Bleeding metastasis of renal cell cancer to anal canal treated with radiation

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Introduction

Renal cell cancer (RCC) has the potential to metastasize to various organs, including the anal canal which is reported to be the rarest location. An 88-year-old male patient who had previously been treated for right RCC subsequently developed distant metastases to the prostate, lungs, and small bowel. Four years following nephrectomy, the patient presented with a bleeding anal mass which was excised and has been proven to be an anal canal metastasis of RCC. Seven months post excision, regrowth occurred. The patient underwent stereotactic ablative body radiotherapy resulting in satisfactory regression during the 2-month follow-up period, without episodes of bleeding. The treatment options for metastatic post-nephrectomy disease should be considered with a multidisciplinary approach in order to achieve satisfactory symptom relief.

Keywords: Anal canal, Metastasis, Radiation therapy, Renal cell cancer
ous surgeries comprehended diabetes mellitus and hypertension and open prostatectomy due to benign prostatic hyperplasia in 2007, respectively. Metastasis from RCC was diagnosed in 2020 and was initially treated with interferon-alpha but due to the patient’s intolerance to the medication, interruption, and replacement with sunitinib followed. During the treatment, the clinical progression of the metastasis was recognized. Therefore, the treatment was converted to doxorubicin + cyclophosphamide with the achievement of a complete clinical response seen on the chest X-ray performed prior to surgical excision of the anal canal lesion. Further, small bowel metastasis occurred in 2020 presented with hematochezia. Hence, segmental intestinal resection was performed.

Almost 4 years following the index surgery for the RCC, the patient complained of rectal bleeding with present anal mass mimicking hemorrhoid disease. He was initially treated for bleeding hemorrhoid disease. The bleeding was recurrent, and the lesion continued to grow, finally resulting in severe secondary anemia at the beginning of the year 2022. In March 2022 he was admitted to the department for colorectal surgery with anemia and a visible mass in the anal canal (Fig. 1). Add following: erythrocytes count of 3.01 × 10^6 U/L, hemoglobin value of 8.2 g/L, hematocrit of 24.4%, neutrophils of 86.6%, C-reactive protein value of 40.4 mg/L, glucose value of 185 mg/dL, serum albumin value of 24.1 g/L, serum creatinine value of 13 U/L, serum urea value of 59 mg/dL, serum total protein value of 47 g/L and serum sodium value of 133 mmol/L. Replacement of blood (4 units) was given in order to correct anemia with hemoglobin value achievement of 12.2 g/L. The patient was operated under spinal anesthesia and the lesion was excised with mucosal defect closure in order to achieve proper hemostasis. The patient’s hospital stay lasted 4 days and the wound was regularly followed and it healed completely after 35 days. The pathology report confirmed R0 resection of RCC metastasis in the anal canal (Fig. 2).

One month after metastasis removal, clinical regrowth was noted. The lesion regrew to an almost identical size as when presented initially over the next 7 months with episodes of bleeding (Fig. 3). Additional R2 resection of the lesion due to bleeding was forced. In addition, the patient was referred to the oncologist where radiation (SABR) was indicated with a total of 25 Gy divided into 10 fractions. Metastasis regression followed with no new episodes of bleeding (Fig. 4). Six months after SABR completion, a complete clinical response was achieved with no macroscopic tumor present in the anal canal. After this time frame, the patient was lost for further follow-up.

Discussion

Approximately 1/3 of the patients diagnosed with RCC present with distant metastases at the initial diagnosis. Twenty to 40% of them will subsequently develop metastases [7]. Distant spread is described to be hematogenous, lymphatic, transcoelomic or by direct invasion [8].

An advanced search of the Cochrane library and PubMed by using the keywords “renal cell cancer,” “metastasis,” and “anal canal” revealed only two case reports of anal canal metastasis from RCC [9,10]. Rare GI tract locations of RCC metastases have also been reported. They are described as solitary or with concomitant involvement of other organs (brain and lungs) as in this case. GI tract organ affection includes the duodenum [9,11], the colon [12], the rectum [3], and the anal canal [9,10]. To the best of our knowledge, the present case is the third report on the occurrence of anal canal metastasis originating from RCC (Table 1).

The diagnosis can be challenging because symptomatology can mimic other primary conditions of the affected organ. It may present with hematochezia [11], rectal bleeding [9], signs of intestinal obstruction, vomiting, and change in stool caliber [13]. Anal canal metastases have been misdiagnosed as hemorrhoids and in some cases treated as such [9]. The same clinical confusion was initially present in this case.

