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Case Report

Tumor to tumor metastasis of renal cell carcinoma in carcinoma stomach: An unusual case presentation

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ABSTRACT

Tumor-to-tumor metastasis (TTM) is a rare phenomenon of hematogenous metastasis of one tumor to another type of tumor. Renal cell carcinoma (RCC) has been involved in the TTM either as a donor or recipient. Herein, we report an unusual case of RCC metastasis to primary carcinoma stomach. This is the first of its kind to be reported in the literature.

1. Introduction

The phenomenon of TTM was first published in 1930 by Fried in a case of bronchogenic carcinoma metastasizing to meningioma.[1] Since then, numerous theories such as "seed and soil theory" and "anatomical-mechanical theory" have been contributed to this phenomenon. The mechanism of metastasis depends on metastatic tumor cells and the tumor microenvironment of the target organ.[2] The incidence of renal cell carcinoma (RCC) with gastric cancer as a second primary malignancy is low (0.11-0.37%). Gastric metastasis of renal cell carcinoma is unusual and only a few cases have been reported in the literature. Herein we report an unusual case of RCC metastasis to primary carcinoma stomach. This is the first of its kind to be reported in the literature.

2. Case Report

A 68-year-old male presented with complaints of nausea, vomiting and weight loss for 1 month. The patient is a known hypertensive with a history of alcohol consumption for 20 years. He was diagnosed with Renal cell carcinoma with lung metastasis 2 years back and he underwent cytoreductive laparoscopic Radical nephrectomy (Outside) and had come to our hospital for follow-up. All the routine blood investigations were normal.

PET-CT showed interval development of metabolically active thickening involving the proximal lesser curvature of the stomach, measuring 4.2 x 1.3 cm. (Figure 1) Few hypodense hepatic lesions, the largest in segment VIII were observed, which were suggestive of metastasis. Also seen were the marginal increase in the size of bilateral pulmonary nodules, few stable small discrete left para-aortic and bilateral cervical lymph nodes.

Upper GI endoscopy performed showed a large ulceroproliferative growth in cardiac end of fundus and higher lesser curvature of stomach (Figure 2).

3. Histopathology

The upper GI endoscopic biopsy consisted of multiple pale brown soft tissue fragments which revealed gastric mucosa with two distinct morphologies. One focus had diffuse sheets of signet ring cells floating in abundant extracellular mucin. Also seen were fragments of smooth muscle tissue infiltrated by 20-30 highly pleomorphic

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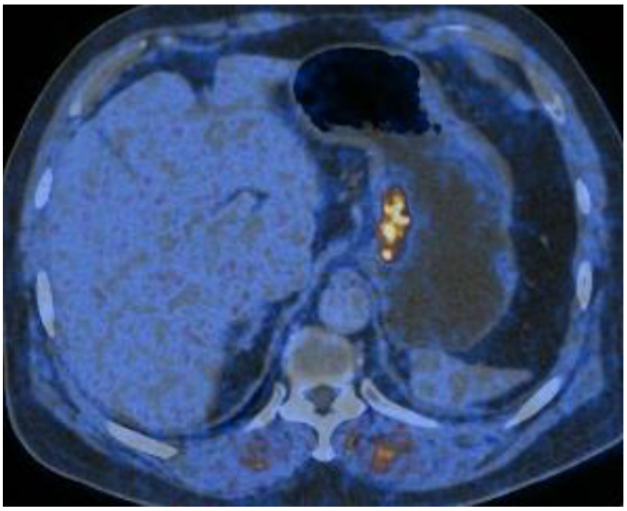

Figure 1: PETCT shows interval development of thickening in the lesser curvature of stomach

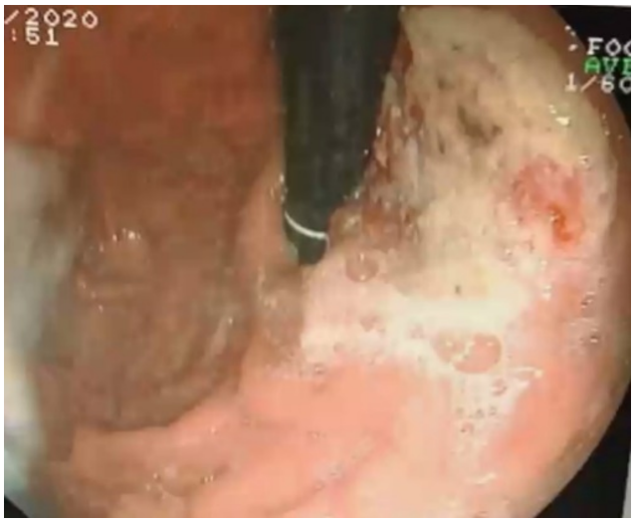

Figure 2: Upper GI endoscopy shows a large irregular ulceroproliferative growth seen in cardiac end of fundus and higher lesser curvature of stomach- Malignant

