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Renal cell carcinoma with rhabdoid features. Divergent differentiation of conventional (clear cell) carcinoma

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Summary

A rare case of renal cell carcinoma (RCC) with rhabdoid features in an adult man is presented. This tumor with rhabdoid features, also known as composite neoplasm, represents a pattern of progression emerging from specific histologic RCC types. RCC with rhabdoid features is a highly aggressive neoplasm and its malignant behavior may be due to the high-cell proliferation activity of the rhabdoid areas. Rhabdoid features in RCC may represent a final pathway of differentiation in clonal progression to a high-grade, aggressive biologic state.

Key words: immunohistochemistry, morphology, renal cell carcinoma, rhabdoid features

Introduction

Adult RCC with rhabdoid features is a recently recognized morphologic variant of kidney carcinoma.

This neoplasm, also known as "Composite" tumor, most frequently is composed of conventional RCC with 10-50% of the tumor consisting of cells with rhabdoid features [1,2]. These cells are characterized by a large abundant eosinophilic cytoplasm containing a globular inclusion and an irregular eccentric nucleus with a prominent nucleolus.

Tumors displaying rhabdoid features have been reported in broad range of epithelial and mesenchymal neoplasms such as malignant melanoma, gastric adenocarcinoma, neuroendocrine carcinomas of the pancreas, pulmonary carcinomas, RCC, meningiomas, endometrial stromal tumors, and soft tissue sarcomas [3-7]. The rhabdoid change has been generally associated with a poor prognosis and is most often present in tumors with a poorly differentiated morphology [2,4,5,8,9].

RCC with rhabdoid features has been reported in a few studies in the literature [8-11]. We present the clinicopathologic features and immunohistochemical findings in a case of rhabdoid RCC.

Case presentation

A 60-year-old man presented with flank discomfort, gross intermittent haematuria and a palpable abdominal mass. CT of the abdomen showed a 13 cm mass in the right kidney. Work-up for metastatic disease was negative. Of interest was the fact that his mother had died from renal carcinoma. Radical nephrectomy was performed and the specimen was sent for pathological examination. The postoperative course was uneventful. No adjuvant therapy was given. Ten months postoperatively the patient is alive without evidence of disease.

Pathologic features

The kidney weighed 900 g and measured 16×10×8

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cm. On bisecting the specimen, a 13 cm in greatest diameter variegated solid mass was identified. Several white circumscribed nodules constituting 30% of the mass, were embedded in a yellow, hemorrhagic and necrotic tumor (Figure 1). The tumor involved the renal pelvis and penetrated the renal capsule.

Microscopically, the yellow hemorrhagic areas and the white nodules of the tumor corresponded with clear cell and eosinophilic cell areas of a RCC, respectively. The clear and eosinophilic cell areas were sharply separated from each other with or without a thin fibrous band (Figure 2).

The clear cell areas consisted of smaller tumor cells with a moderate amount of clear cytoplasm and centrally placed, moderately atypical nuclei with distinct to prominent nucleoli (nuclear grade 3, according to the Fuhrman scheme). Numerous arborising capillaries were present in the clear cell areas but not in the eosinophilic cell areas.

The eosinophilic cell areas were comprised of high grade round or polygonal cells with abundant eosinophilic cytoplasm and a globular intracytoplasmic inclusion body (Figure 3). The nuclei were large, eccentrically placed with macronucleoli. Architecturally, most of the eosinophilic areas showed a sheet-like or pseudoglandular pattern. Tumor necrosis was focally present. The eosinophilic cells were observed at the area of capsular invasion.

Immunohistochemical studies showed that the clear cells were positive for vimentin, neuron-specific enolase (NSE), pancytokeratins AE1/AE3, and negative for CK7. The eosinophilic inclusion bodies were immunostained by cytokeratins AE1/AE3 (Figure 4) and vimentin (Figure 5). EMA (epithelial membrane antigen) was positive and decorated the cytoplasmic membrane. Stains for CK7, CD117 and HMB-45 were negative. Immunostains indicative of muscle differentiation (desmin, a-smooth muscle actin and myoglobin) were negative in the eosinophilic rhabdoid cells. A nuclear positivity for p53 was detected in a small number of tumor cells (less than 5% of nuclei were positive).

