

Bilateral and Synchronous Metastatic Sarcomatoid Renal Cell Carcinoma: Case Report

İki Taraflı ve Eş Zamanlı Metastatik Sarkomatoid Renal Hücreli Karsinom

Ferhat ATEŞ, MD,^a
Kenan KARADEMİR, MD,^a
İlker AKYOL, MD,^a
Ercan MALKOÇ, MD,^a
Zafer KÜÇÜKODACI, MD,^a
Kadir BAYKAL, MD^a

^aDepartment of Urology,
GATA Haydarpaşa Teaching Hospital,
İstanbul

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Yazışma Adresi/Correspondence:
Ferhat ATEŞ, MD
GATA Haydarpaşa Teaching Hospital,
Department of Urology, İstanbul,
TÜRKİYE/TURKEY
drferhatates@yahoo.com

ABSTRACT Renal cell carcinoma (RCC) accounts for 3% of all adult tumors. Between 1 to 4% of renal tumors are bilateral, whereas synchronous bilateral renal tumours occur rarely. Sarcomatoid variants of almost all histologic subtypes of RCC have been described and consist of 1 to 5% of RCC. Sarcomatoid RCC is an uncommon tumor of the renal parenchyma. We report a rare case of synchronous bilateral sarcomatoid renal cell carcinoma that affected a 70 year-old man who presented with fatigue, weight loss and severe bone pain. Biopsies of the renal tumors and hepatic mass demonstrated sarcomatoid renal cell carcinoma. Chest X-ray revealed two lesions in the inferior part of the right lung and bone scanning revealed multiple bone metastases. A few days after the establishment of definite diagnosis, the patient died before initiation of any treatment.

Key Words: Renal cell carcinoma; neoplasm metastasis; neoplasms, multiple primary

ÖZET Renal hücreli kanser (RHK) tüm erişkin tümörlerinin %3'ünü oluşturur. Renal tümörlerin %1 ile 4'ü iki taraflıdır, halbuki eş zamanlı ve iki taraflı renal tümör nadiren görülür. Renal hücreli kanserin hemen hemen tüm histolojik alt tiplerinde sarkomatoid varyant tanımlanmıştır ve RHK'nın %1 ile 5'ini oluşturur. Sarkomatoid RHK renal parankimin sık görülmeyen bir tümördür. Biz, halsizlik, kilo kaybı ve şiddetli kemik ağrısı ile başvuran 70 yaşındaki bir erkek hastada, nadir görülen, iki taraflı ve eş zamanlı sarkomatoid renal hücreli karsinom vakasını bildirmekteyiz. Renal tümörden ve karaciğerdeki kitleden alınan biyopsilerin sonucu renal hücreli karsinom olarak bulunmuştur. Akciğer grafisinde, akciğerin inferior bölümünde iki lezyon gösterilmiş ve kemik sintigrafisinde çok sayıda kemik metastazları saptanmıştır. Hasta tanının konulmasından birkaç gün sonra herhangi bir tedavi başlatılmadan önce kaybedilmiştir.

Anahtar Kelimeler: Renal hücreli karsinom; tümör metastazı; tümörler, çoklu primer

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Renal cell carcinoma (RCC) accounts for 3% of all adult tumors. Between 1 to 4% of renal tumors are bilateral, whereas synchronous bilateral renal tumours occur rarely.¹ Sarcomatoid variants of almost all histologic subtypes of RCC have been described and consist of 1 to 5% of RCC.² Sarcomatoid RCC is an uncommon tumor of the renal parenchyma. Major symptoms are the same as in the classic RCC: haematuria and flank pain. Tumor consists of a bimorphic feature of clear cells with areas of spindle cells and giant cells, resembling a sarcoma. Therapy is essentially surgical but in some cases chemotherapy may be beneficial.³

