Orijinal Araştırma / Original Article

SARCOMATOID RENAL CELL CARCINOMA: CLINICOPATHOLOGIC FINDINGS IN 27 CASES

SARKOMATOİD RENAL HÜCRELİ KARSİNOM: 27 OLGUNUN KLİNİK VE PATOLOJİK BULGULARI

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Received / Başvuru Tarihi: 10-10-2011

Revised / Revizyon Tarihi: 18-11-2011

Accepted / Kabul Tarihi: 06-12-2011

ÖZET

Giriş: Renal hücreli karsinom (RCC) böbreğin en sık görülen malign neoplazmı olup sarkomatoid renal hücreli karsinom agresif bir tipidir. Sarkomatoid RCC'nin prognozu sarkomatoid olmayan RCC'lere göre oldukça agresiftir. Sarkomatoid RCC'de olgular lokalize evrede olsalar bile kür sıklıkla mümkün olmamaktadır. Bu çalışmada sarkomatoid diferansiasyonun literatürler eşliğinde progresyon ve sağkalıma olan etkisi değerlendirildi.

Materyal ve Metod: Ocak 1998 ve Ocak 2009 tarihleri arasında, renal hücreli karsinom ön tanısı ile radikal nefrektomi yapılan toplam 27 hasta retrospektif olarak değerlendirildi. Bütün hastalar fizik muayene, rutin hematolojik ve biyokimyasal tetkikler, abdominal tomografi, akciğer grafisi ve gerektiğinde Doppler ultrasonografi olmak üzere radyolojik tetkiklerle ve selektif bazı olgularda manyetik rezonans inceleme ile değerlendirildiler.

Bulgular: Hastaların ortanca yaşı 59.3 yıl ve ortalama takip süreleri 6 ay ile 4 yıl arasında değişmekte olup ortalama 1.25 yıl idi. Tümör çapları 3.5 cm ile 14 cm arasındaydı. Hastaların evrelere göre dağılımında pT1 evresinde 2 olgu, pT2 evresinde 14 olgu, pT3 evresinde 9 olgu ve pT4 evresinde ise 2 olgu bulunmaktaydı. Radikal nefrektomi materyalinin incelenmesi bütün hastalarsa sarkomatoid RCC olduğunu gösterdi. Bütün hastalarda Fuhrman Grade IV tümör bulunduğu görüldü. Evre pT3 ve pT4'de bulunan bütün hastalar kaybedildi. Takipler sonunda ortalama sağkalım oranı %25.9 (n=7) idi.

Tartışma: Bu çalışmanın sonuçları sarkomatoid RCC'nin agresif olduğunu ve genel sağkalımın bu tümör tipinde olukça kötü olduğunu göstermiştir. Erken tanı ve radikal cerrahi yaklaşım bu hastalarda yaşam beklentisinin artırılmasındaki temel seçeneklerdir. Bununla birlikte bu hastalarda radikal cerrahi yaklaşımlara rağmen kötü prognoz ve kısa sağkalım oranlarının olduğu gözönünde bulundurulmalıdır.

Anahtar Kelimeler: Böbrek, kanser, sarkomatoid diferansiasyon, radikal nefrektomi, sağkalım.

Abstract

Introduction: Renal cell carcinoma (RCC) is the most common malignant neoplasm of the kidney, and sarcomatoid RCC is an aggressive variant. The prognosis of sarcomatoid RCC is much more aggressive than that of nonsarcomatoid renal cell carcinoma tumors. Sarcomatoid renal cell carcinoma is often incurable, even when patients present with localized disease. In this study, the effects of sarcomatoid differentiation on progression and survival rate were evaluated and discussed in relation to the relevant findings in the literature.

Materials and Methods: Between January 1998 and January 2009, a total of 27 patients who underwent radical nephrectomy for renal cell carcinoma were retrospectively evaluated. All patients were evaluated by physical examination, routine hematologic and biochemical analysis, and radiologic studies, including abdominal computed tomography, chest X-ray, renal Doppler ultrasonography, if necessary, and in selected cases, magnetic resonance imaging.

Results: The median age of the patients was 59.3 years, and the mean follow-up period was 1.25 years, ranging from 6 months to 4 years. The tumor size ranged from 3.5 cm to 14.0 cm. The stage distribution was pT1 in 2 patients, pT2 in 14 patients, pT3 in 9 patients and pT4 in 2 patients. Histopathological examination of radical nephrectomy material showed sarcomatous differentiation in all patients. All patients had Fuhrman Grade IV tumors. All patients with tumors at stage pT3 and pT4 died. The mean survival rate was 25.9% (n=7) at the end of the follow-up period.

Conclusions: The results of this study demonstrate that sarcomatoid RCC is aggressive and that the overall prognosis is very poor with this tumor type. Early diagnosis and radical surgery are the only options available to increase life expectancy for these patients. However, the poor prognosis and short survival times of these patients despite radical surgical approaches should be considered.

