ARAŞTIRMA MAKALESİ/ORIGINAL RESEARCH

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Synchronized Ampulla Vater Adenocarcinoma and Renal Cell Carcinoma: A Case Report and a Review of the Literature

Senkronize Ampulla Vater Adenokarsinom ve Renal Hücreli Harsinom: Bir Olgu Sunumu ve Literatürün Gözden Geçirilmesi

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ABSTRACT

INTRODUCTION: Synchronous primary tumors of the pancreas and kidney are extremely rare and poorly documented in the literature. The aim of this study is to present a case with primary synchronous pancreatic adenocarcinoma and renal cell carcinoma in light of the literature.
METHODS: A 60-year-old female patient was admitted to our outpatient clinic with a history of intermittent epigastric pain, nausea and vomiting for about 3 months. There was no family history of pancreatic and kidney disease or familial genetic syndromes. After the multidisciplinary team evaluation right nephrectomy with a Whipple procedure in the same session was performed.
RESULTS: In laboratory examinations serum carbohydrate antigen 19-9 and carcinoembryonic antigen levels were elevated. Endoscopic retrograde cholangiopancreatography, protruding and infiltrating ampulla was observed. In magnetic resonance imaging of the entire abdomen; A space-occupied lesion with hyperintense necrotic areas is observed anteriorly at the junction of the upper and middle poles of the right kidney, and was reported as a suggestion of renal cell carcinoma. In positron emission tomography; Heterogeneous hypermetabolism appearance was noted in the focus thought to belong to the duodenal loops and in the region corresponding to the level of the ampulla of Vater, and distant metastasis was not defined.
DISCUSSION AND CONCLUSION: More detailed epidemiological and molecular studies are needed to define the relationship between primary synchronous pancreatic and kidney tumors. In resectable cases radical surgical treatment is safe and should be considered as the primary treatment.
Keywords: pancreatic adenocarcinoma, renal cell carcinoma, synchronous primary cancers

ÖZ

GİRİŞ ve AMAÇ: Pankreas ve böbrekte senkron primer tümörler oldukça nadirdir. Ayrıca literatürde bu iki organda senkronize tümörler çok az sayıda ve yetersiz belgelenmiştir. Bu çalışmanın amacı; primer pankreas adenokarsinomu ile senkronize böbrek hücreli karsinom tanısı alan hasta ile birlikte literatürün gözden geçirilmesi ile pankreas kanserine eşlik edebilecek senkronize tümörlerin olabileceği ve bunun göz önünde bulundurulması gerekliliğini vurgulamaktır.
YÖNTEM ve GEREÇLER: Atmış yaşında kadın hasta, 3 aylık aralıklı epigastrik ağrı ile ilişkili bulantı ve kusma şikayeti ile polikliniğe başvurdu. Ailede pankreas ve böbrek hastalıkları veya ailesel genetik sendrom öyküsü yoktu. Tanısal tetkikler sonucu multidisipliner yaklaşım ile hasta değerlendirildi ve cerrahi kararı verildi. Whipple prosedürü ile birlikte aynı seansta sağ nefrektomi uygulandı.
BULGULAR: Labaratuvar incelemelerinde; serum karbonhidrat antijeni 19-9 ve karsinoembriyonik antijen seviyesinde yükseklik tespit edildi. Endoskopik retrograd kolanjio pankreatografi' de; ampullanın protrüze ve infiltratif olduğu izlendi ve mutipl biyopsi alındı. Tüm batın manyetik rezonans görüntülemede ise; sağ böbrek üst, orta pol bileşkesinde yer kaplayıcı lezyon izlenmektedir ve ön planda renal hücreli karsinom düşündürmektedir şeklinde raporlandı. Pozitron emisyon tomografisinde; ampulla vateri seviyesine uyan bölgede heterojen hipermetabolizma görünümü dikkati çekmiş olup, uzak metastaz tanımlanmadı şeklinde yorumlandı.
TARTIŞMA ve SONUÇ: Senkronize pankreas ve böbrek primer tümörleri arasındaki ilişkiyi tanımlayabilmek için, daha ayrıntılı epidemiyolojik ve moleküler araştırmalara ihtiyaç vardır. Ayrıca rezektabl vakalarda radikal cerrahi tedavinin güvenli olduğuna ve öncelikli tedavi olarak düşünülmesi gerektiğine inanmaktayız.
Anahtar Kelimeler: pankreas adenokarsinomu, böbrek hücreli karsinom, senkron primer kanserler