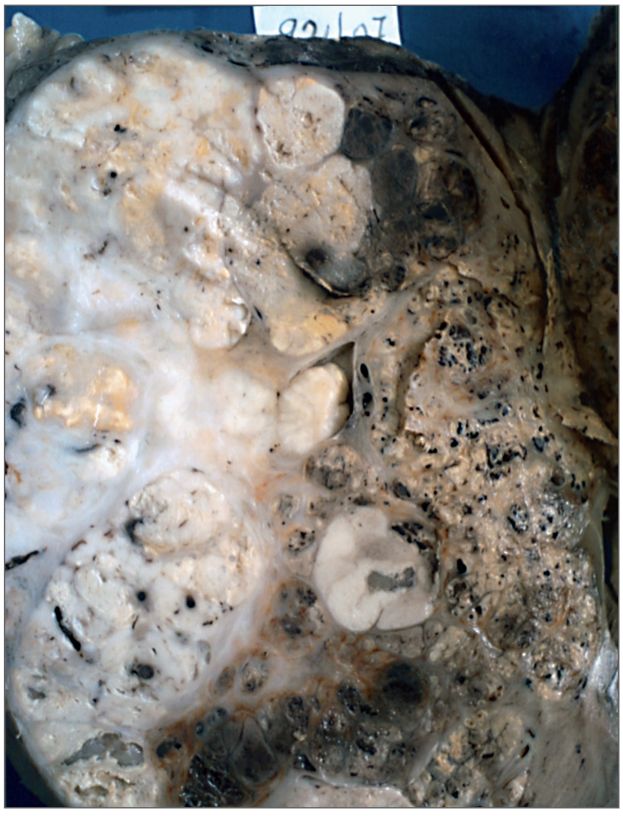

Figure 1. Gross appearance of the tumor: the yellow hemorrhagic areas represent clear RCC whereas the white areas represent the rhabdoid foci.

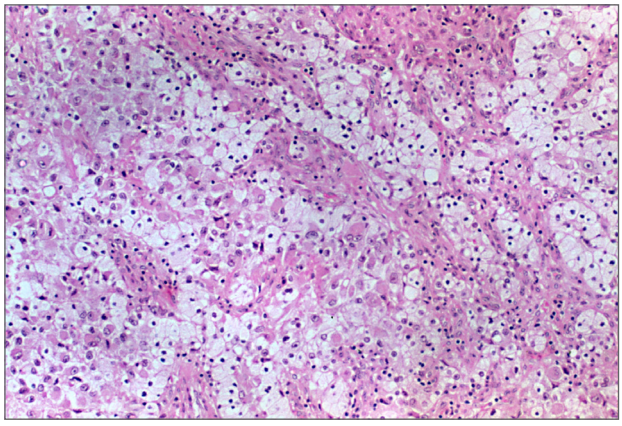

Figure 2. Transition between rhabdoid cells and conventional clear cell carcinoma cells (H&E × 125).

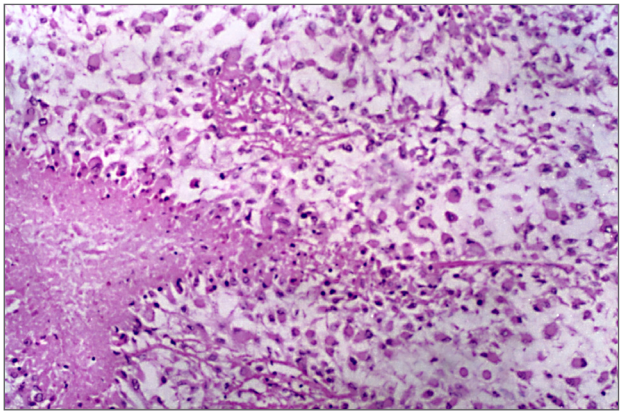

Figure 3. Rhabdoid tumor cells with eccentric nuclei and prominent nucleoli, and large paranuclear intracytoplasmic globules (H&E × 125).

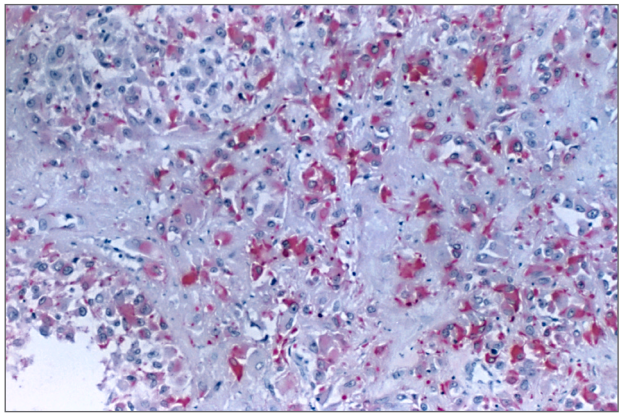

Figure 4. Strong positivity with cytokeratins AE1/AE3 is seen in the globoid cytoplasmic inclusions of rhabdoid cells (ABC × 125).

