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Clear Cell Carcinoma Leading to Gastrointestinal Bleed

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Abstract

The incidence of renal cell cancer has risen over the recent years, and with the use of new diagnostic imaging modalities, the detection rate has also increased. Clear cell carcinoma is the most common type amongst them (70% of cases). The most common sites of distant metastases are the lungs, lymph nodes, liver, bone, and brain. This advanced renal cell cancer is being treated by biologicals like cabozantinib, an antiangiogenic tyrosine kinase inhibitor (TKI). This case report highlights an 84-year-old male with a complex medical history, including metastatic renal cell carcinoma (RCC) on cabozantinib therapy, presenting with gastrointestinal bleeding. Despite the infrequency of gastric involvement, evaluating GI bleeds is crucial to rule out such complications. The patient's hematemesis prompted further investigation, such as an endoscopy, revealing a 7 mm polypoid area with ulceration and active bleeding in the stomach. The endoscopic intervention included snare resection, histologically confirmed as metastatic clear cell carcinoma. Gastric metastasis from RCC is uncommon, often manifesting later in the disease course. The simultaneous occurrence of metastases in other organs is common, emphasizing the significance of gastric findings in indicating RCC progression and severity. The patient's favorable response to the intervention highlights the diagnostic and therapeutic challenges associated with such cases. This report contributes to the limited literature on RCC-associated gastrointestinal bleeding, illustrating the importance of maintaining a high index of suspicion in patients with atypical presentations. The overall poor prognosis of metastatic RCC further underscores the importance of timely diagnosis and intervention.

Keywords

Anemia, Targeted Therapy, Prostate Cancer, GI Bleed, Clear Cell Carcinoma

1. Introduction

Renal cell carcinomas (RCCs) primarily arise in the renal cortex and present with either the classic triad of flank pain, hematuria, and a palpable abdominal renal mass (9 percent of cases), indicative of locally advanced disease or local invasion, or commonly so with paraneoplastic syndrome [1]. Other symptoms are fever, weight loss, anemia, and a varicocele. Some can be detected by incidental imaging (CT or MRI). This has markedly increased the 5-year survival for patients with RCC and increased nephron-sparing surgery use.

Paraneoplastic syndromes involve systemic symptoms due to ectopic hormone production [2]. Hormones implicated include erythropoietin, parathyroid hormone-related protein (PTHrP), gonadotropins, human chorionic somatomammotropin, an adrenocorticotropic hormone (ACTH)-like substance, renin, glucagon, and insulin. Recognition of these varied clinical presentations is crucial for timely diagnosis and appropriate management of RCC [3].

Metastasis of renal cell carcinoma (RCC) predominantly occurs in the lungs, bones, and lymph nodes, with gastrointestinal involvement less frequent [4]. Historically, gastric manifestations are associated with symptoms such as abdominal pain, early satiety, changes in bowel habits, and, infrequently, acute anemia due to blood loss. Gastric metastasis, when observed, typically manifests later in the disease progression. The simultaneous occurrence of metastases in other organs is commonly reported. Consequently, detecting gastric involvement may indicate the advancement and severity of RCC. Malignant lesions contribute to less than 5% of such bleeding episodes [5].

2. Case Presentation

An 84-year-old male with a past medical history of end-stage renal disease on nightly peritoneal dialysis, metastatic renal cancer, and prostate cancer presented following a fall and subsequent hematemesis. For renal carcinoma diagnosed six years ago, the patient underwent left nephrectomy and radiation and has been currently on cabozantinib daily for six months. The patient also had prostate cancer in the remote past treated with surgical resection. The patient reported weight loss, loss of appetite, and fullness at the flanks. He noted mild dizziness and shortness of breath on exertion.

The patient was unclear if the episode of hematemesis occurred right after or during the fall. He described a single episode of dark coffee-ground emesis, denying any prior or subsequent events. He denied recent exposure to nonsteroidal anti-inflammatory drugs (NSAIDs) due to his renal failure. The patient denies any alcohol intake in the recent past. He denies any forceful vomiting history. Physical examination revealed pallor and abdomen fullness. The patient had undergone an upper endoscopy a year ago, showing a gastric ulcer, which was then cauterized.

Pertinent negatives included abdominal pain, chest pain, constipation, diarrhea, or blood in the stool. The patient's last bowel movement was the same morning, which he described as normal. The patient started treatment for heartburn

symptoms (burning sensation after food intake) and hoarse voice two weeks ago with omeprazole 20 mg daily. The symptoms resolved following medication onset. However, the hoarse voice in this case could be due to recurrent laryngeal nerve compression due to mediastinal lymph node enlargement in advanced malignancy.

On admission, vitals were as in Table 1.

Lab work was significant, as in Table 2.

Table 1. Vitals on admission.