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INTRODUCTION

Multiple primary malignancies are uncommon conditions that account for approximately 1-3% of all cancers (1). In addition, the more widespread use of computed tomography for diagnosis and screening and also frequently using of ultrasonography for different indications have led to the finding of much more synchronized primary tumors (2).

The consequence of substantial improvements in cancer treatment has resulted in cure or longer survival. As a result of this, the incidence of primary, and secondary cancers, and also the incidence of multiple primary malignant tumors were expected to increase (3). In various studies, the incidence of primary pancreatic cancer with primary cancers of other organs has been reported to be between 1% and 20% (4). The most common secondary malignancies with pancreatic cancer are; tumors of the stomach, colon, thyroid gland, and genitourinary system (5).

Secondary malignancies reported to be associated with renal cell carcinoma include bladder, prostate, rectum, and lung cancer, as well as non-Hodginkin lymphoma and melanoma (6). Synchronized primary pancreatic and kidney tumors are extremely rare and poorly documented.

Renal cell carcinoma is the most common subtype of adult kidney cancer and surgical resection is the standard treatment (7). On the other hand, pancreatic adenocarcinoma is one of the deadliest cancers, and surgery is the standard treatment for resectable cancers (8).

The aim of this study is to present a unique case diagnosed with synchronous primary pancreatic adenocarcinoma and renal cell carcinoma and reviewed the literature.

CASE REPORT

A 60-year-old female patient was admitted to our outpatient clinic with a history of intermittent epigastric pain and nausea and vomiting for about 3 months associated with 12 kilograms of weight loss. There was no known co-morbidity, smoking or alchole abuse, family history of pancreatic and kidney diseases, or familial genetic syndrome.

On physical examination, no significant abnormalities were revealed. Laboratory investigations showed an increased level of total bilirubin (9.76 mg/dl), direct bilirubin (5.25 mg/dl), serum carbohydrate antigen 19-9 (CA 19-9) (44.36 Iu/ml) and carcinoembryonic antigen (CEA) (22.53 Iu/ ml) was detected. Endoscopic retrograde cholangiopancreatography (ERCP), protruding and infiltrating ampulla was observed and multiple biopsies was performed. Ampulla biopsy was reported as intraampullary neoplasia. In magnetic resonance imaging of the entire abdomen; A space-occupied lesion with hyperintense necrotic areas of approximately 58*40 mm is observed anteriorly at

the junction of the upper and middle poles of the right kidney, and it was reported as a suggestion of renal cell carcinoma in the foreground (Figure 1). In positron emission tomography; Heterogeneous hypermetabolism appearance was noted in the focus thought to belong to the duodenal loops and in the region corresponding to the level of the ampulla of Vater, and it was interpreted as malignant processes could not be ruled out on this basis (Figure 2).

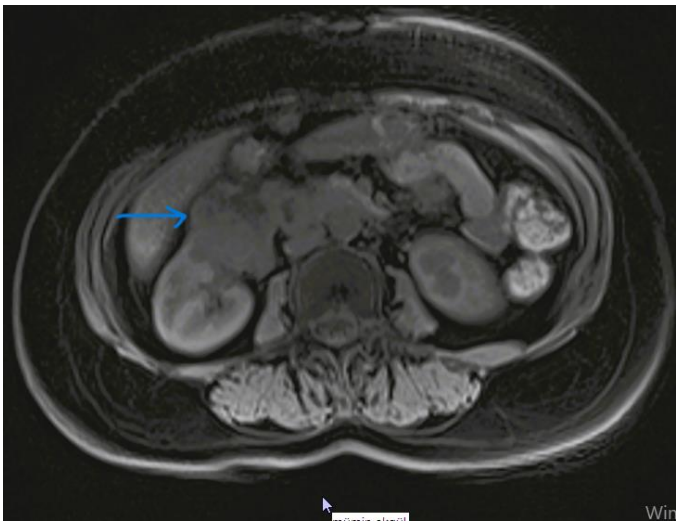

Figure 1: Heterogeneous right renal mass.