CASE REPORT

A 70-year-old male presented with fatigue, weight loss and severe bone pain for the last month. No significant abnormality could be detected on physical examination. He had microscopic haematuria, normochromic anemia (Hb:9.2 gr/dl), elevated erythrocyte sedimentation rate (109 mm/h) and alkaline phosphatase level (1400 IU/dL) at presentation. Chest X-ray revealed two lesions with diameters of 2 and 3 cm in the right inferior pulmonary lobe. Abdominal ultrasonography and subsequent tomography revealed bilateral renal masses (4 cm on the right and 6 cm on the left, respectively) and multiple hepatic lesions (Figure 1). No abnormality was detected on abdominal computed tomography (CT) which had been performed for an irrelevant problem ten months ago. The diagnosis of sarcomatoid type RCC was made upon the histopathological examination of the biopsies from the lesions in both kidneys and the liver. Hepatic masses were proven to be metastases of RCC.

Tru-cut biopsy of the renal mass revealed a solid tumoral infiltration consisting of cells with clear cytoplasm in a small area and spindle cells in other parts (Figure 2). Tumor cells had big hyperchromatic nuclei, some of which had big nucleoli, and narrow eosinophilic cytoplasm. A few tumor giant cells were seen as well. Tumor tissue showed



FIGURE 1: Abdominal computed tomography (CT) shows bilateral renal and hepatic masses.

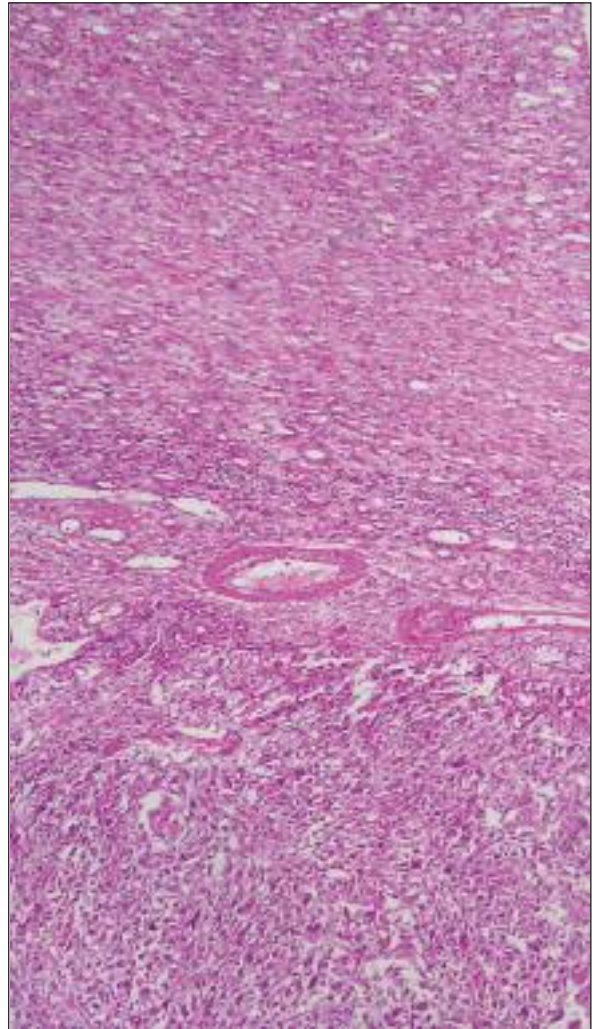


FIGURE 2: Kidney tissue in the upper part and tumoral infiltration in the lower part of the picture (HE, x40).

high mitotic activity with some atypical mitoses. Immunohistochemical evaluation showed positive staining of tumor cells with Vimentin (Figure 3), Epithelial Membrane Antigen (EMA) and pancytokeratin. Tru-cut biopsy of the lesion in the liver revealed a tumoral infiltration with similar morphology and immunohistochemical feature (Figure 4).

Bone scanning revealed multiple bone lesions that were interpreted as metastases. The general health status of the patient deteriorated during these studies and he died a few days after the establishment of the definite diagnosis and completion of the staging procedures.

