

Sarcomatoid renal cell carcinoma with rhabdoid features

Nagla Ahmed Al-Saidi, Mohammed Akhtar

From the King Faisal Specialist Hospital and Research Center - Pathology & Lab Medicine, Riyadh, Saudi Arabia

Correspondence: Dr. Mohammed Akhtar · King Faisal Specialist Hospital and Research Center - Pathology & Laboratory Medicine, DPLM - MBC 10 PO Box 3354 Riyadh 11211 Saudi Arabia · T: +966-11-4424280 F: +966-11-4424280 · makhtar69@kfshrc.edu.sa

Ann Saudi Med 2013; 33(5): 495-499

DOI: 10.5144/0256-4947.2013.495

Sarcomatoid renal cell carcinoma (SRCC) with rhabdoid features is a rare tumor with aggressive behavior and poor prognosis. We report a case of a 71-year-old man with a large left-sided renal mass. Nephrectomy specimen revealed clear cell carcinoma with sarcomatoid and rhabdoid tumor cells. The rhabdoid cells were immunoreactive for mesenchymal markers such as vimentin, epithelial markers such as cytokeratin, and epithelial membrane antigen. These cells were also positive for p53 and had a high proliferation index. The rhabdoid component also demonstrated the loss of immunostaining for integrase interactor 1 (INI1), which stained the other components of the tumor. Only a few cases are available in the published reports documenting rhabdoid cells in SRCC. None of these cases were studied by INI1 immunostain.

Rhabdoid tumor cells are characterized by large eccentric nuclei with prominent nucleoli and abundant eosinophilic cytoplasm containing globular paranuclear eosinophilic inclusions. These "rhabdoid inclusions" are composed of intermediate filaments that are consistently immunoreactive for vimentin with variable reactivity for other types of intermediate filaments.¹⁻⁴ Neoplasms with rhabdoid features have been encountered in many anatomic sites. In the kidney, malignant rhabdoid tumor was first recognized as a highly aggressive neoplasm in infants and children. Subsequently, several cases of rhabdoid tumor arising in a background of renal cell carcinoma in adults were reported. In a few studies, rhabdoid cells have been recognized as one of the cellular components in sarcomatoid renal carcinoma.²⁻⁶

In this report we described another case of SRCC with a rhabdoid component and briefly outlined histologic and immunohistochemical findings. We also briefly reviewed relevant published reports.

CASE

A 71-year-old man was found to have a left renal mass during a routine medical checkup. The patient was an ex-smoker and had a history of hypertension. He reported 2 episodes of hematuria during the past year, although he did not seek medical advice at that time.

His physical examination was otherwise unremarkable. The laboratory workup was within normal limits except for mildly elevated creatinine. Computed tomography (CT) revealed a heterogeneous, partly circumscribed, irregular (13×11×11 cm) mass occupying the upper and middle parts of the left kidney (**Figure 1**). A preoperative diagnosis was of a solid renal mass, most likely malignant. The patient underwent a transperitoneal left radical nephrectomy. A chest CT scan revealed multiple ill-defined small pulmonary nodules, more prominent in the right upper and middle lobes along with mildly enlarged mediastinal and retroperitoneal lymph nodes. These findings however, were not considered to be metastatic disease and were not pursued further.

PATHOLOGIC FINDINGS

The radical nephrectomy specimen weighed 1534 g and measured 15×13×11 cm. The cut surface revealed a variegated, partly cystic mass with grayish white nodularity and the areas of hemorrhage and necrosis. The mass virtually replaced the entire kidney except for a rim of uninvolved renal tissue in the lower pole (**Figure 2**). The tumor invaded the renal sinus, perirenal adipose tissue and renal vein.

Microscopically, the tumor was composed of clear cell carcinoma component constituting approximately 30% of the mass. The Furhman nuclear grade varied

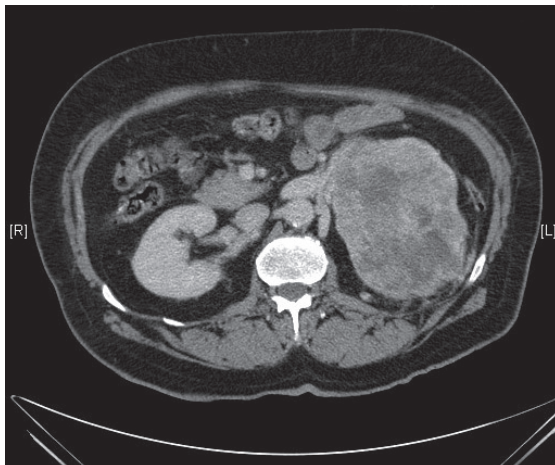


Figure 1. CT scans showing a large heterogeneous, irregular mass occupying the left kidney.