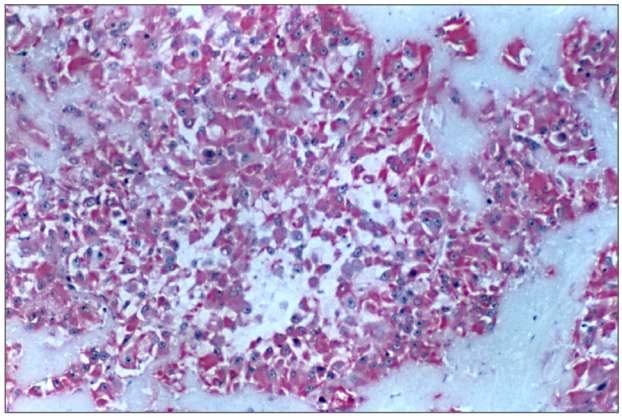

Figure 5. Strong immunoreactivity for vimentin accentuating in the paranuclear regions of the rhabdoid tumor cells (ABC × 125).

Immunoreactivity for K1-67 antigen, a cell-proliferation factor, has been investigated. The mean K1-67 labeling index of the rhabdoid areas was significantly higher than that in the clear cell area: 8.30% and 2.65%, respectively.

Discussion

Adult RCC with rhabdoid features, described herein, represents an unusual morphologic variant of clear cell RCC. A rhabdoid component may be also observed in papillary, chromophobe, or collecting duct carcinomas [8-12].

Clinically, our patient presented with the classic triad of flank pain, gross haematuria and palpable abdominal mass. In their study of 14 RCCs with rhabdoid features, Leroy et al. [1] reported that the flank discomfort occurred in 21.4%, macroscopic haematuria in 14.2% and a palpable lumbar mass in 28.5% of patients. RCCs with rhabdoid features occur in adults with a mean age of 61.8 years (range 33-84) [8]. The ultrasonographic appearance of RCC with rhabdoid features was similar to other renal solid tumors.

The overall incidence of rhabdoid features in RCC varies considerably. Godken et al. identified 23 (4.7%) RCCs with rhabdoid features among 480 cases [8]. Rhabdoid tumors accounted for 7.4% of RCCs in the study of Shannon et al. [10] and 3.2% of RCCs reported by Kuroiwa et al. [9]. The rhabdoid areas constituted 10-90% of the tumor mass. The rhabdoid component ranged in size from 1 mm to more than 2 cm in maximum dimensions. Such foci were present in RCCs with a mean diameter of 8.8 cm (range 4-15) [7]. In our case the size of the rhabdoid component was 4 cm, whereas the entire tumor size was 13.0 cm.

The gross appearance, histology and immunohistochemistry of the rhabdoid cells in RCC are similar to that of the pediatric rhabdoid tumor of the kidney [1,8-11]. Macroscopically, the white firmer areas with homogeneous cut surface often represent the rhabdoid components while the hemorrhagic areas are composed of conventional RCC, reflecting the greater vascularity of conventional RCC component.

Microscopically, rhabdoid cells are characteristically large, round or oval with abundant cytoplasm containing an eosinophilic globular paranuclear inclusion. Nuclei are large, eccentrically placed with macronucleoli. Rhabdoid cells are arranged in sheets or sometimes in pseudoglandular formations. Tumor necrosis is very common in rhabdoid areas. The rhabdoid cells, in our case, were of higher nuclear grade (Fuhrman grade 4/4) than the surrounding conventional RCC.

Immunohistochemically, the rhabdoid cells have marked positivity for vimentin. Rhabdoid cells also have an epithelial phenotype with expression of pan-cytokeratins and EMA. This profile is consistent with the previous description of rhabdoid cells in RCC with rhabdoid features. [1,8-10].

No staining is obtained for CK7, CK20, HMB-45 and CD117. Despite the rhabdoid appearance of the cells there is no evidence of myogenic differentiation by immunohistochemistry.

p53 in our study was expressed in less than 5% of the nuclei. This was also noted by Miyagi et al. [6] in their report of 3 cases. Leroy et al. [1] found positive expression of p53 in 10 of 14 tumors in the rhabdoid areas (5-50% of tumor cells stained) and only in 5 of 14 cases in usual clear renal cell areas. An overexpression of p53 in the rhabdoid component may be implicated

in the tumor differentiation [1,13]. p53 overexpression also appeared to be of value in predicting tumor recurrence and progression [1,13-15]. In our case, K1-67 labeling index of the rhabdoid areas was higher than that of the carcinomatous areas. K1-67 is considered as an index of tumor proliferative activity and as an additional prognostic indicator of progressive aggressiveness in RCC with rhabdoid component [4-6,10].

Pathologists should carefully search for a rhabdoid component in RCC, and, when present, it should be reported because it is a marker of high risk for metastasis and a very poor prognosis even when the rhabdoid area is limited. Rhabdoid features represent an endpoint of clonal evolution in RCC [8].

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