Vital	Value
Temperature	98.4 F
Heart Rate	104 beats per minute
Blood Pressure	130/90 mm of Mercury

Table 2. Patient's presenting CBC.

Test	Value
Hemoglobin in g/dL (12 - 15)	6.5 (Patient's baseline 9)
Platelets (K/microliter) (150 - 450)	107
WBC (K/microliter) (4.5 - 10.5)	4.6

The patient was treated with intravenous pantoprazole 40 mg given an episode of hematemesis. The patient underwent a trauma workup, which was negative for any acute process. He was started on maintenance fluids and given a unit of packed red blood cell transfusion, improving hemoglobin to 7.1 g/dL. CT demonstrated two newly enlarged lymph nodes in the gastrohepatic ligament. Liver function tests and erythropoietin levels were within normal limits.

Gastroenterology was consulted for upper gastrointestinal bleeding, and the decision was made to proceed with upper endoscopy to make a definitive diagnosis and possibly control bleeding. Endoscopic findings included a 7 mm polypoid area with ulceration and active bleeding at the mid-body of the stomach posterior wall. This was removed using the hot snare technique and retrieved as a single piece for histology. After this, three endo clips were placed for the closure of the defect.

Follow-up histopathology demonstrated metastatic clear cell carcinoma. Following the intervention, the patient had no further episodes of bleeding, and hemoglobin remained stable at around 8 g/dL without further transfusions. The patient was then transferred to a tertiary care center for an endoscopic ultrasound to check the further involvement of the gastric thickness.

3. Discussion

An 84-year-old male presented with a recent history of hematemesis. He is a known case of metastatic renal cell carcinoma on cabozantinib therapy and post-operative prostatic carcinoma. Malignant lesions, though infrequently causing

acute upper gastrointestinal (GI) bleeding, contribute to less than 5% of such bleeding episodes [6]. In 2019, around 63,000 individuals in the USA received a diagnosis of renal cell carcinoma (RCC) [7]. Common locations for RCC metastasis are lungs, bones, and lymph nodes. On the contrary, common malignancies with gastrointestinal spread are breast, lung, and skin.

Other causes of hematemesis, like forceful retching, Mallory-Weiss tear, Boerhaave syndrome, NSAID use, liver cirrhosis, and trauma, are ruled out from the historical aspect. This patient is on cabozantinib, a tyrosine kinase inhibitor, which is associated with bleeding events, including gastrointestinal bleeding [8]. Awareness of this risk is crucial for evaluating hematemesis in patients on targeted therapies.

In a patient with metastatic carcinoma presenting with unexplained anemia, a clinician should have a lower threshold for endoscopy. Hence, it is done for both diagnostic and therapeutic purposes. This patient demonstrated a 7 mm polypoidal growth, and the biopsy finding indicated metastatic clear cells, which is highly suggestive of the clear cell variety of renal cell carcinoma. Past cases of hematemesis have demonstrated metastasis involving the stomach presenting with symptoms such as abdominal pain, chronic gastrointestinal bleeding, early satiety, bowel habit alterations, and acute anemia due to blood loss [9]. Gastric metastasis from RCC typically occurs later in the disease course. Concurrent metastases to other organs are frequently reported, making gastric disease findings indicative of RCC progression and severity.

Overall, metastatic RCC carries a poor prognosis with a 5-year survival rate of 12% [10]. Given the high mortality, maintaining a clinical suspicion for metastatic disease is crucial in patients with atypical presentations. Studies suggest that patients with gastrointestinal metastases should be assessed for the risk of hemorrhages. The prognosis becomes even poorer in these patients as compared to metastasis on more commoner sites. Notably, the patient also had prostate cancer, an even rarer entity known to spread to the stomach. Hence, a biopsy is needed to rule out the cause of the GI bleed. In this patient, biopsy showed clear cells suggesting renal cell carcinoma.

Treatment for this patient should focus on improving the quality of life, as in palliative care. However, endoscopic management significantly reduces the GI bleeding while reducing morbidity.

4. Conclusions

Patients with any malignancy, even ones with infrequent gastrointestinal metastasis, should be evaluated by an upper endoscope for upper gastrointestinal spread. Even though suspicion of peptic causes is higher, metastasis cannot be ruled out. Adequate biopsies from any ulcers should be taken before intervention.

From a diagnostic standpoint, the patient needs to be evaluated by endoscopic ultrasound (EUS) to determine the extent of involvement. In this patient, the role of the endoscopic ultrasound is to control the bleeding lesion and decide on anti-

coagulation if the patient has been on it for thromboembolism associated with malignancy. Usage of EUS for tumor staging or prognosis is of less value in this patient, as it won't change the overall management of metastatic RCC.

Overall prognosis of metastatic RCC is poor; hence, the aim of the management is to improve patient outcomes, reduce complications, and offer palliative care. A higher index of suspicion is needed to find out the cause, particularly when faced with an unusual presentation such as the above patient.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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