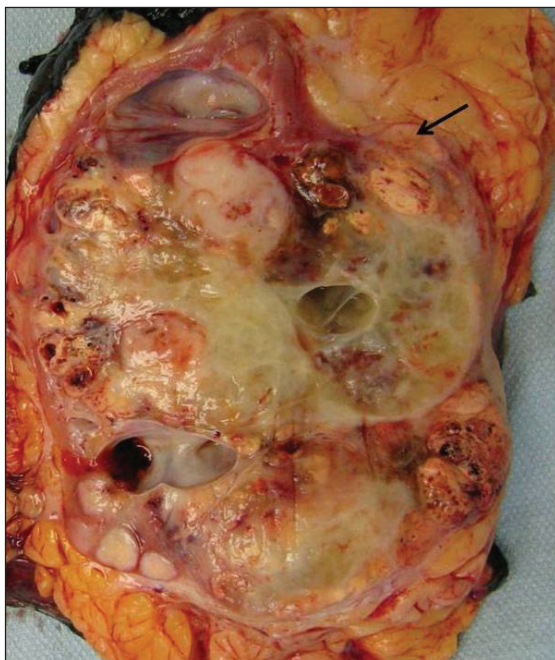


Figure 2. Variegated cystic and solid growth replacing most of the kidney and extending to the perirenal adipose tissue (arrow).

from 2 to 4. Approximately half the tumor consisted of spindle cell sarcomatous elements with large pleomorphic nuclei and brisk mitotic activity (Figures 3 and 4). The rest of the tumor was composed of discohesive polygonal to round cells with abundant cytoplasm containing eosinophilic rhabdoid inclusions (Figure 5). These cells also manifested large vesicular nuclei with prominent nucleoli and were present as variably sized aggregates among the spindle cells.

Immunohistochemical studies revealed all cellular

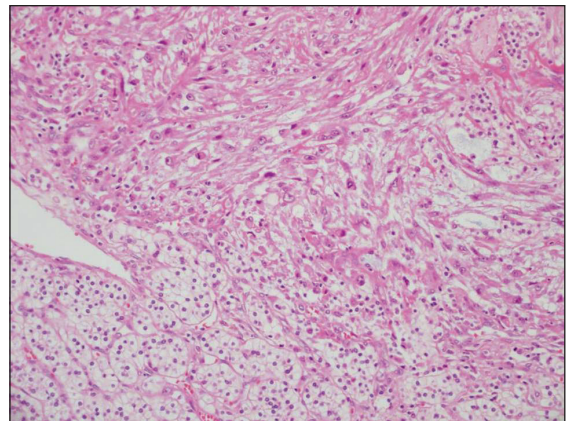


Figure 3. Photomicrograph depicting clear cell carcinoma (lower part) and spindle cell sarcomatoid carcinoma component (hematoxylin–eosin–safran, original magnification 100×).

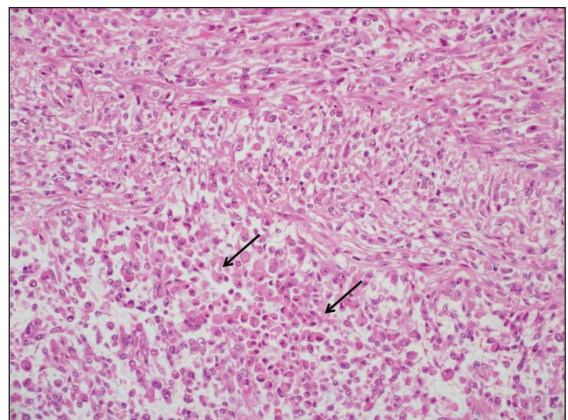


Figure 4. Photomicrograph showing transition between sarcomatoid and rhabdoid tumor cells (arrows) (hematoxylin and eosin stain, original magnification 200×).

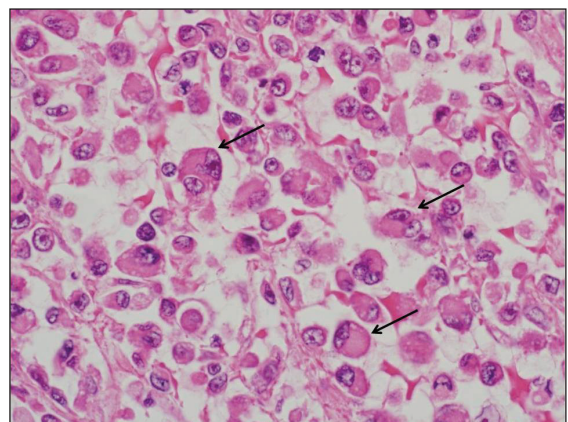


Figure 5. Higher magnification photomicrograph featuring large numbers of discohesive rhabdoid tumor cells (arrows) (hematoxylin and eosin stain, original magnification 400×).

