

# Double Primary Tumors-Renal Cell Carcinoma and Duodenal Mucinous Adenocarcinoma

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## ABSTRACT

A 59-year old patient was admitted to the Gastroenterology Clinic with the signs of gastrointestinal bleeding. Computerized tomography (CT) and a barium-meal radiography revealed a circumferential nodular wall narrowing and incomplete stricture at the D2 part of the duodenum. CT also showed a poorly demarcated mass in the upper and lower poles of the left kidney. During the operation, the whole kidney together with the tumor was removed and also a part of the duodenum. Morphological features of both tumors were typical and distinctive enough to set the diagnosis of two independent primary tumors. The possibility of one being the metastasis of the other was excluded. The diagnosis of double primary malignant neoplasms - renal cell carcinoma and duodenal mucinous adenocarcinoma was made.

**Key Words:** Duodenal cancer, mucinous adenocarcinoma, renal cell carcinoma, multiple primary neoplasms

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## Introduction

The incidence of multiple primary malignant neoplasms (MPMNs) is increasing, not only as a result of aging of the population, but also as a result of advances in medical technology (1). Based on the definition of Warren and Gates, each of the tumors must present a definite picture of malignancy, each must be distinct, and the probability of one being a metastasis of the other must be excluded (1, 2). MPMNs can be classified as antecedent, synchronous, and subsequent (1).

Some authors claim that genitourinary organs appear to be at high risk for multiple primary malignancies, because these organs are at high risk of primary tumors (1). Sato et al. (1) analyzed MPMNs in patients with renal cell carcinoma (RCC). MPMNs were detected in 12% of patients with RCC, most often simultaneous with RCC. Out of the total of 42 malignancies (other than RCC), 22 were gastrointestinal (mostly stomach, followed by colorectal malignancies), which is in accordance with Nakata et al. (3). Clear cell RCC was diagnosed in 61% of patients. Patients with other primary malignancies were about five years older than those without them, and their RCCs were most commonly incidental, small (<4 cm) and low stage tumors (T1-2N0M0) (1).

Primary duodenal cancer (PDC) was first described by Hamburger in 1746 (4). Excluding the duodenal carcinoma of the Ampulla of Vater, PDC is extremely rare, accounting for approximately 0.019-0.5% of all gastrointestinal (GI) cancers, and 30%-45% of small bowel cancers (2, 4).

Zhang et al. (4) reported 1.02% of PDC in 8.879 patients diagnosed with GI cancer during a 14-year period, with a predominance of male and elderly patients. Tumors are mostly located in the second portion of the duodenum (5). Histologically, adenocarcinoma is the most common type of PDC (74.7%). Most of the PDCs are diagnosed at stage II, III and IV, whereas 30-40% of them are poorly differentiated (4). The most common initial symptoms include abdominal pain, weight loss, vomiting, jaundice and GI bleeding (5). Due to the vague symptoms, it is common to miss or delay the diagnosis, with an average delay of six to eight months between the time of symptom onset and diagnosis (4).

To the best of our knowledge, there are no reports on the occurrence of renal cell carcinoma and duodenal mucinous adenocarcinoma as double primary malignant tumors. .

## Case Report

A 59-year old patient was admitted to the Gastroenterology Clinic due to signs of gastrointestinal bleeding-anemia and black, tarry stools, dizziness and exhaustion in the previous three days. The regional lymph nodes were not palpable. The abdomen was soft, without tenderness or palpable masses. A digital rectal examination showed traces of black stool. Kidneys were painless, and not palpable. In the past ten years the patient had been treated for diabetes.

Esophagogastroduodenoscopy revealed a swelling of the duodenal mucosa in the descending portion of the duodenum

(D2) and a narrowing of the canal. Mucosal biopsy showed signs of chronic active inflammation of the duodenum, but no tumor was present.

Computerized tomography (CT) and a barium-meal radiograph (Figure 1) revealed a circumferential nodular wall thickening, narrowing and incomplete stricture (50 mm in length) at the D2 part of the duodenum. The CT also showed a poorly demarcated mass in the upper and lower poles of the left kidney (Figure 2). The mass in the upper pole was in close contact with the renal hilum, but there were no definite signs of ureteral, arterial or venous infiltrations.

Left radical nephrectomy was performed, along with partial excision of the duodenal mass.



