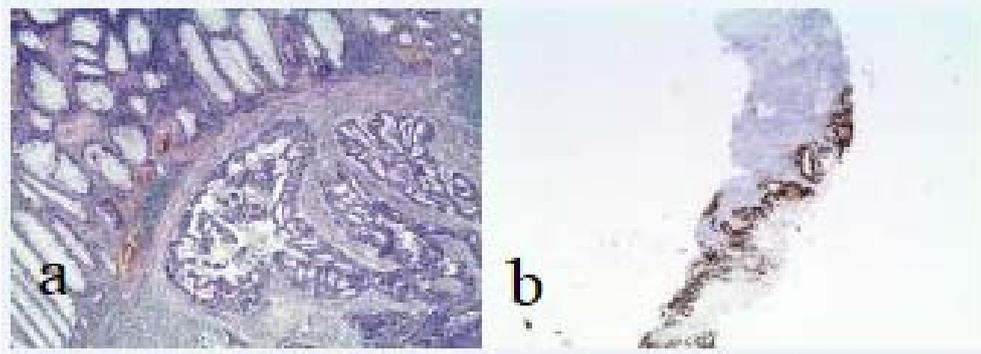


Figure 1: Microscopically, tumor showed a moderate differentiated, serosa-invading adenocarcinoma (a) and immunohistochemical section of kidney mass positive to CDX2 (b).

showed lung disease progression and a 23 mm solid mass in the cortical site of the left lower kidney (Figure 2). A biopsy of the kidney was performed and histological examination of the tissue showed renal metastases from RC. The tumoral cells stained positively for Cytokeratin (CK) 20 and CDX2 (Figure 1b). Thereafter, third-line therapy was undertaken consisting of irinotecan, folinic acid and fluorouracil plus aflibercept. Twenty-four cycles of therapy were administered and a CT scan of the whole body revealed dimensional reduction of lung and kidney metastases with disappearance of microhematuria. Thirteen months after diagnosis of renal metastases, the patient started to suffer from headaches in September 2019 and a new CT scan of the whole body showed a single brain metastases in the left fronto-parietal site with dimensional increase in lung metastases, while the mediastinal lymph nodes and renal metastases appeared unchanged. Third-line therapy was immediately stopped and a brain metastasectomy with subsequent stereotaxic radiation therapy was performed. He then underwent fourth-line chemotherapy with oral TAS-102 (trifluridine-tipiracil) that was administered for 3 cycles until March 2020 and a fifth line of therapy with the reintroduction of oxaliplatin for three months. After ascertaining a recurrence of brain metastases, best supportive care was suggested to the patient who died in November of the same year, more than 5 years after the onset of metastatic disease.

Discussion

Secondary kidney involvement is notoriously rare and the primitive cancers that are responsible are generally those of the lungs, followed by those of the breast [6]. The appearance of renal metastases from CRC is undoubtedly even rarer. Metastatic lesions generally manifest themselves as expansile solitary exophytic masses. More rarely they are multifocal and have an infiltrative growth pattern appearing radiologically as renal enlargement [2]. Their manifestation from colon cancer was primarily justified through diffusion *via* the lymphatic and venous system, with three levels of lymph nodes: Pericolonic, intermediate, and principal. Renal metastasization from RC has been described only once in the literature and has instead been demonstrated through intraluminal diffusion secondary to an infiltration of the urinary tract by the primary tumor [5]. Although arterial renal metastases are also possible for colon cancers, we believe that in our case they were essentially due to the primary localization of the tumor in the lower rectum with drainage of blood through the inferior vena cava.

Even if they are mostly detectable in later stages of the disease and in the presence of other secondary metastatic lesions, a biopsy

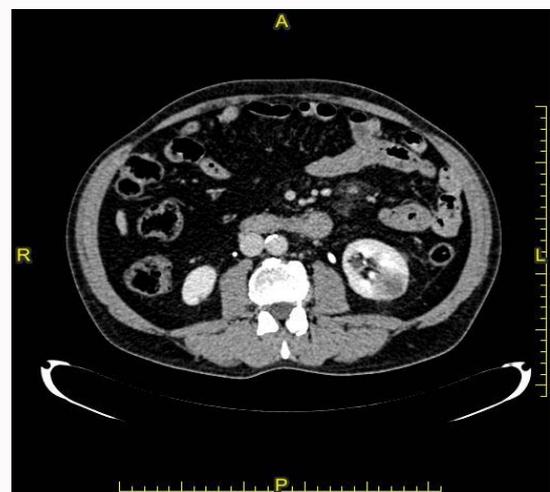


Figure 2: Abdominal computed tomography scan revealing a mass in the cortical site of the left lower kidney.

should be performed because, when renal metastases occur as a single nodule, they may be radiologically indistinguishable from a primary kidney tumor [2,7]. Immunohistochemistry and positivity of CDX2 is necessary in attributing the colorectal origin of metastases, as described in literature [8,9] and as documented in this case. However, nephrectomy should only be recommended in extreme cases, such as in patients suffering from intense pain, perirenal hematoma with risk of rupture or uncontrollable hematuria. On the other hand, microhematuria in our patient could also have been related to a side effect of regorafenib [10], without forgetting that even a partial nephrectomy could have resulted in decreased renal clearance and compromised the use of subsequent full-dose chemotherapy. So, the suspension of regorafenib for documented disease progression and third-line therapy ensured the resolution of microhematuria and the dimensional reduction of all secondary metastatic lesions with improvement in the quality of life of our patient and increase in his survival.

In conclusion, while noting the rarity of renal metastases from CRC, we believe that their biopsy assessment and early diagnosis are always necessary in order to maximize clinical outcome.

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