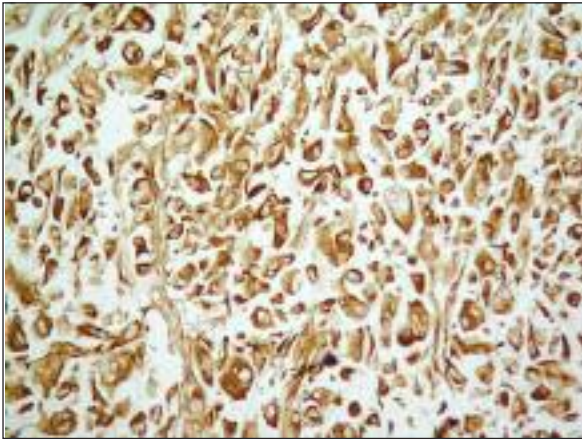


FIGURE 3: Immunoreactivity of tumor cells with vimentin (x400).

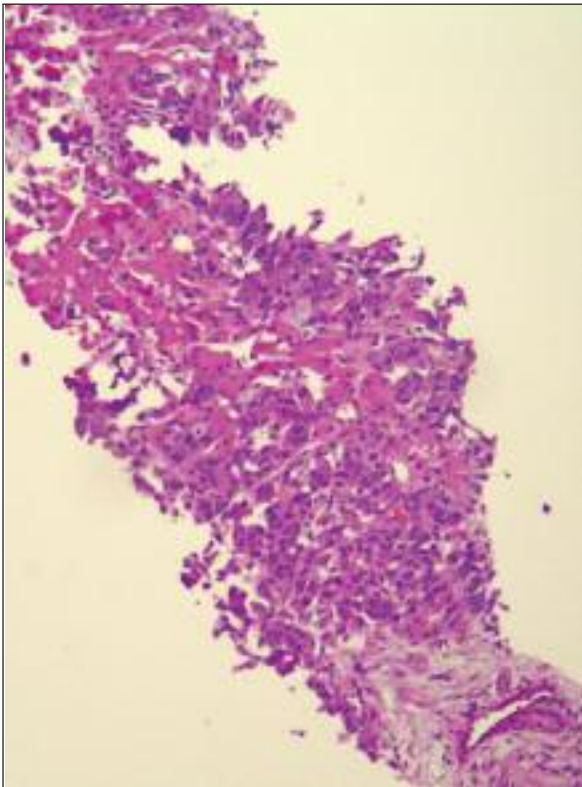


FIGURE 4: Tumoral infiltration in the liver (HE, x40).

DISCUSSION

Recent data suggest that sarcomatoid variants represent a poorly differentiated group of other histologic subtypes of RCC, rather than being independently derived tumors.¹ Histologic evaluations of the sarcomatoid tumors have frequently shown a mixed configuration of histologic subtypes of

RCC, especially clear cell and others as well, and pure sarcomatoid tumor is found rarely.² Thus, sarcomatoid RCC is no longer considered a distinct histologic subtype of RCC.

Followings have been proposed as indications for percutaneous biopsy for a renal mass: prior history of nonrenal malignancy, metastatic disease of unknown primary origin, previous contralateral nephrectomy for a renal cell neoplasm, a renal transplant mass, suspected renal lymphoma, history of tuberous sclerosis, and poor surgical candidacy.⁴ Discovery of novel targeted treatments for metastatic disease are now leading to wider indications for renal tumor biopsy.⁵

Pretreatment percutaneous biopsy can assist the urologist in clinical decision making, especially for elderly and unfit patients who are possible candidates for active surveillance and/or minimally invasive ablative therapies. Finally, there is potential for stratifying initial therapy of metastatic RCC by histological subtype and in the future molecular characteristics on needle biopsies.^{5,6} In the setting of metastatic disease, the histological characterization of a renal tumor may also be helpful to select the most suitable targeted treatment. With the development of new and improved techniques and increasing expertise, percutaneous needle core biopsy of renal masses is a safe and accurate diagnostic procedure.⁷ In our case, percutaneous biopsies from both renal and hepatic lesions were obtained in order to establish the primary histopathologic diagnosis and initiate systemic therapy accordingly. Hepatic metastases were reported as high grade RCC, whereas renal mass biopsies were typical of sarcomatoid RCC. This finding is in accordance with the fact that pure sarcomatoid tumor is very rare and its metastasis can be RCC.