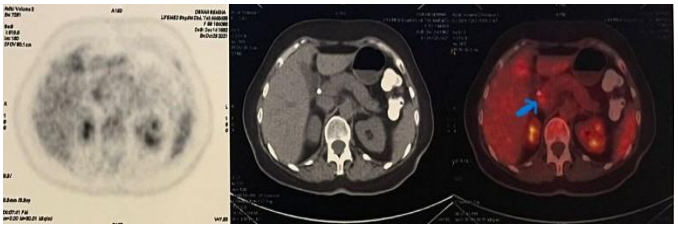

Figure 2: Heterogeneous hypermetabolism appearance in the ampulla vateri region.

The patient was evaluated by a team of medical oncology, radiology, urology, and surgery, and the surgical approach was the decision of the multidisciplinary team. The patient underwent right nephrectomy with a Whipple procedure in the same session (Figure 3). The operation was uneventful; during the postoperative follow-up, the patient was stable and discharged on the postoperative ninth day. The histopathological examination of the specimens was reported as synchronized primary renal cell carcinoma and adenocarcinoma of the ampulla vater (Figure 4).

Postoperative adjuvant chemotherapy is given, and a 14th-month close followed up was done. No problems were detected and follow-up continues.

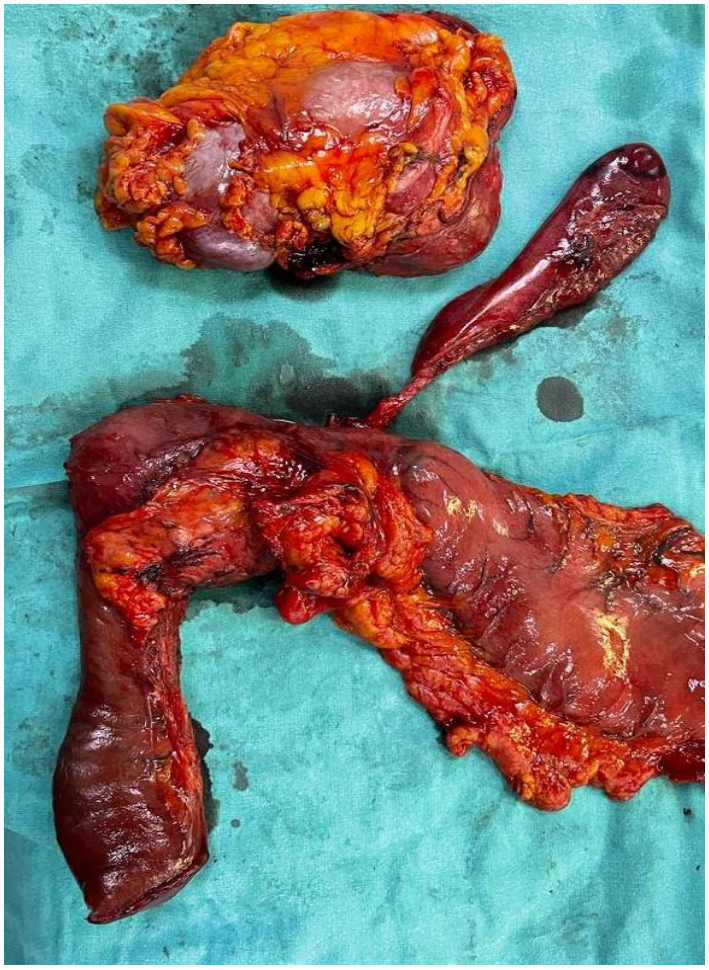

Figure 3: Gross specimen; Whipple procedure and right nephrectomy.

