OLGU SUNUMU CASE REPORT

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GASTRIC METASTASIS OF RENAL CELL CARCINOMA: A CASE REPORT

RENAL HÜCRELİ KARSİNOMUN MİDEYE METASTAZI: OLGU SUNUMU

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Öz

Primer mide tümörlerine, metastatik tümörlerinden daha sık rastlanır. Berrak hücreli renal hücreli karsinomun (BHRHK) mideye metastazı çok nadirdir. Bu yazıda BHRHK'un mideye metastazı olgusunu sunduk. Altmış yaşında erkek hasta radikal nefrektomi geçirdi ve adjuvan kemoterapi aldı. Takibinde ikinci yılda pulmoner metastaz izlendi ve relaps için interferon alfa-2a kullanıldı. Akciğer metastazlarından iki yıl sonra dispepsi ile başvuran hastanın bilgisayarlı tomografik incelemesinde mide duvarında (boyunca) 11 mm kalınlık saptandı. Endoskopik inceleme nöroendokrin tümörü düşündürdü.

Histopatolojik incelemede berrak vakuolize sitoplazmalı solid paternde tümöral hücre grupları gözlendi. Tümör hücreleri RCC, PAX8, CD10, Vimentin ile pozitif olup immünhistokimyasal sonuçlar ilk tümör ile benzerdi. Sonuç olarak olguya BHRHK'un mide metastazı tanısı verildi ve çok hedefli bir reseptör tirozin kinaz inhibitörü ile tedavi edildi.

Anahtar Kelimeler: Mide metastazı, berrak hücre, renal karsinom, immünhistokimya.

Abstract

Primary gastric tumors are encountered more frequently than metastatic tumors. The gastric metastasis of clear cell renal cell carcinoma (CCRC) is very rare. We herein report a case of gastric metastasis of CCRC.

A sixty-year-old man patient underwent a radical nephrectomy and received adjuvant chemotherapy. Pulmonary metastasis occurred at the second-year follow-up, and interferon alpha-2a was used for relapse. The Computed Tomography examination of the patient presented with dyspepsia two years after pulmonary metastases revealed 11 mm thickness in the (along) gastric wall. Endoscopic examination was suggestive of a neuroendocrine tumor.

Histopathologic evaluation of endoscopic biopsies showed tumoral cell groups in a solid pattern composed of clear, vacuolated cytoplasm. These tumor cells were positive for RCC, PAX8 CD-10, Vimentin, and immunohistochemistry findings were similar to the initial tumor at diagnosis. Finally, the patient was diagnosed with CCRC's gastric metastasis and treated with a multi-targeted receptor tyrosine kinase inhibitor.

Keywords: gastric metastasis, clear cell, renal carcinoma, immunohistochemistry

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Introduction

Primary gastric malignancies have been observed more commonly than metastatic gastric tumors (1). The incidence of metastatic gastric tumors was reported as 0.2-0.7% in the autopsy series (2-4). The most common origins of gastric metastasis were reported to be breast (27.9%), lungs (23.8%), and esophagus (19.1%) (1). The gastric metastasis of clear cell renal cell carcinoma (CCRC) is very rare (2). We present here a rare case of a CCRC with multifocal gastric metastasis.

Case Report

Clinical Findings

A 60 years old man with a history of CCRC had treated with radical nephrectomy and adjuvant chemotherapy. In the second year of patient follow-up, multiple bilateral pulmonary nodules with the largest diameter of 24 mm without increased metabolic activity were detected on Positron Emission Tomography-Computed Tomography (PET-CT) and considered as pulmonary metastasis. The patient underwent interferon (IFN) alpha-2a therapy. On the control PET-CT at the third month of IFN therapy, significant regression in the pulmonary nodules' size was considered a partial response to the IFN therapy. The patient was monitored for two years with stable disease following second-year pulmonary relapse.

The patient was admitted to the hospital with dyspepsia 4 years after the diagnosis of CCRC. Laboratory findings were as; hemoglobin; 12.5(13,6-17,2) g/dL, hematocrite; 37.8 (39,5-50,3) %, and MCV; 68.3 (80,7-95,5) fL, urea; 41.25 (10-40) mg/dL, BUN; 19 (5-18) mg/dL, creatinin; 1.38 (0,67-1,17) mg/dL, uric acid; 8.9 (3.5-7.2) mg/dL. Hypochromic microcytic anemia and mild elevation in kidney function were detected.

Abdominal CT evaluation revealed 11 mm gastric wall thickening of the cardia. Further evaluation with endoscopy was suggested (Figure 1A). Endoscopy showed gastric mucosal edema of the corpus and 3-4 mm hyperemic polypoid lesion originating from the cardia's anterior wall, the proximal of the greater curvature, and lesser curvature of the corpus (Figure 1B). Numerous endoscopic biopsies were taken with a pre-diagnosis of neuroendocrine tumor.