Mian et al have reported 108 cases of sarcomatoid RCC. All of these tumors were unilateral and median survival of the metastatic patients was 8.5 months.³ Rothman et al reported that in cases of bilateral sporadic localized synchronous renal masses, a diagnosis of ipsilateral RCC was associated with contralateral RCC in the vast majority of patients. The rate of malignant concordance of the

histologic diagnoses between the two kidneys was 99% and 84-95% in their series and Fox Chase Cancer Center series, respectively.⁸

Stabellini et al reported a 52 year-old female presenting with uremia due to bilateral urinary tract obstruction caused by bilateral sarcomatoid RCC. The patient underwent bilateral nephrectomy and was on chronic hemodialysis treatment when she died from cachexia one month after the diagnosis.⁹

Minagawa et al reported a 68 year-old woman who had bilateral sarcomatoid RCC associated with von Hippel-Lindau disease. Synchronous bilateral RCCs were found in her kidney with metastases to lungs and liver. Right radical nephrectomy followed by transcatheter arterial embolization was performed for the tumor in the left kidney and interferon therapy was commenced. Interferon therapy was effective on both the tumors in left kidney and the metastatic masses in the lung. Four years after nephrectomy, the tumor in the left kidney grew progressively in size and partial left nephrectomy was performed. The patient eventually died of her disease 5 years after the resection of the primary tumor.¹⁰

Von Hippel-Lindau (VHL) syndrome is characterized by hemangioblastomas of the brain, spinal cord, and retina; renal cysts and clear cell renal cell carcinoma; pheochromocytoma; and endolymphatic sac tumors. Renal cell carcinoma occurs in about 40% of individuals with VHL.¹¹ Since our case had sarcomatoid RCC, and there were no signs of the tumors listed above, no evaluation to reveal a VHL gene mutation was planned. As a matter of fact, this might not have provided a prognostic benefit due to the unfavorable natural history of the disease.

Bird et al reported an unusual metastatic sarcomatoid RCC with cardiac, pulmonary and adrenal

metastases. The patient died fifteen months after nephrectomy, and autopsy revealed massive tumor infiltration of the heart, pulmonary and adrenal metastases and tumor nodules at the incision site.¹²

Our case had no lesion on abdominal CT ten months ago. He became symptomatic and died within 2 months after the initiation of symptoms. We suggest that bilaterality, sarcomatoid histology of the tumor and widespread metastases at presentation may have had a negative impact on the course of the disease.

Due to very poor prognosis of metastatic RCC with a median survival of 6-12 months, surgery is considered standard treatment in localized and metastatic diseases. Attempts to treat metastatic RCC have been unsuccessful. A few chemotherapeutic agents have limited efficacy. Currently, if surgery is unsuitable, combination of interleukin-2 and interferon- α is an acceptable treatment modality. However, the success of this treatment modality is limited and short-lived. There have been promising advances in proliferation-inhibiting agents in the management of metastatic RCC, and these might serve as a treatment option.¹³

Sarcomatoid renal cell carcinomas are rare renal tumors. They have a rapid course and are generally fatal. The median survival is less than 12 months even in patients diagnosed at an early stage. Radical nephrectomy is not curative. Several chemotherapy and immunotherapy protocols have been tried but none of them proved to be useful. Upon detecting bilateral renal masses, immediate action must be taken to make the histopathological diagnosis and to detect possible metastases. All of the appropriate treatment modalities should be initiated as soon as possible in these patients due to low survival. Studies on new treatment modalities for bilateral metastatic renal cell carcinoma are needed.

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