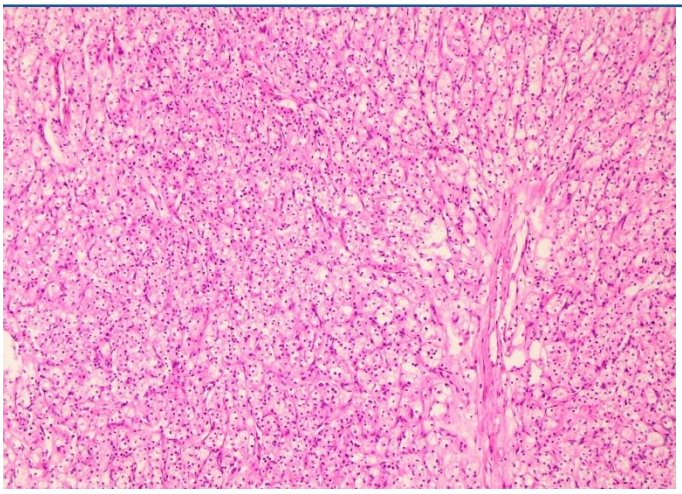

Figure 4a: Renal cell carcinoma, clear cell type area (Hematoxylin & Eosin 100x).

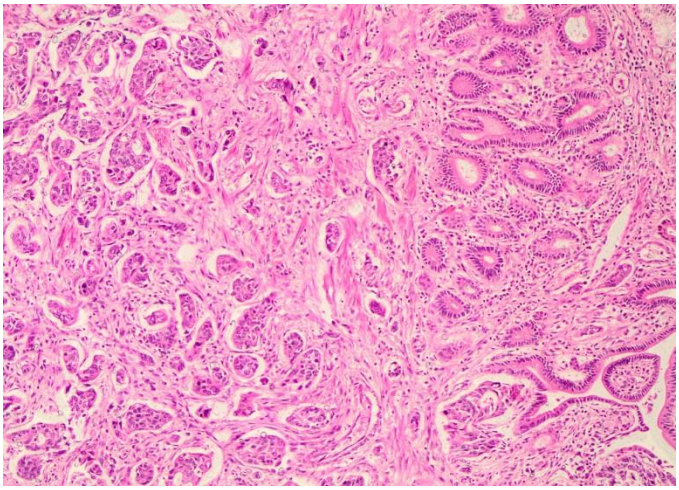

Figure 4b: Moderately differentiated adenocarcinoma of pancreatic origin (Hematoxylin & Eosin 100x).

DISCUSSION

Nowadays, there has been an increase in the rate of detection of second primary synchronous and metachronous cancers. This is due to improvements in radiologic diagnostic tools, mass screening, increasing patient age, and improving survival rates for patients with neoplastic disease (9). Most synchronous tumors involve the gastrointestinal tract and the genitourinary system, followed by the breast and gastrointestinal tract or the breast and genitourinary tract (1).

Several factors have been impacted in the development of synchronous primary tumors; however, the mechanisms of cancer development are not fully understood. Lifestyle, environmental factors (alcohol, smoking, occupational and environmental pollution), genetic predisposition, oncological treatments, immunological and hormonal factors, mutations in stem cells are the accused factor (10). Synchronized primary pancreatic and kidney tumors are extremely rare and have been reported in very few cases.

Sasaki et al. reported the first case of pancreatic and kidney synchronized tumors (11). Kontor et al. showed that a second primary cancer developed in 5% of 4176 patients with renal cell cancer, and only 6 of them had pancreatic cancer (0.14%); however, they did not find a statistically significant relationship (12). Alexakis et al. reported synchronous renal cell carcinoma in one case in their analysis of 373 patients with pancreatic cancer (13). In another series consisting of 763 patients who were operated for kidney cancer, synchronized pancreatic ductal adenocarcinoma was reported in 3 patients (14). Similarly, Muller et al. reported that synchronized pancreatic cancer was seen in 6 of 1178 patients who underwent an operation for kidney

cancer, and metachronous pancreatic cancer in 10 patients (9). Other publications concern only a few case reports (Table 1)