Histopathological Findings

The biopsies have been taken from the stomach, cardia, corpus, and antrum, with the largest 0,4 cm and the smallest 0,2 cm in diameter. The samples were dirty-white-colored. Microscopic findings of endoscopic biopsies were in Hematoxylin & eosin (H&E) stained section samples taken from the gastric cardia and corpus; tumoral cell groups in solid pattern beneath the surface epithelium, which had abundant vacuolated cytoplasm, prominent nucleoli, indistinct cell borders were observed (Figure 2A, 2B). Gastric xanthomas, signet-ring cell (poorly cohesive) carcinoma of the stomach, renal cell carcinoma metastasis were considered in the differential diagnosis. For ruling out the differential diagnosis, some ancillary immunohistochemical markers were solicited. RCC, PanCK, CD10, vimentin, PAX8, AMACR, CDX2, CK20, CK7, chromogranin, SATB2, and CD68 were applied in the panel. Tumor cells showed diffuse expression with RCC (Figure 3A), PanCK (Figure 3B), CD10, vimentin, PAX8 (Figure 3C), and local expression with AMACR. No specific staining was observed in tumor cells with CDX2, CK20, CK7 (Figure 3D), chromogranin, SATB2, and CD68. As a result of the immunohistochemical

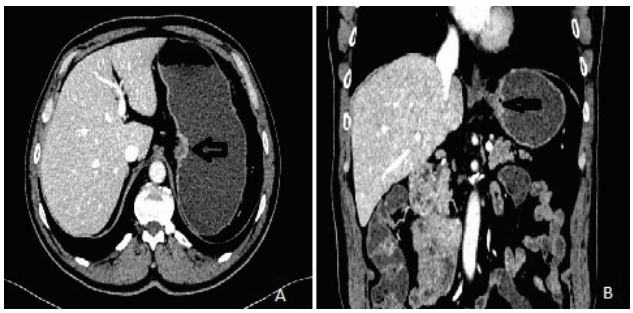

Figure 1a
Gastric wall thickening was seen at cardia (arrow) on axial and coronal contrast-enhanced Abdomen CT (1A: Axial contrast-enhanced Abdomen CT, 1B: Coronal contrast-enhanced Abdomen CT).

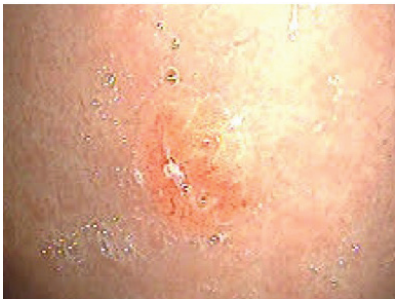

Figure 1b
Gastric endoscopy showing a collapsed 3-4 mm polypoid lesion in the gastric cardia

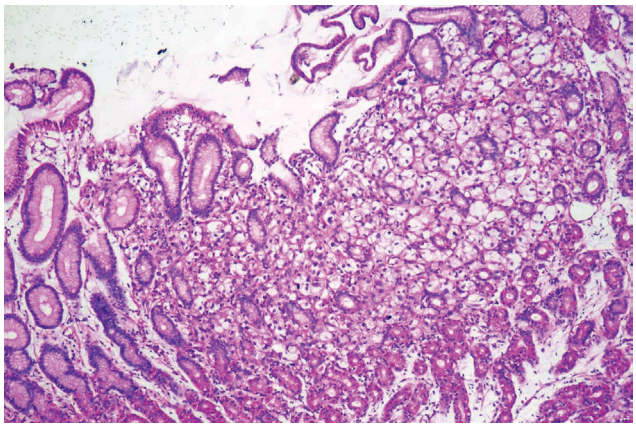

Figure 2a
Tumor cell groups in solid pattern beneath the surface epithelium (H&E, 100x)

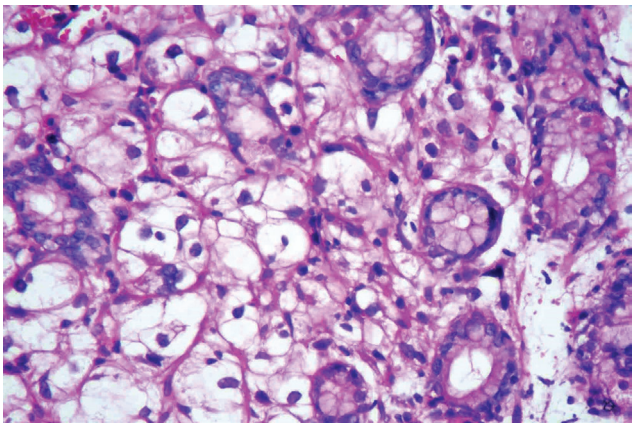

Figure 2b
Tumor cell groups in solid pattern beneath the surface epithelium, which had an abundant cytoplasm, that is, vacuolated, prominent nucleoli, indistinct cell borders (H&E 400x)