Figure 1. Barium meal radiography of the duodenum

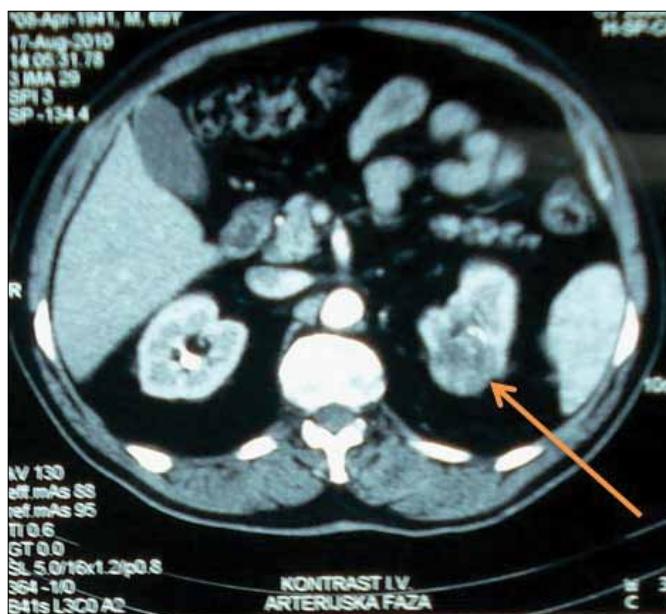


Figure 2. Computerized tomography of the abdomen. Arrow points to the tumor

During the partial excision of the duodenal mass, the tissue sample was examined on frozen sections, which showed the presence of mucinous adenocarcinoma, infiltrating the mucosa and the muscle layer of the duodenal wall. After surgery, kidney and duodenal tissue samples were prepared for routine histopathological examination. The tissues were fixed in 10% formalin saline, sampled, embedded in paraffin, cut on a microtome in 5 $\mu$ m sections, and stained with hematoxylin and eosin (H&E).

Macroscopic examination of the kidney revealed a well circumscribed, yellowish-orange mass in the lower (4.5 cm) and upper (3.5 cm) parts of the kidney. Several smaller nodules in the hilar region were present. The ureteral lumen was dilated.

Renal cell carcinoma (RCC), mainly of clear cell type (Figure 3A) and a minor population of eosinophilic cells (Figure 3B) was infiltrating the capsule (Figure 3C), but without penetrating through. Tumor cells were also observed inside the lumen of some blood vessel groups. There were no signs of invasion of lymph nodes or the adrenal gland. Hilar nodules were enlarged, reactive lymph nodes.

Two duodenal tissue samples, up to 1cm, were obtained surgically and submitted to histopathological analysis. Pathological examination showed a typical, papillary mucinous adenocarcinoma (Figure 3D) infiltrated into the muscle wall of the duodenum. During the operation, partial resection of the duodenal mass was performed for diagnostic purposes because on the first biopsy, no tumor was obtained. Resection of the duodenum was performed in the second operation, after obtaining the patient's consent, and the diagnosis was confirmed.

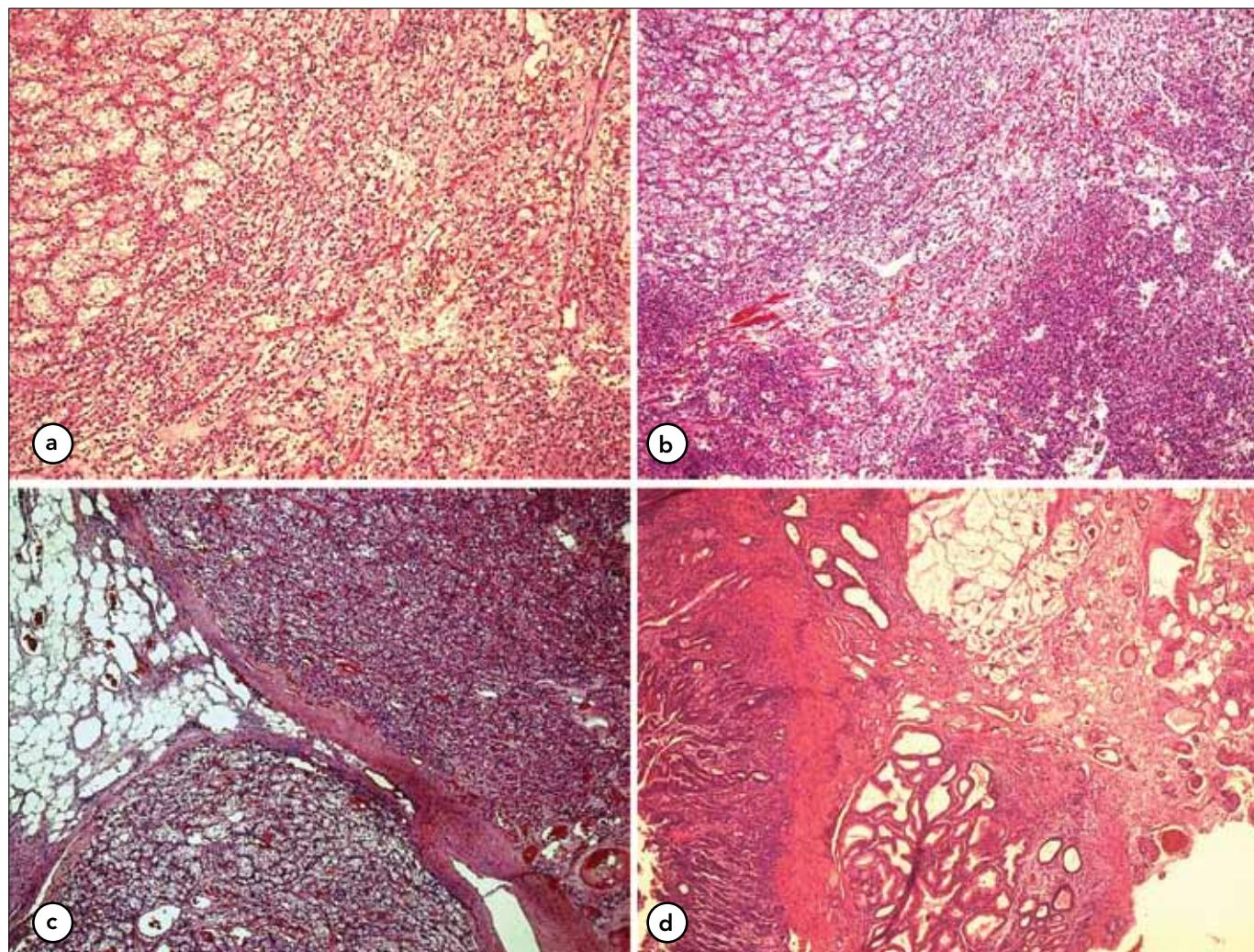
Both tumors have typical and quite different morphological appearances and two independent pathologists gave the same diagnosis. The probability of one tumor being the metastasis of the other was excluded due to the quite different histomorphologic appearances.