Table 1: Overview of the literature on synchronous pancreatic adenocarcinoma and renal cell carcinoma

Authors	Type of study	Cases, n	Procedure for PAC	Procedure for RCC	Short description
Ismail et al. (1)	Case report	1	Not resected.	Right nephrectomy	The patient underwent right radical nephrectomy and pancreatic biopsy (the reason for this management was the encasement of the celiac trunk). The patient was referred to the oncology department.
Müller et al. (9)	1,178 patients with pancreatic tumors and 518 patients with renal carcinoma	6	Total pancreatectomy was performed in 1 patient and Whipple was performed in 5 patients.	Partial nephrectomy was performed in 3 patients and nephrectomy was performed in 3 patients.	The median follow-up duration was 12.6 months. During the follow-up period 3 patients died because of either pancreatic cancer or its recurrence, whereas no patient died due to recurrent RCC.
Sasaki et al. (11)	Case report	1	No details.	No details.	Single patient with PAC, polyposis coli and RCC; No other details.
Kantor et al. (12)	4,176 patients with renal cell carcinoma in the Connecticut Tumor Registry	6	No details.	No details.	No details.
Alexakis et al. (13)	373 patients with pancreatic cancer in a single unit	1	Whipple	Left nephrectomy	He underwent a left nephrectomy and 6 weeks later he underwent a pylorus-preserving pancreaticoduodenectomy.
Rabbani et al. (14)	763 patients undergoing resection for RCC in a single unit	3	No details.	No details.	No details.
Olgyai et al. (17)	Case report	1	Distal pancreatectomy	Left nephrectomy	She received chemotherapy treatment after radical surgery in the same session.
Nobili et al. (18)	Case report	1	Whipple	Partial left nephrectomy	Mildly differentiated papillary carcinoma of kidney; intraductal papillary neoplasm without atypia of the pancreatic. No other details.
Mahfoud et al. (19)	Case report	1	Not resected	Not resected	Bone metastasis from clear cell renal cell carcinoma; In view of this association of a locally advanced pancreatic adenocarcinoma with the patient was treated with chemotherapy.
Present case	Case Report	1	Whipple	Right nephrectomy	She received chemotherapy treatment after radical surgery in the same session.

Most articles reporting an association between pancreatic and kidney cancer can provide few clinical details due to the low number of cases (6,9,11,12) such as the majority of patients are over 60 years of age and resection could be performed on small synchronized tumors detected in the early period. Environmental or genetic factors can be considered among the possible reasons for the synchronized appearance of these two tumors. Smoking is one of the most important environmental risk factors that increases the risk of pancreatic and renal cell cancer approximately two times (13). Although our case did not have a history of smoking, the region where she lived was a heavily industrialized region with intense environmental pollution. In some studies, genetic changes have been investigated to show the relationship in the development of synchronous tumors. Satake et al. detected a mutation in the 12th codon of the K-ras gene in a patient with synchronous pancreatic and kidney tumors (15). Molecular studies were not performed in our case, since there was no known history of familial genetic syndrome. However, genetic analysis of synchronized tumors seen in different organs can provide information about the etiology of genetic changes (16).

We believe that further analytical, epidemiological studies, and molecular investigations, including evaluation of genetic and environmental interactions, are necessary to specifically identify the causes of synchronized pancreatic and kidney tumors.

CONCLUSION

Synchronous pancreatic adenocarcinoma and primary renal cell carcinoma are extremely rare, but this possibility should always be kept in mind. We believe that radical surgical treatment is safe and should be considered as the primary treatment in resectable cases.

Conflict of Interest: The authors declare that they have no conflict of interests regarding content of this article.

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Informed Consent: Informed consent was obtained from all participants.

REFERENCES

1 Ismail TO, Janane A, Hajji F, Dekkak Y, Bekkali S, Sossa J, et al. Synchronous primary tumors of the kidney and pancreas: case report. Afr J Urol. 2010;16:128–131.

2 Porena M, Vespasiani G, Rosi P, Costantini E, Virgili G, Mearini E, et al. Incidentally detected renal cell carcinoma: role of ultrasonography. J Clin Ultrasound. 1992;20:395–400.