Keywords: Kidney, cancer, sarcomatoid differentiation, radical nephrectomy, survival.

INTRODUCTION

Renal cell carcinoma (RCC) is the most common (85%) primary malignancy of the renal parenchyma and accounts for approximately 3.8% of all adult neoplasms. RCC displays a wide range of biological behavior, and up to 30% of RCC patients present at advanced stages; approximately 40% of patients who undergo curative surgical resection experience recurrence during the follow-up period (1,2). In the prediction of the prognosis of RCC, several important factors have been identified, including tumor volume, tumor stage, platelet count, age and histologic subtype (3,4). In renal cell carcinoma, known histologic subtypes include clear-cell adenocarcinoma (80%) and papillary (15%), chromophobe (5%), collecting-duct (1%), and unclassified (4%) carcinomas (5). Sarcomatoid renal cell carcinoma, characterized by the presence of intercellular bridges or keratinization, is an uncommon variant of renal malignancy (6). Sarcomatoid differentiation occurs in 10–20% of renal cell carcinomas. Sarcomatoid components can occur in all histologic subtypes of RCC. Patients with sarcomatoid renal cell carcinoma are rare and often present an aggressive clinical course characterized by rapid disease progression. However, there are conflicting reports concerning the prognostic value of quantifying the sarcomatoid component of RCC composition. In this study, the effects of sarcomatoid differentiation on progression and survival rate were evaluated and discussed based on a review of the relevant literature.

MATERIALS AND METHODS

Between January 1998 and January 2009, a total of 27 patients (19 men and 8 women) who underwent radical nephrectomy for RCC were retrospectively evaluated. All the patients had histologically verified RCC. Sixteen patients had a tumor on the right side, and 11 had a tumor on the left side.

All patients were evaluated with respect to pathologic stage, grade and prognosis. Preoperatively, all patients were evaluated with physical examination, routine hematologic and biochemical analysis, and radiologic studies including abdominal computed tomography, chest X-ray, renal Doppler ultrasonography, if necessary, and in selected cases, magnetic resonance imaging. Pathologic staging was performed according to the 1997 TNM (Tumor, node, metastasis) classification as stage pT1 (confined to the kidney), stage pT2 (involving perirenal fat but confined to Gerota's fascia), stage pT3 (gross renal vein involvement, lymphatic involvement, or both), or stage pT4 (adjacent organ involvement or distant metastasis), and the Fuhrman grading system was used for tumor grading. All patients were evaluated postoperatively every 3 to 6 months for the first 2 years and every 6 months thereafter. Follow-up consisted of physical examination, chest radiography, abdominal and thoracic CT, ultrasonography, biochemical and hematologic analysis, and, if indicated, cranial CT or radionuclide bone scanning.

RESULTS

The median age of the patients was 59.3 years, and the mean follow-up period was 1.25 years (range: 6 months to 4 years). The tumor size ranged from 3.5 cm to 14.0 cm. The stage distribution was pT1 in 2 patients, pT2 in 14 patients, pT3 in 9 patients and pT4 in 2 patients. Histopathological examination of radical nephrectomy material showed sarcomatous differentiation in all patients. All patients had Fuhrman grade IV tumors. The rates of sarcomatoid differentiation were 62.96% (n=17) in conventional RCC, 14.81% (n=4) in chromophobe RCC, 11.11% (n=3) in papillary RCC, and 11.11% (n=3) in collecting duct carcinoma. Although these tumors were diagnosed in the advanced

stages, three of our cases were incidentally discovered in the early stages. All patients with tumor stages pT3 and pT4 died. The mean survival rate was 25.9% (n=7) at the end of the follow-up period.