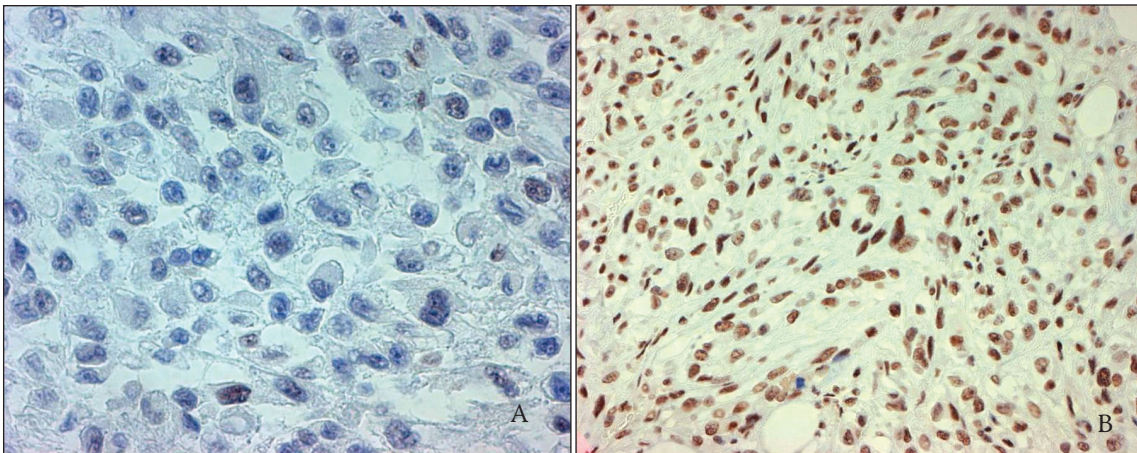


Figure 6. (A) Rhabdoid tumor cells with mostly negative staining for INI1 (original magnification 400 \times). (B) Sarcomatoid component of the tumor with prominent nuclear immunostaining for INI1 (original magnification 400 \times).

components of the tumor to be reactive for cytokeratin (AE1–AE3) (Figure 4). Vimentin was strongly and diffusely reactive in clear cell carcinoma as well as in spindle cell and rhabdoid components. Approximately 20% of the spindle cells and rhabdoid cells were reactive for p53, whereas the carcinoma component was mostly negative. Proliferation index (Ki67) was >90% in the spindle and rhabdoid cells, but was low (<1%) in the carcinomatous component. Epithelial membrane antigen (EMA) decorated most of the carcinoma cells (70%), but stained only a few scattered cells in the sarcomatoid and rhabdoid cellular elements. None of the tumor cells reacted with smooth muscle actin and desmin. Immunostaining for INI1 revealed strong diffuse reactivity in the sarcomatoid component with little or no staining in the rhabdoid tumor cells (Figure 6A and B).

DISCUSSION

Sarcomatoid renal cell carcinoma (SRCC) was first described by Farrow et al. as a tumor, exhibiting marked cytologic atypia and containing enlarged pleomorphic and malignant spindle cells reminiscent of sarcoma.⁷ SRCC represents 5%–8% of renal cell carcinomas (RCCs) and may arise from any of the subtypes including clear cell, papillary, chromophobe, and collecting duct carcinoma, among others. SRCC is characterized by a spindle cell histologic appearance with ultrastructural and immunohistochemical evidence of epithelial and mesenchymal differentiation. SRCC is highly aggressive with a high metastatic potential and extremely poor prognosis and with a median survival of less than 1 year following diagnosis. The mean age of the patients with SRCC is 60 years (range 33–80 years) with a male-to-female ratio of 1.6–15.8–10.

