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CASE REPORT

A Not-So-Clear Case of Renal Cell Carcinoma

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Abstract

Renal cell carcinoma (RCC) has a relatively high rate of metastasis which carries a grave prognosis, yet the location and presentation of metastatic disease can be quite unpredictable. We present a case of metastatic clear cell RCC presenting with nonspecific gastrointestinal symptoms before imaging revealed hepatoduodenal fistulization and multiple masses concerning for abscess vs metastases. Subsequent biopsy revealed an uncommon tumor marker profile. The ultimate diagnosis depended on piecing together the patient's clinical history, current presentation, and histopathological features.

Introduction

Renal cell carcinoma (RCC) has a relatively high rate of metastatic spread that corresponds to a grave prognosis. While approximately 33% of all RCC patients will demonstrate metastases, up to 50% of RCC patients have been reported to develop metastases post-nephrectomy [1]. When RCC metastasizes, it's location and presentation can be quite unpredictable. Most common locations include bone, lymph node, lung, liver, adrenals and contralateral kidney, yet metastasis to the mesentery, omentum, or peritoneum represent less than 2% of cases [2]. Thus, histopathological confirmation is critical in securing an accurate diagnosis.

Case presentation

A 56-year-old man with a history of hypertension presented to the emergency room with one week of severe epigastric abdominal pain radiating to his right upper quadrant and back. The pain was associated with nausea, vomiting, and feeding intolerance. Notably, the patient reported having a right radical nephrectomy for "cancer" performed in Mexico four months prior to his current presentation.

On arrival, he was mildly tachycardic and tachypneic, but otherwise afebrile and normotensive. His physical exam was remarkable for epigastric and right upper quadrant tenderness to palpation without hepatomegaly. Laboratory studies revealed leukocytosis of 30.79 with a neutrophilic predominance as well as a normocytic anemia with a hemoglobin of 10.6. Platelets were elevated to 414. Alkaline phosphatase was elevated at 143 with otherwise normal transaminases. Lipase was normal. Abdominal CT revealed an apparent fistula between the second portion of the duodenum and right lobe of the liver as well as multiple rim-enhancing peritoneal implants with surrounding inflammatory changes.

At the time, the patient's presentation, labs, and imaging raised concern for potential abscesses versus metastatic malignancy, either of which were presumed to be complicated by hepatoduodenal fistulization. He was admitted for broad spectrum IV antibiotic therapy and further management. The patient subsequently underwent CT-guided core needle biopsy of the right lobe liver mass and perihepatic soft tissue nodule. Preliminary results showed poorly differentiated carcinoma with sarcomatoid features. Immunostaining was positive for CA-IX, CK AE1/AE3, and CAM 5.2 tumor markers but notably negative for PAX8. Operative and histopathological reports from the patient's nephrectomy were obtained indicating invasive clear cell RCC at the time of surgery. A

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diagnosis of metastatic clear cell RCC was made despite PAX8-negative immunostaining. IV antibiotics were discontinued, and oncology was consulted for further recommendations and ongoing management. Patient eventually underwent drain placement for liver masses and feeding tube placement due to presence of fistula, was discharged from the hospital with plans for outpatient follow-up.

Discussion

The renal PAX8 gene encodes pro-survival factors expressed in normal renal tissue that allow for apoptosis evasion. Accordingly, expression of this gene is increased in the setting of RCC and therefore widely used in diagnosing both primary and metastatic RCC [3]. Despite this feature, PAX8 expression is not uniformly distributed among sub-types of RCC. A 2015 study comparing PAX8 expression found that 96% of normal renal tissue was PAX8-positive compared to 83% of RCC tumors. Among RCC subtypes, PAX8-positivity was 100% in chromophobe tumors and 95% in papillary tumors. However, only 80% of clear cell tumors were PAX8-positive [4], thus providing sound precedence for PAX8-negativity in clear cell RCC as seen in our patient. What makes our case particularly unique is that the patient's PAX8-negative biopsies were obtained from sites of metastatic clear cell RCC. Barr and colleagues reported significantly higher rates of PAX8-positivity in metastatic RCC tumors compared to primary RCC tumors. Only 3% of metastatic RCC tumors were found to be PAX8-negative, introducing potential doubt in our diagnosis. Yet importantly, our patient's biopsies were uniformly CA-IX, CK AE1/AE3, and CAM 5.2-postiive, all of which are important markers that together support a diagnosis of metastatic clear cell RCC, particularly in the setting of the patient's specimen-proven history of clear cell RCC per previous nephrectomy. Our case is also unique because hepatoduodenal fistula is not a well-known complication of RCC, most cases reported are renocolic fistulas which can lead to infection, ischemia, or necrosis [5].

Conclusion

Though rare, PAX8-negative tumors do not preclude a diagnosis of clear cell RCC, whether primary or metastatic. This case emphasized the importance of taking the patient's entire clinical picture into consideration. While the patient's histopathological evidence certainly supported a diagnosis of RCC, the diagnosis of metastatic clear cell RCC despite being unexpectedly PAX8-negative was informed by the full histological profile (including both immunostaining and tumor morphology) and the patient's history of specimen-proven clear cell RCC. Moreover, this case highlights the highly variable presentations of RCC including development of hepatoduodenal fistula.

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