Fig. 1. Clinical presentation of the metastasis in the anal canal.
Renal cell cancer metastasis to anal canal

Fig. 2. Histopathology findings of the primary tumor and the anal canal metastasis. (A) Metastatic renal cell cancer (RCC) in perianal region. Metastatic tumor caused skin ulceration (hematoxylin and eosin stain ×40). (B) Primary RCC and renal parenchyma interface (hematoxylin and eosin stain ×40). (C) RCC composed of cells with abundant eosinophilic cytoplasm, rhabdoid features and prominent nucleoli (hematoxylin and eosin stain ×100). (D) Diffuse carbonic anhydrase-IX (CAIX) stain in neoplastic cells (×40).

In general, the indication for SABR in RCC has not yet been clearly defined for different stages of the disease. Surgery remains the standard treatment option for localized RCC. Having in mind the cases with locally advanced RCC and/or the present comorbidities in some patients, radiation therapy should be considered as the proper treatment option. In the multi-center analysis from the International Radiosurgery Consortium of the Kidney, primary inoperable RCC in 96 patients was treated with stereotactic ablative body radiotherapy delivered as single or multiple fractions of more than 5 Gy. The reported cumulative incidence of local failure at 5 years was 5.5% [14]. In the German S3 guideline for renal cell carcinoma stereotactic body radiotherapy is favored for local tumor control. At the same time, the oligometastatic treatment with higher local doses or stereotactic treatment should be considered after interdisciplinary discussion [15].

The use of palliative radiotherapy in patients with metastases occurrence after prior nephrectomy is reported. In the systematic review of Kothari et al. [16], the effect of SABR on extracranial metastatic renal cell carcinoma was analyzed. The reported average marginal range was 15–50 Gy with a range of fractions from single one to 10. Weighted local control was achieved in 89% with a median overall survival range of 11.7–22 months. In the meta-analysis of Zaorsky et al. [17] on the use of stereotactic ablative radiation therapy for extracranial oligometastatic renal cell carcinoma, the 1-year overall survival rate ranged from 48.9–100% with a 1-year local control rate range from 72.4–99.4%.

Due to the lack of data and recommendations for the standard treatment of the metastatic disease to the anal canal from RCC, surgical excision was initially performed in this case. The clinical symptomatic regrowth forced the use of palliative radiation. The used 25 Gy/10 fraction radiation was lower than the standard one for soft-tissue conventional palliative radiation dose. The advanced age of the patient influenced the radiation dose decision.

In the proposed algorithm of the Mayo Clinic on the diagnosis
and treatment of RCC, metastatic stage IV disease should be treated with molecularly targeted therapy +/- cytoreductive nephrectomy. In cases with oligometastases presence, surgical excision or stereotactic body radiotherapy are the treatment options [18].

Metastatectomy is still an effective treatment in selected patients with soft-tissue metastases from RCC. In this case, the surgery failed and led to symptomatic local recurrence. On the contrary, local radiation therapy resulted in satisfactory metastasis regression with no post-radiation bleeding during the follow-up period. Therefore, initial radiotherapy could be the choice of treatment for local metastases in the anal canal from RCC instead of local excision in selected cases. To summarize, the recurrent local metastatic RCC disease requires a multidisciplinary approach in order to achieve symptom relief.

**Statement of Ethics**

Written informed consent was obtained from the patient.

**Conflict of Interest**

No potential conflict of interest relevant to this article was reported.

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Table 1. Literature review of cases with metastases from renal cell cancer in the anal canal

<table>
<thead>
<tr>
<th>Study, year</th>
<th>Age (yr)/Sex</th>
<th>Symptoms</th>
<th>Metastasis treatment</th>
<th>Local recurrence after treatment</th>
<th>Treatment after recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sawh et al. [9], 2002</td>
<td>53/M</td>
<td>Bleeding, anal mass</td>
<td>Local excision</td>
<td>Not reported</td>
<td>-</td>
</tr>
<tr>
<td>Davies et al. [10], 2015</td>
<td>76/M</td>
<td>Anal mass</td>
<td>Local excision</td>
<td>Not reported</td>
<td>-</td>
</tr>
<tr>
<td>This study</td>
<td>88/M</td>
<td>Bleeding, anal mass</td>
<td>Local excision</td>
<td>Yes</td>
<td>R2 excision + radiation</td>
</tr>
</tbody>
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Fig. 3. Regrowth of metastasis with evident bleeding.

Fig. 4. Local finding 2 months after radiotherapy completion with evident metastasis regression.
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**Author Contributions**

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**References**