Rhabdoid tumor was first described in 1978 as a rare malignancy of the kidney in children and was initially thought to represent rhabdomyosarcomatous differentiation in Wilms tumor, with particularly aggressive behavior. Subsequently, similar tumors were recognized arising in other parts of the body.^{11,12} Furthermore, several types of high-grade sarcomas, such as synovial sarcomas, extraskeletal myxoid chondrosarcoma, and leiomyosarcoma, may also manifest rhabdoid differentiation.^{13–16} Rhabdoid features may also be encountered rarely in adult RCC. Gokden et al reported 23 cases of adult RCC with rhabdoid morphology and described their histologic, immunohistochemical, and ultrastructural features. Their study showed that RCCs with rhabdoid cells is an aggressive neoplasm with frequent fatal outcome even when rhabdoid component is only focal and limited to small areas within the tumor.¹

Presence of rhabdoid elements in SRCC is rare. In a study of 101 cases of SRCC, Mariza et al found 2 tumors with rhabdoid elements.⁵ Kuroiwa et al, studied eight cases of RCC with rhabdoid features and found sarcomatoid component in four of these cases.² In another study Leroy et al, reported their findings in 14 cases of RCC with rhabdoid features and found sarcomatous elements in one of these cases.³ The last case of RCC with sarcomatoid and rhabdoid element is reported by Fukata et al.⁶

Sarcomatoid and rhabdoid components of renal cell carcinoma show immunoreactivity for epithelial markers such as cytokeratin (AE1–AE3) and EMA, which is consistent with their presumed epithelial derivation. These cells, in addition, show strong positivity for vimentin, indicating additional mesenchymal differentiation in these cells. However, as reported in previous studies, sarcomatoid and rhabdoid cells lack any

myoblastic differentiation as indicated by the absence of staining for desmin and smooth muscle actin. It is also worth noting that in spite of their markedly different phenotypes, sarcomatoid, and rhabdoid cells appear to have similar immunohistochemical staining profile. This would support a common origin for these cells and also support the concept that both rhabdoid and sarcomatoid elements represent the final common dedifferentiation pathway of renal epithelial malignancies.^{1-3,5,17}

In our case, the carcinoma and the sarcomatoid components were strongly reactive for *INI1*, but the rhabdoid component was negative. *INI1* is a tumor suppressor gene, ubiquitously present in virtually all the cells. Molecular genetic investigations of malignant rhabdoid tumors have identified a characteristic loss or mutation of the *INI1* gene in chromosome band 22q11.² *INI1* is part of the SWI/SNF chromatin remodeling complex, which acts as both a transcriptional repressor and activator and is constitutively expressed in all cells. Germline mutations or deletions of *INI1* predispose patients to the development of rhabdoid tumors, and homozygous inactivation of *INI1* in human tumors supports its role as a tumor suppressor gene. Deletion and/or mutation of both copies of the *INI1* gene results in the loss of *INI1* expression at the protein level, which can be detected using immunohistochemistry with an anti-*INI1* antibody. *INI1* immunohistochemistry has been demonstrated to be sensitive and relatively specific for the diagnosis of malignant rhabdoid tumor. Recently *INI1* has also been implicated in the pathogenesis of additional tumor types including

renal medullary carcinomas and epithelioid sarcomas, a subset of epithelioid malignant peripheral nerve sheath tumors, myoepithelial carcinomas, extraskeletal myxoid chondrosarcomas, and pediatric undifferentiated sarcomas.^{18,19}

In most of the renal and extra renal rhabdoid tumors, immunohistochemistry has demonstrated a loss in the expression of *INI1*. Composite rhabdoid tumors in which rhabdoid cells represent 1 of several tumor components have been evaluated in 2 studies for *INI1* expression. Perry et al studied 14 composite rhabdoid tumors including meningiomas, carcinomas, melanomas, glioblastomas, and a neuroblastoma.²⁰ *INI1* expression was retained in all of the tumors except for 1 retroperitoneal leiomyosarcoma. Donner et al studied 2 endometrial carcinomas with rhabdoid cells and demonstrated the loss of *INI1* in 1 case.²¹ To the best of our knowledge, none of the previously described SRCCs with rhabdoid elements have been studied for *INI1* expression.

SRCC is known to have a poor prognosis. From the small number of cases reported so far, it is not clear whether the presence of rhabdoid elements in these tumors has any additional adverse prognostic impact. In our case, as reported in previous studies, both cellular elements were reactive for p53 and showed a high proliferation index on Ki67 staining. These findings are consistent with the aggressive nature of each one of these elements. It may be suggested that the presence of either one of these components is predictive of aggressive behavior and poor clinical outcome.

