Sarcomatoid Chromophobe Renal Cell Carcinoma With Heterologous Sarcomatoid Elements

A Case Report and Review of the Literature

Gabriela Quiroga-Garza, MD; Hema Khurana, MD; Steven Shen, MD; Alberto G. Ayala, MD; Jae Y. Ro, MD

Chromophobe renal cell carcinoma (CRCC) is a distinct subtype of renal cell carcinoma (RCC) that is well known for its relatively good prognosis. Sarcomatoid transformation in this tumor, although rare, has been well documented in the literature and, as in other types of RCC, carries an ominous prognosis for the patient. The finding of heterologous elements in the sarcomatoid component of CRCC is an extraordinary event, which has been reported in only 2 previous cases. Here, we present the third such case, occurring in the left kidney of a previously healthy 63-year-old woman. The nephrectomy specimen showed CRCC with extensive sarcomatoid changes displaying heterologous elements in the form of chondrosarcomatous and osteosarcomatous differentiation. As in other sarcomatoid RCCs, this tumor behaves aggressively, with frequent distant metastases. It is important to recognize the sarcomatoid component in these tumors because of its consequential adverse prognosis for the patient.

(Arch Pathol Lab Med. 2009;133:1857–1860)

CLINICAL HISTORY

The patient is a 63-year-old previously healthy woman who presented in August 2006 complaining of episodes of nausea and mild left flank pain that started 2 months prior to her first medical visit. A computed tomography scan was obtained, which showed an upper pole left renal mass with renal vein involvement. Under the clinical diagnosis of RCC, she underwent a left radical nephrectomy with a periaortic lymph node dissection, as well as a left adrenalectomy and splenectomy. Three months after surgery, the patient was found to have multiple pulmonary nodules, along with hepatic and bone (sacral) metastases. The patient was treated with radiotherapy and chemotherapy for her distant metastatic disease. She is currently alive with disease 10 months after the diagnosis.

PATHOLOGY

Macroscopic Features

A radical nephrectomy specimen consisted of left kidney surrounded by perinephric adipose tissue and Gerota fascia (592 g), with the kidney alone measuring 12.0 × 8.0 × 6.0 cm. A 6.0 × 6.0 × 5.5 cm mass occupied most of the upper pole and displayed a gray-tan to yellow-tan tumor with areas of necrosis (40% of tumor), fibrosis, and calcification. The tumor invaded the overlying perinephric adipose tissue posteriorly. It also invaded the renal vein, forming an embolus (4.5 × 2.1 × 2.0 cm), with obstruction and dilatation of the vessel extending to within less than 0.1 cm of the margin. The tumor also appeared to involve the renal pelvis. Grossly, 1 of 12 submitted lymph nodes showed tumor metastasis. The adrenal gland was normal and free of tumor.

Microscopic Features

The sections of kidney showed a biphasic, malignant epithelial and sarcomatoid neoplasm, with CRCC as the carcinomatous element and a high-grade pleomorphic sarcoma as the sarcomatoid component (Figure 1). The latter displayed areas of osteosarcoma and chondrosarcoma (Figure 2). The sarcomatous element represented about 70% of the tumor, with 5% composed of osteosarcomatous and chondrosarcomatous components. Areas of calcification were seen at the periphery of the tumor, and there
was invasion into the perinephric fat and renal vein. One of the 12 lymph nodes showed metastatic disease exclusively composed of sarcomatoid component without the CRCC element. Tumor necrosis was about 40% of the total tumor volume. The adrenal gland and spleen were both free of tumor (T3bN1MX).

**Histochemistry and Immunohistochemistry**

The epithelial component was diffusely positive for Hale colloidal iron stain (Figure 3). The following immunohistochemical stains were used: AE1/AE3 (1:100; clone AE1/AE3, DAKO, Carpinteria, California); kidney-specific cadherin (1:75; clone 4H6/P9, Zymed, San Francisco, California); cytokeratin 7 (1:50; clone OV-TL12/30, DAKO); vimentin (1:500; clone V9, DAKO); c-kit (1:400; clone P145, DAKO); smooth muscle actin (SMA; 1:5; clone 1A4, Biogenex, San Ramon, California); MIB-1 (prediluted; clone Ki67, DAKO); and p53 (1:2000; clone DO-7, DAKO).

AE1/AE3 stain showed diffuse positivity, but there was only focal positivity for cytokeratin 7 in the epithelial component. Kidney-specific cadherin was also diffusely positive in the epithelial component (Figure 4), whereas vimentin, SMA, and c-kit were negative. In the sarcomatoid component, diffuse vimentin positivity (Figure 5) and focal SMA positivity were observed, whereas other markers, as well as Hale colloidal iron stain, were negative. Stain for MIB-1 showed strong positivity in more than 30% of the sarcomatoid cells, but only 10% in the epithelial component (Figure 6). Stain for p53 was negative in both the epithelial and sarcomatoid components.