DISCUSSION

In the United States, the incidence of RCC has steadily increased over the past 50 years. Each year, RCC is responsible for approximately 2% of the new cancer cases in the United States and for the highest proportion of cancer-associated deaths compared with all other malignant urological diseases (7). Based on various cytogenetic and immunohistochemical features, there are several different histologic subtypes of RCC including clear-cell adenocarcinoma and papillary, chromophobe, collecting duct, and unclassified carcinomas. In addition, sarcomatoid components have been reported in RCC. Sarcomatoid RCC was first described by Farrow et al. in 1968. Sarcomatoid renal cell carcinoma is currently defined in the 2004 World Health Organization (WHO) classification of renal tumors as any histologic type of renal cell carcinoma (RCC) containing foci of high-grade malignant spindle cells (8). Sarcomatoid RCC is a distinct pathologic variant of RCC that is defined histologically by the presence of highly pleomorphic spindle cells and/or giant cells resembling sarcoma, along with a varying degree of clear or granular epithelial cells that typify RCC (9). Sarcomatoid RCC is a biphasic lesion with both mesenchymal (sarcomatous) and epithelial (carcinomatous) elements. The reported incidence of sarcomatoid RCC in the contemporary studies is between 1.2% and 13.90% of all kidney tumors (4,6,10). Although sarcomatoid components can occur in all histologic subtypes of RCC, several reports have indicated that sarcomatoid change more commonly occurs in chromophobe RCC compared with clear cell or papillary RCCs. Akthar et al. found 6 patients with an underlying chromophobe subtype among 11 patients with sarcomatoid RCC (11). In another study, Peralta-Venturina et al. studied 100 kidney tumors and found the rates for sarcomatoid differentiation to be 8% in conventional RCC, 9% in chromophobe RCC, 3% in papillary RCC, 29% in collecting-duct carcinoma and 11% in unclassified RCC (12). However, in another study, the authors found no chromophobe RCC, and the clear cell subtype was identified in half the cases (7). In present study the rates of sarcomatoid differentiation were 62.96% in conventional RCC and 14.81% in chromophobe RCC. Although these tumors were diagnosed in the advanced stages, three of our cases were incidentally discovered in the early stages.

In sarcomatoid RCC, the clinical symptoms and diagnosis do not differ from those of other RCCs. In addition to the classical prognostic factors, such as tumor stage and Fuhrman grade, several factors including necrosis and proportion of the sarcomatous component have been reported as factors in the prediction of the course of the disease. Cheville et al. reported that although a higher proportion of sarcomatoid change was associated with a poorer prognosis, this difference was not statistically significant (13). However, the majority of studies have revealed a strong relationship between sarcomatoid differentiation and prognosis. In this context, it has been reported that sarcomatoid RCC typically presents at an advanced stage. Sarcomatous differentiation is usually found in moderate- to high-grade tumors, often with deeply invasive behavior (9,12,13). In present study, all patients had Fuhrman grade IV tumors. Most authors have reported that the presence of a sarcomatoid component in RCC is generally associated with a poor prognosis, with a median survival following diagnosis of less than 1 year reported in the majority of studies. The median survival of this patient group is much shorter than for patients with conventional RCC presenting with localized disease. Klatte et al. reported that a sarcomatoid component accompanies

50% of metastatic RCC cases, that these cases have a tendency to display hepatic metastases and unresponsiveness to immunotherapy and that the prognosis is unfavorable (14). Cheville et al. studied 2381 patients treated with radical nephrectomy for clinically localized RCC. In that study, a total of 120 (5.0%) patients had RCC with sarcomatoid components, including 940 who died of RCC at a mean of 1.4 years after nephrectomy (13). The cancer-specific survival rates at 2 and 5 years following nephrectomy were 33.3% and 14.5%, respectively. The most important prognostic factors were the presence of distant metastases at the time of radical nephrectomy and histologic tumor necrosis. In a study of 101 patients with sarcomatoid RCC, de Peralta et al. reported a cancer-specific survival rate at 5 years of 22% and identified TNM stage as an independent predictor of patient outcome (12). Similarly, Mian et al. reported poor overall survival among 108 patients with sarcomatoid RCC and stated that patients with clinically localized disease survived significantly longer than patients with metastases (15). For this reason, careful postoperative follow-up for potential histological progression of RCC to the sarcomatoid subtype has been suggested. Similarly in our study the mean survival rate was detected as 25.9%.

In patients with sarcomatoid RCC, the reported median survival durations from the time of diagnosis are 3.8 to 6.8 months when no treatment is provided (16,17). Radical nephrectomy alone is often inadequate to achieve tumor control, even in those patients who present with localized disease. Several different regimens of systemic therapy, including chemotherapy and/or immunotherapy, have been used for the treatment of sarcomatoid renal cell carcinoma during the last 2 decades (18). The relationship between sarcomatoid differentiation and survival in patients with RCC who underwent radical nephrectomy or a variety of adjuvant therapies after radical nephrectomy has been evaluated in different studies. The response of RCC to chemotherapy and immunotherapy has been controversial. Although several studies based on small numbers of patients have shown occasional complete and few partial remissions, the overall results remain disappointing. Cangiano et al. suggested that surgical resection with high-dose IL-2-based immunotherapy may play a role in the treatment of sarcomatoid RCC in select patients (19). In another study, Sella et al. studied patients who were treated with various chemotherapeutic and immunotherapeutic agents and found longer median survival duration in treated patients than in untreated patients (16). In the current series, the addition of chemotherapy or radiotherapy after surgical resection did not appear to affect survival. The role of nephrectomy in patients with sarcomatoid renal cell carcinoma who present with metastatic disease thus remains uncertain. Based on the results of our study, we can state that renal cell carcinoma with a sarcomatoid component often shows local invasion, distant metastasis and a poor prognosis.

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