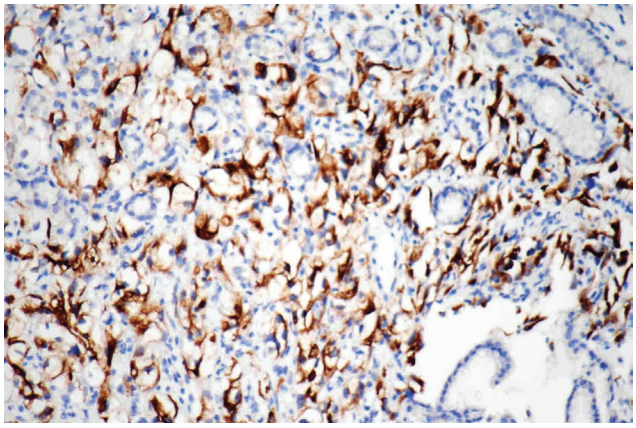

Figure 3a
Diffuse expression was observed in tumor cells of immunohistochemical RCC (400x)

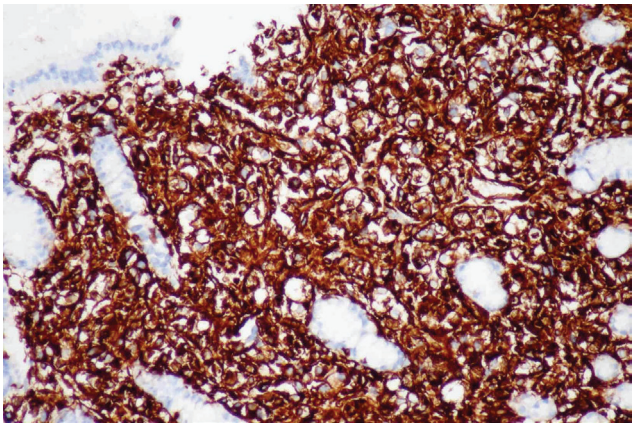

Figure 3b
Diffuse expression was observed in tumor cells of immunohistochemical vimentin (400x)

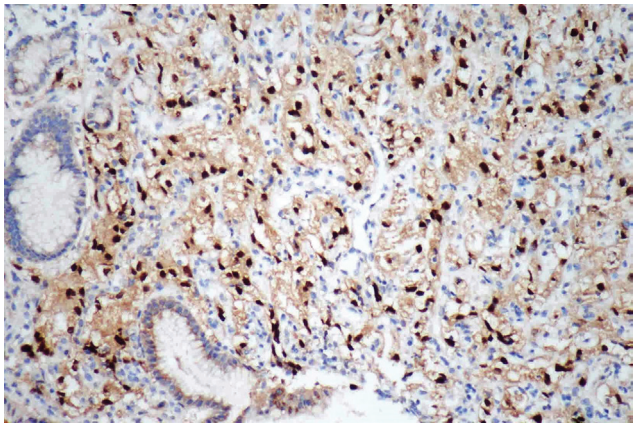

Figure 3c
Diffuse nuclear expression was observed in tumor cells of immunohistochemical PAX8 (400x)

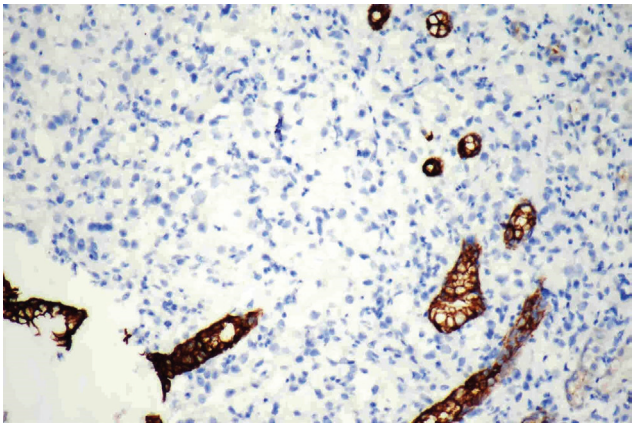

Figure 3d
While staining was observed in the normal gastric epithelial, there was no expression in tumor cells of immunohistochemical cytokeratin 7 (200x)

findings, suspicious for Renal Cell Carcinoma (RCC) concomitant evaluation of the current gastric biopsy and a previous nephrectomy slide was performed. It was observed that the tumor in the radical nephrectomy material and the tumor under the gastric epithelium showed similar histopathological and immunohistochemical findings. With this combination, the case was diagnosed with gastric metastasis of CCRC.