**COMMENT**

Chromophobe renal cell carcinoma is an infrequent subtype of RCC, representing about 5.9% of total RCCs. The age of presentation may have a wide range, but it tends to occur in patients between 20 and 40 years old, which is a younger age presentation than that seen in other RCC subtypes. Chromophobe renal cell carcinoma is generally detected incidentally, but when symptomatic, it can present with hematuria, flank pain, and/or a mass. Radiologically, CRCC presents as a well-defined, homogeneously echoic, and hypovascular mass. Clinically, CRCC pa-
tients have been reported to have a more favorable prognosis than that associated with other histologic subtypes of RCC.2

In general, the incidence of sarcomatoid transformation in RCC is around 5%.3 This process is thought to result from dedifferentiation of the epithelial component, and so the sarcomatoid cells are expected to show the original genomic pattern of the “parent” cells. X-chromosome inactivation analysis has confirmed this hypothesis by showing different patterns of allelic loss in multiple chromosomal regions, indicating divergence during the clonal evolution of RCC.7 The sarcomatoid dedifferentiation in any type of RCC carries a poor prognosis for most patients,4 and most of them present with advanced stage at initial diagnosis. The disease-specific survival rate of sarcomatoid RCC is decreased compared with RCC without sarcomatoid change. The amount of sarcomatoid component (equal to or more than 50%) and lymphovascular invasion are also associated with decreased survival.8

Heterologous sarcomatoid transformation also has been reported in other histologic subtypes of sarcomatoid RCC, and conventional RCC is the main type of tumor to undergo this heterologous transformation. Its incidence is about 1.5% of all sarcomatoid RCCs.

Akhtar et al2 in 1997 first documented the sarcomatoid transformation in CRCC, and thereafter additional reports have been published.9–14 The incidence of sarcomatoid transformation observed in a large series of CRCC was 8.7%.3 Akhtar et al2 suggested that the sarcomatoid development in CRCC might be associated with its peculiar genetic profile, which would make the cells prone to hyperploidization. This observation has been extensively studied by Brunelli et al,15 who found that both the epithelial and sarcomatoid elements in a CRCC show different genetic abnormalities than those considered a “hallmark” of CRCC. The sarcomatoid CRCC shows multiple gains of chromosomes 1, 2, 6, 10, and 17.15

In most cases, the dedifferentiated elements, referred to as sarcomatoid components, are homologous in type, with a malignant fibrous histiocytoma-like or fibrosarcoma-like
pattern. However, there are only 2 previously reported patients whose tumors disclosed heterologous differentiation of the sarcomatoid component. The first case, published in 1999 by Hes et al., occurred in a 74-year-old patient with a sarcomatoid CRCC that exhibited osteosarcomatous, chondrosarcomatous, and rhabdomyosarcomatous elements. The second case, reported in 2002 by Itoh et al., was a 74-year-old man who had a CRCC with osteosarcomatous and chondrosarcomatous differentiation. The Table summarizes the major clinical and pathologic features of the previously reported cases, including the current case.

Chromophobe renal cell carcinoma is diffusely positive for Hale colloidal iron stain and usually expresses E-cadherin or kidney-specific cadherin, pancytokeratin (AE1/AE3), and CK7, but is negative for vimentin, c-kit, and SMA. The sarcomatoid component is positive for vimentin and negative for cytokeratin, colloidal iron, and cadherin. Our case revealed typical histochemical and immunohistochemical findings in the carcinomatous component, with AE1/AE3, kidney-specific cadherin, and CK7 positivity, and negativity with vimentin, SMA, and c-kit. In the sarcomatoid component, there was diffuse vimentin positivity and focal SMA positivity and negativity for colloidal iron stain as well as AE1/AE3, CK7, and kidney-specific cadherin. In addition, stain for MIB-1 showed strong positivity in more than 30% of the sarcomatoid cells, but only 10% in the epithelial component. Stain for p53 was negative in both the epithelial and sarcomatoid components.

Most of the previously reported cases of sarcomatoid CRCC are in concordance with the above-mentioned data. The mean age of presentation in the sarcomatoid CRCCs was higher than that of the ordinary CRCCs; sarcomatoid CRCCs were usually locally aggressive and patients presented with metastatic disease at the time of diagnosis. In general, survival of these patients was very short. As with any other type of RCC, these tumors are highly resistant to chemotherapy.

The primary histologic subtype of RCC, whether it has homologous or heterologous sarcomatoid components, is no longer significant to predict outcome, since the stage (TNM) of the lesion appears to be the only risk factor to predict outcome.

In the case of sarcomatoid CRCC, the situation is similar: the usual 5-year disease-specific survival rate of CRCC that is close to 100% and the 5-year progression-free survival of 94% drop to the levels comparable to those of other sarcomatoid RCCs.

It is very important to recognize CRCC as a distinct subtype of renal neoplasm, so much as the diagnosis implies a favorable prognosis to the patient. However, if sarcomatoid transformation develops, the patient's prognosis is very poor.

We report a case of CRCC with heterologous sarcomatoid elements with osteosarcomatous and chondrosarcomatous elements that is apparently the third reported case of heterologous sarcomatoid CRCC.

References