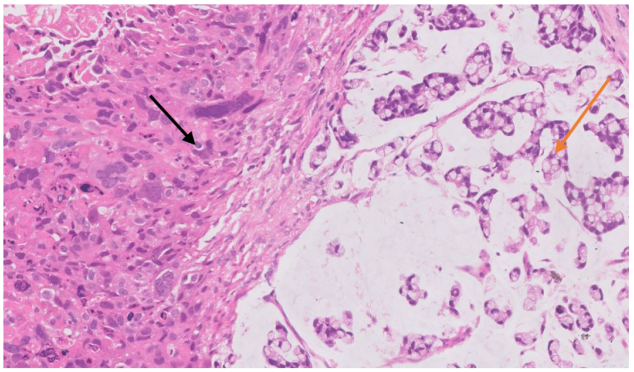

Figure 3: H&E 40X: Shows signet ring cells (red arrow) with a focus of pleomorphic bizarre cells (black arrow)

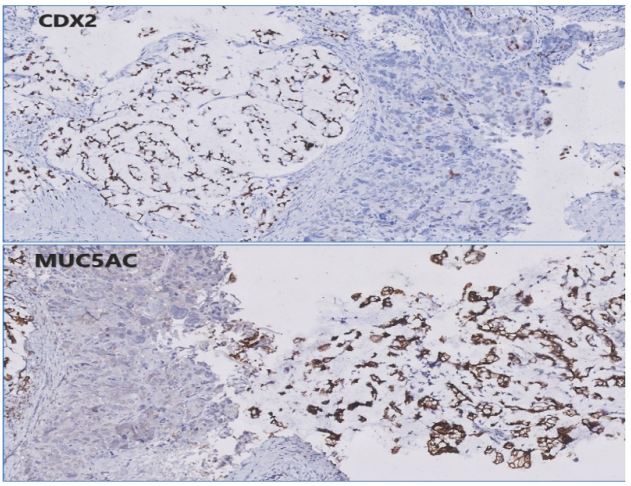

Figure 4: IHC 40X: CDX2 and MUC5AC positive in signet ring cells and negative in bizarre cells

bizarre cells. (Figure 3)

On immunohistochemistry, the signet ring cells were positive for CDX2 and MUC5AC with focal positivity for CK7, CK20 and SATB2. These signet ring cells were immuno-negative for RCC, CD10 and PAX8. (Figure 4)

The bizarre cells expressed RCC, CD10 and PAX8(focally) and were negative for CK7, CK20, CDX2, MUC5AC and SATB2. (Figure 5)

Based on the morphology and different IHC expression of the two areas, a diagnosis of Clear Cell Renal Cell Carcinoma metastatic to Adenocarcinoma stomach was made. As the patient also had interval development of liver metastasis, liver biopsy was performed to differentiate a gastric primary v/s renal primary. Liver biopsy showed extensive necrosis with a small focus of tumor cells arranged in glandular pattern lined by pleomorphic cells with moderate amount of eosinophilic cytoplasm and enlarged vesicular to hyperchromatic nucleus with prominent nucleoli.

On immunohistochemistry, these tumor cells were positive for CK7(few cells), CK19 and MUC5AC (weak& patchy). These cells were immunonegative for CK20, CD10, PAX8, RCC, m-CEA, Arginase, and HepPar. (Figure 6) This is an unusual case of Renal cell carcinoma metastatic to Adenocarcinoma stomach and adenocarcinoma stomach metastatic to the liver. As the patient had lung lesions prior to the development of gastric lesion, the lung lesions were not biopsied. The genomic evaluation did not reveal any VHL or actionable mutations. The patient was treated with 6 cycles of chemotherapy of the DOF regimen (Docetaxel, Oxaliplatin and 5- Fluorouracil) and the 12-month follow-up was uneventful. As the patient

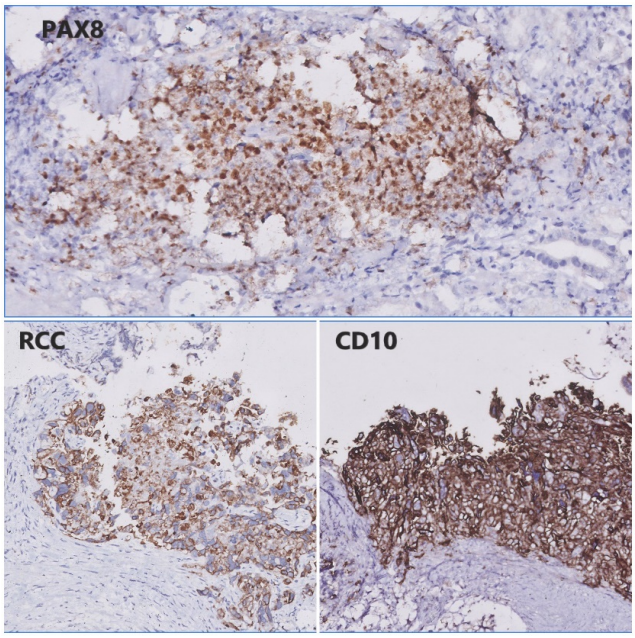

Figure 5: IHC 40X: The pleomorphic bizarre tumor cells showing positivity for PAX8, RCC and CD10.