## Discussion

In surgery specimens (left radical nephrectomy and partial duodenectomy), a unique combination of a clear cell RCC and papillary mucinous adenocarcinoma of the duodenum were found. Based on the time of diagnosis, they were classified as simultaneous double primary malignant neoplasms.

To the best of our knowledge, this is the first case of such a combination of double primary malignant tumors described in the literature.

Although the small intestine contains 75% of mucosal surface in the gastrointestinal tract, only 1% of all GI tract adenocarcinomas are located in the duodenum (6). Small bowel adenocarcinomas are most frequent in the duodenum and they are often associated with a second simultaneous, (as in our patient), or after some period of time a primary malignancy at another intestine site (6). Scelo et al. (7) reported that there was a 68% increase in risk of a new cancer after a small intestine carcinoma. Most tumors are at an advanced stage when clinically diagnosed and the prognosis is poor (1). This is probably related to the liquid content of the small bowel, so the signs of obstruction are late or absent (6).



**Figure 3.** Microscopic appearance of renal cell carcinoma and duodenal mucinous adenocarcinoma, a) clear cell area of RCC (HE staining, 50x), b) clear cell and eosinophilic component of RCC (HE staining, 50x), c) RCC tumor cells do not penetrate capsule (HE staining, 50x) d) duodenal mucinous adenocarcinoma (HE staining, 50x)

HE: hematoxylin and eosin, RCC: Renal cell carcinoma

Conventional or clear cell RCC is the most common type of RCC, and it was diagnosed in our patient (1). According to a 2006 study, patients with papillary renal cell carcinoma are significantly more likely to have multiple malignancies, compared to patients with clear cell renal cell carcinoma, although no significant difference was found in the incidence of other primary tumors among histological subtypes of RCC (8).

There are various data, according to which other primary malignant tumors are the most frequently associated with RCC. Some authors found that GI tract tumors are the most common tumors (in accordance with our case), while others believe that prostate, breast, colon, bladder cancer and non-Hodgkin's lymphoma are the most common among double malignancies (1, 9).

Multiple tumors are usually found incidentally, during the preoperative workup of the primary tumor, or by physical examination and improved radiologic imaging (10). In our case, the patient was sent for further preoperative examination due to gastrointestinal symptoms, and the existence of another

tumor was diagnosed. According to the literature, incidentally detected RCC in MPMN is usually <4 cm in diameter, while in our case it was >4 cm in the lower half of the kidney and in the upper half in the hilar region (1).

Surgery was performed simultaneously, as suggested in most reports, especially if lesions require a single incision, and the patient's medical condition allows longer anesthesia exposure (9, 11). Although the imaging methods showed two tumors, the diagnosis of MPMN could not have been made without histopathological examination. RCC showed typical features of clear cell carcinoma cells with clear cytoplasm with solid, alveolar and acinar patterns, and a minor population of eosinophilic cells. On the other hand, the duodenal tumor showed tubular and papillary formations, cellular and nuclear pleomorphism with extracellular mucin production. Morphological features of both tumors were distinctive enough to set the diagnosis of two independent tumors, and exclude the possibility of one being the metastasis of the other. All findings confirmed the existence of MPMN in our patient.

## Conclusion

It is very important that clinicians and pathologists are open-minded and without prejudice when interpreting histological and imaging findings (12). Through this case, we wanted to point out the possibility of the occurrence of two primary tumors. As rare as they may be, they should always be taken into consideration.

## Conflict of Interest

No conflict of interest was declared by the authors.

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