3 Mariotto AB, Rowland JH, Yabroff KR, Scoppa S, Hachey M, Ries L, et al. Long-term survivors of childhood cancers in the United States. Cancer Epidemiol Biomarkers Prev. 2009;18:1033–1040.

4 Eriguchi N, Aoyagi S, Hara M, Okuda K, Tamae T, Fukuda S, et al. Synchronous or metachronous double cancers of the pancreas and other organs: report on 12 cases. Surgery today.2000;30(8):718-721.

5 Gerdes B, Ziegler A, Ramaswamy A, Wild A, Langer P, Bartsch DK. Multiple primaries in pancreatic cancer patients: indicator of a genetic predisposition?. International journal of epidemiology. 2000;29(6): 999-1003.

6 Rabbani F, Grimaldi G, Russo P. Multiple primary malignancies in renal cell carcinoma. J Urol. 1998;160:1255–1259.

7 Kalra S, Atkinson BJ, Matrana MR, Matin SF, Wood CG, Karam JA, et al. Prognosis of patients with metastatic renal cell carcinoma and pancreatic metastases. J Clin Oncol. 2014;32:527–531.

8 Shima Y, Okabayashi T, Kozuki A, Sumiyoshi T, Tokumaru T, Saisaka Y, et al. Completion pancreatectomy for recurrent pancreatic cancer in the remnant pancreas: report of six cases and a review of the literature. Langenbeck's archives of surgery. 2015;400(8):973-978.

9 Müller SA, Pahernik S, Hinz U, Martin DJ, Wente MN, Hackert T, et al. Renal tumors and second primary pancreatic tumors: a relationship with clinical impact?. Patient Safety in Surgery. 2012; 6(1): 1-6.

10 Tomasetti C, Vogelstein B. Variation in cancer risk among tissues can be explained by the number of stem cell divisions. Science. 2015; 347(6217): 78-81.

11 Sasaki E, Kushida S, Okinaka T, Sasaki K, Abe S. Case report of double cancer of the pancreas and the kidney with polyposis of the large intestine. Gan no rinsho. Japan Journal of Cancer Clinics. 1969; 15(2). 203-206.

12 Kantor AF, McLaughlin JK, Curtis RE, Flannery JT, Fraumeni JR. Risk of second malignancy after cancers of the renal parenchyma, renal pelvis, and ureter. Cancer. 1986; 58(5): 1158-1161.

13 Alexakis N, Bosonnet L, Connor S, Ellis I, Sutton R, Campbell F, et al. Double resection for patients with pancreatic cancer and a second primary renal cell cancer. Digestive surgery. 2003; 20(5): 428-432.

14 Rabbani F, Reuter VE, Katz J, Russo P. Second primary malignancies associated with renal cell carcinoma: influence of histologic type. Urology. 2000;56(3):399-403.

15 Satake, K. Gene expression in synchronous tumors in different organs: Pancreas and other organs. Journal of Hepato-Biliary-Pancreatic Surgery. 1996; 3(2): 167-171.

16 Beisland C, Talleraas O, Bakke A, Norstein J.

Multiple primary malignancies in patients with renal cell carcinoma: a national population-based cohort study. BJU Int. 2006; 97: 698–702.

17 Olgyai G, Haulik L, Oláh A. Double resection for synchronous pancreatic and renal cell cancer-case report. Magyar Sebeszet. 2004; 57(5): 287-289.

18 Nobili C, Franciosi C, Degrate L, Caprotti R, Romano F, Perego E, et al. A case of pancreatic heterotopy of duodenal wall, intraductal papillary mucinous tumor and intraepithelial neoplasm of pancreas, papillary carcinoma of kidney in a single patient. Tumori Journal. 2006; 92(5): 455-458.

19 Mahfoud T, Tanz R, Khmamouche MR, Allaoui M, Belbaraka R, Khouchani M, et al. Synchronous primary renal cell carcinoma and pancreatic ductal adenocarcinoma: case report and literature review. Case Reports in Oncology. 2017; 10(3): 1050-1056.