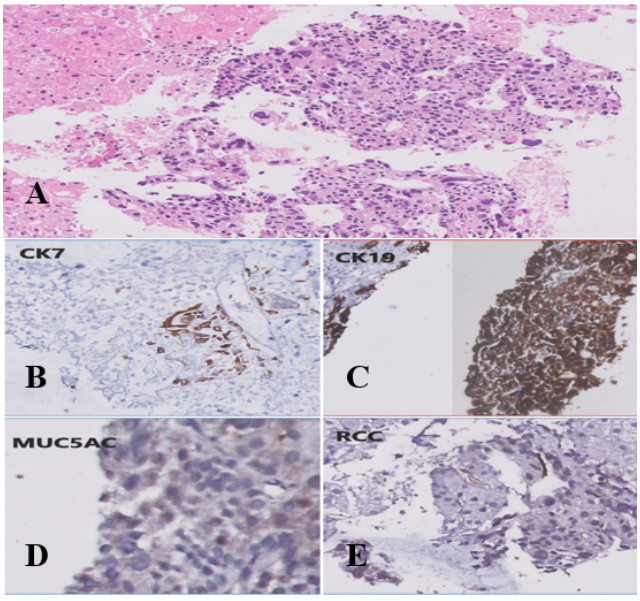

Figure 6: A): H&E 40X: Shows tumor cells in glandular pattern lined by cells with enlarged vesicular to hyperchromatic nucleus with prominent nucleoli. **B-E)**: IHC 40X: The tumor cells show positivity for CK 19, focally positive for CK7 and weak positive for MUC5AC. These tumor cells are immunonegative for RCC

underwent laparoscopic radical nephrectomy elsewhere, the morphology of the primary specimen couldn't be determined.

4. Discussion

TTM is a relatively rare phenomenon in which a secondary tumor is established when one tumor hematogenously spreads to another as a donor to the recipient.[3] Several proposed criteria are to be fulfilled to define a tumor-to-tumor metastasis, such as: (1) There must be two or more primary tumors.; (2) the host tumor (recipient) must be a true neoplasm; (3) It is necessary for the metastatic tumor (donor) to establish growth inside the host tumor rather than a contiguous growth or embolization; and (4) the host tumor should not be a lymph node that is associated with leukemia or lymphoma.[4] To date, only around 150 cases of TTM have been reported in studies worldwide.Meningiomas have been described to be the most frequent tumor to harbor metastasis with breast and lung being the donor. This phenomenon of metastatic seedling has been attributed to the expression of cell adhesion molecule E-cadherin in both meningiomas and breast adenocarcinomas.[5,6] Our case of RCC (donor) to adenocarcinoma stomach (recipient) TTM is the first reported case in the literature worldwide. It has also been described that tumor microenvironment and epithelial-mesenchymal transition could play a role in this metastasis.[7]

Tumors metastasizing to the stomach are uncommon, occurring in only 0.2% to 0.7% of the cases.[8] While RCC often metastasizes to the lungs, bones, and liver, metastasis to the stomach is extremely rare. In medical literature, there have been few reports of gastric metastases from RCC, accounting for only 0.2% of RCC cases in clinical settings.[9] Among primary tumor entities spreading to the stomach, the most prevalent is breast cancer (27%), followed by lung cancer (23%), renal cell cancer (7.6%) and malignant melanoma (7%).[10] The incidence of multiple primary cancers is reported to be 0.734% to 11.7%.[11] Among them, the incidence of carcinoma stomach in presentation with another second primary malignancy varies from 0.7–11%.[12]

Sakurai et al. conducted a review of 44 RCC patients with gastric metastasis and found that only 13 patients had single or isolated gastric metastasis without any other organ metastasis. This suggests that gastric metastasis could be the initial site of metastasis, but in our case, the patient had lung metastasis at the time of RCC diagnosis. When the patient was diagnosed with carcinoma stomach as a second primary, the patient already had a liver metastasis of gastric origin. Also, 14 cases (60.9%) had concomitant tumor spread to other organs and 8 cases (34.8%) had isolated gastric metastasis. The median survival time after treatment of gastric metastasis was 6 months (1-84 months).[13] Therefore, early detection of RCC metastasis is crucial for improving patient survival. Furthermore,

patients with solitary gastric metastasis of RCC tend to have better survival outcomes compared to those with multiple metastases. [14]

There have been very few reports about the preferred treatment modality to improve the clinical prognosis of patients with synchronous gastric cancer and RCC. The primary factor that influences the treatment modality for these patients is the pathological stage of the second primary cancer. Most patients who have resectable synchronous tumors, have both tumors operated at the same time, and reduces postoperative mortality. [15]

5. Conclusion

As renal cell carcinoma has a higher incidence of metastasis, a regular follow-up is required for the early diagnosis of metastasis and occurrence of second primary malignancies. There should be a meticulous histopathological and immunohistochemical evaluation to rule out concomitant metastatic foci in a second primary malignancy.

6. Ethics Approval and Consent to Participate

There is no participation of human subjects or animals. Therefore, ethics approval and informed consent are waived.

7. Conflict of Interest

The authors declare that they have no competing interests.

8. Source of Funding

This study received no funding.

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