After the gastric CCRC metastasis was diagnosed, the patient underwent Sunitinib treatment, a multi-targeted receptor tyrosine kinase inhibitor. The patient was monitored for two years with stable. After the signed out, the patient was still alive for six months.

Discussion

The incidence of tumor metastasis to the stomach in the clinical and autopsy series was reported to be 0.2-0.7%. Literature is observed considerably rarely (3, 4, 7, 8). RCC frequently metastasis hematogenously to the lungs, bone, and liver (8). Metastasis to the stomach can develop years after the treatment of the primary tumor. RCC and breast tumor metastasis to the stomach can be given as examples of this type of metastasis (1). In our case, lung metastasis was detected two years after the diagnosis of CCRC. The gastric metastasis was detected four years after the diagnosis.

Primary gastric tumors can present with anemia, upper gastrointestinal bleeding, dyspepsia, and epigastric pain. It is impossible to differentiate gastric metastasis from the primary gastric tumors with clinical symptoms (9-11). Melena and microcytic anemia can be observed of the gastric metastasis of RCC in 64% and 45%, respectively (12, 13). Our case had microcytic anemia at the time of diagnosis.

In a previous study, 26 of the 35 cases with gastric metastasis were male, and the mean age was 67 (14). Our case was a 60-year old male and coherent with the cases in the literature.

Endoscopy, imaging findings, and histopathological findings can differentiate between primary and metastatic gastric tumors while it is almost impossible clinically (1, 10, 15). Doughnut-like, volcano-like ulcers observed on esophagogastroduodenoscopy (EGD) can be considered as findings of gastric metastasis (1). Metastatic tumors are mostly multifocal and seen in the gastric corpus and fundus (8). Metastatic tumors resemble submucosal tumors or present with deep ulceration similar to the primary tumors (10). The general appearance of gastric metastasis from RCC usually consists of a polypoid submucosal-like tumor with a central depression (2). It is not always possible to differentiate primary and metastatic gastric tumors due to the different presentations of primary gastric tumors (10). 90-92.2% of the metastasis suspected cases on endoscopy are proven histopathologically (10). In our case, the endoscopist had suspected neuroendocrine tumors.

In our case, lung metastasis was detected on PET-CT 2 years after CCRC diagnosis, and there was no increased metabolic activity on PET-CT. PET is a promising method for the diagnosis of lung, breast, esophagus, and colorectal cancer. Unfortunately, its sensitivity for the detection of gastric tumors is low (16). Gastric wall thickening of the cardia was seen on abdominal CT after four years from the primary tumor diagnosis. Taken endoscopic biopsy results proved the gastric metastasis histopathologically.

Nonetheless, histopathological assessment is the gold standard for the differentiation between primary and metastatic gastric tumors. Suppose the microscopic examination shows the tumor with clear cytoplasm underneath the epithelium in the lamina propria. In that case, we should be consider signet-ring (poorly cohesive) carcinoma, gastric xanthoma, and metastatic tumors, which are like RCC, the most common with cytoplasmic clearance. Routine H&E stained sections may not always be sufficient for diagnosis. Immunohistochemical methods have a crucial place in confirming the diagnosis. For signet-ring carcinoma in the differential diagnosis, we should need some immunohistochemical stain positivity like CDX2, CK7, and intracellular mucin as identified by periodic acid-Schiff (PAS) positivity histochemically. Immunohistochemical other ancillary stains are vimentin, CD10, AMACR, EMA positivity point out RCC metastasis. On the other hand, CD68 positivity will prove gastric xanthoma (17). In our case, both primary and metastatic tumor cells showed staining with RCC, Vimentin, AMACR, CD10, and no expression was observed with CK7, CDX2, SATB2, CD68.

The survival is less than one year in approximately half of the metastatic RCC cases, but survival has been reported to be more than five years in 10% of the cases (18). The median survival of metastatic RCC is 13 months (19). There is limited data on the clinical course of the cases with gastric metastasis. In a previous study, monitoring 22 cases demonstrated seven deaths within weeks after diagnosis, while other cases were still alive during the one year (10).

The five-year survival rate for kidney cancer has become two-fold over the last 60 years, from 2009 to 2015 (20). Our case has been still alive for six months after the detection of gastric metastasis.

In conclusion, primary signet ring cell carcinoma is primarily considered for the diagnosis when subepithelial cells with clear cytoplasm are seen in gastric biopsies in the clinical routine. However, gastric metastasis of RCC should also be kept in mind for the differential diagnosis. It is crucial to verify the diagnosis immunohistochemically.

Conflict of Interest Statement
The authors have no conflicts of interest to declare.

Consent to Participate and Publish
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Data Curation: GE, ŞB, SB, ŞE, OE, AŞ, BÇ
Writing- Original Draft: GE, ŞB, SB, ŞE, OE, AŞ, BÇ

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