REFERENCES

1. Gokden N, Nappi O, Swanson PE, et al. Renal cell carcinoma with rhabdoid features. *Am J Surg Pathol.* Oct 2000; 24:1329-38.
2. Kuroiwa K, Kinoshita Y, Shiratsuchi H, et al. Renal cell carcinoma with rhabdoid features: an aggressive neoplasm. *Histopathology.* Dec 2002; 41:538-48.
3. Leroy X, Zini L, Buob D, Ballereau C, Villers A, Aubert S. Renal cell carcinoma with rhabdoid features: an aggressive neoplasm with over expression of p53. *Arch Pathol Lab Med.* Jan 2007; 131:102-6.
4. Haas JE, Palmer NF, Weinberg AG, Beckwith JB. Ultrastructure of malignant rhabdoid tumor of the kidney; a distinctive renal tumor of children. *Hum Pathol.* 1981;12:646-657.
5. Mariza de Peralta-Venturina M, Moch H, Amin M, et al. Sarcomatoid differentiation in renal cell carcinoma: a study of 101 cases. *Am J Surg Pathol.* Mar 2001; 25:275-84.
6. Fukata, Satoshi K, Takashi T, Makoto K, Naoto S, Taro. Renal cell carcinoma with Rhabdoid features and sarcomatoid change. *Acta Urologica Japonica.* 2010; 65(4).
7. Farrow GM, Harrison AG, Utz DC. Sarcoma and sarcomatoid and mixed malignant tumors of the kidney in adults. Part III. *Cancer.* 1968; 22:556-563.
8. Cheville JC, Lohse CM, Zincke H, Weaver AL, Leibovich BC, Frank I, et al. Sarcomatoid renal cell carcinoma: an examination of underlying histologic subtype and an analysis of associations with patient outcome. *Am J Surg Pathol* 2004; 28:435-40
9. Cheol K, Young H.P, et al. Sarcomatoid differentiation as a prognostic factor for Immunotherapy in metastatic Renal Cell Carcinoma. *J. Surg. Oncol.* 2007; 95:317-323
10. Oda H, Nakatsuru Y, Ishikawa T. Mutations of the p53 gene and p53 protein over expression are associated with sarcomatoid transformation in renal cell carcinomas. *Cancer Res.* 1995; 55:658-662.
11. Beckwith JB, Palmar NF. Histopathology and prognosis of Wilms' tumors: results from the first National Wilms' Tumor Study. *Cancer* 1978; 41; 1937-1948.
12. Peng HQ, Stanek AE, Teichberg S, Shepard B, Kahn E. Malignant rhabdoid tumor of the kidney in an adult: a case report and review of the literature. *Arch Pathol Lab Med.* Sep 2003; 127(9):e371-3.
13. Yumi Oshiro, Hideki Shiratsuchi, Yoshinao Oda, Satoshi Toyoshima, Masazumi Tsuneyoshi. Rhabdoid Features in Leiomyosarcoma of Soft Tissue: With Special Reference to Aggressive Behavior. *Mod Pathol* 2000;13:1211-1218.
14. J Knapik, AT Yachnis, D Ripley, JA Biegel, S Rathor, NS Hardt, A Talerman, EJ Wilkinson. Aggressive uterine sarcoma with rhabdoid features: diagnosis by peritoneal fluid cytology. *Hum Pathol* 2001; 32: 884-6.
15. Mauricio A. Paláu L, Tina Thu Pham, Nicola Barnard, and Maria J. Merino. Primary sarcoma of the kidney with rhabdoid features *Int J surg Pathol.* October 2007; 15: 421-428.
16. Oshiro y, Shiratsuchi H, Tamiya S, Oda Y, Toyoshima S. Tsuneyoshi M. Extraskelletal Myxoid Chondrosarcoma with Rhabdoid Features, with Special Reference to Its Aggressive Behavior. *Int J Surg Pathol.* 2000; 8: 145-152.
17. DeLong W, Grignon DJ, Eberwein P, Shum DT, Wyatt JK. Sarcomatoid renal cell carcinoma. An immuno-histochemical study of 18 cases. *Arch Pathol Lab Med.* 1993; 117: 636-40
18. Hollman TJ, Homick JL. INI1-deficient tumors: diagnostic features and molecular genetics. *Am J Surg Pathol* 2011, 35: e47-63
19. Kreiger PA, Judkins AR, Russo PA, Biegel JA, Lestini BJ, Assanasen C, Pawel BR. Loss of INI1 expression defines a unique subset of pediatric undifferentiated soft tissue sarcomas. *Modern Pathology* 2009; 22: 142-150.
20. Perry A, Fuller CE, Judkins AR, Dehner LP and Biegel JA. INI1 expression is retained in composite rhabdoid tumors, including rhabdoid meningiomas. *Modern Pathology* 2005; 951-958.
21. Donner LR, Wainwright LM, Zhang F, Biegel JA. Mutation of the INI1 gene in composite rhabdoid tumor of the endometrium. *Human Pathology* 2007; 38: 935- 939.