



Urothelial carcinoma with rhabdoid features: report of 6 cases

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Received 1 September 2005; revised 6 October 2005; accepted 11 October 2005

Keywords:

Extrarenal rhabdoid tumors;
Hematuria;
Obstructive symptoms;
Cytokeratin markers

Summary Extrarenal rhabdoid tumors have been described in a variety of primary sites with only rare case reports of urothelial carcinomas with rhabdoid features in the literature. In this report, we describe the clinicopathologic characteristics, including clinical follow-up on 6 cases of urothelial carcinoma with prominent rhabdoid features. Four cases were retrieved from the consultation files of one of the authors and 2 were retrieved from the surgical pathology files at our institution. The patients were all men, with ages ranging from 53 to 86 years (mean, 66.5 years). Patients initially presented with hematuria or obstructive symptoms. The sites included bladder (n = 4) and renal pelvis (n = 2). All cases had a prominent rhabdoid component (mean, 60%), ranging from 40% to 80%. In addition to the rhabdoid component, multiple coexistent histological components were seen, including in situ urothelial carcinoma (carcinoma in situ) and high-grade papillary urothelial carcinoma (n = 2), poorly differentiated carcinoma with small-cell features (n = 1), sarcomatoid (n = 2), and a myxoid component (n = 2). All cases in this series had focal or diffuse positive staining with one or more cytokeratin markers (epithelial membrane antigen, CAM 5.2, AE1/AE3). Of the 6 patients, 4 were treated initially with surgery (radical cystoprostatectomy, n = 2; radical nephrectomy, n = 2). Of 6 patients, 2 died within 1 month, whereas a third patient died within 4 months. The remaining 3 patients were alive at 3, 3, and 9 months after diagnosis. The histological and immunohistochemical findings in this study serve to broaden the morphological spectrum of urothelial carcinomas with prominent rhabdoid features and add further evidence as to their poor prognosis.

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1. Introduction

Urothelial carcinomas with rhabdoid differentiation are rare with only a limited number of case reports described in the literature. Rhabdoid cells are large and round or oval, with abundant cytoplasm containing a brightly eosinophilic

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Table 1 Clinicopathologic features

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Age (y)/sex	68/Male	53/Male	62/Male	68/Male	86/Male	62/Male
Clinical presentation	Hematuria	Hematuria	Hematuria	Repeated UTI, recurrent urethral stricture	Hematuria, dysuria, prostate adenocarcinoma, renal failure	Hematuria
Tumor location	Posterior wall bladder	Left lateral wall bladder	Left renal pelvis	Bladder and lower aspect of abdominal wall	Trigone bladder with obstruction of ureters	Left kidney, renal pelvis, with extension into adrenal
Tumor size (cm)	4 × 4 × 3	3 × 2.5 × 0.3	7 × 3.2 × 3	10 × 8 × 10.6	NA	5.5 × 2.5 × 0.6
Treatment	Radical cystoprostatectomy	Radical cystoprostatectomy	Radical nephrectomy	None	Bilateral nephrostomy tubes	Radical nephrectomy
Clinical follow-up	Died	Alive	Died	Died	Alive	Alive
Survival (mo)	4	9	1	1	3	3

Abbreviation: UTI, urinary tract infection; NA, not assessed.

body, vesicular nuclei, and a prominent nucleolus. The exact cell of origin is still not known. Ultrastructural studies have confirmed that the eosinophilic body corresponds to whorls of intermediate filaments [1].

Tumors with a rhabdoid differentiation have been described in a variety of primary sites with only rare reports of urothelial carcinomas with rhabdoid features in the literature [2-6]. In this report, we describe the clinicopathologic characteristics including clinical follow-up of 6 cases of urothelial carcinoma with prominent rhabdoid features.

2. Materials and methods

We prospectively identified cases of urothelial carcinoma with a rhabdoid phenotype from 1990 to 2003 from our consultation and surgical pathology files. Four cases were retrieved from the consultation files of one of the authors (J. I. E.). Two of the cases were retrieved from the surgical pathology files at our institutions. Clinical information including follow-up was obtained when available. In addition to submitted immunohistochemical stains, unstained paraffin sections from representative slides were immunostained using standard protocols with a 3-step biotin-streptavidin procedure. The antibodies used included cytokeratin AE1/AE3 (1:4000; Chemicon, Temecula, Calif), cytokeratin CAM 5.2 (1:2; Beckton, San Jose, Calif), cytokeratin 7 (1:500; DAKO, Carpinteria, Calif), chromogranin (1:4000; Chemicon), desmin (1:100; DAKO), epithelial membrane antigen (EMA, 1:1000; DAKO), HMB45 (1:500; DAKO), Melan A (1:200; DAKO), neuron-specific enolase (NSE, 1:2000; DAKO), S-100 (1:6000; DAKO), smooth muscle actin (1:200; DAKO), and thrombomodulin (1:100; DAKO). For all analyses, appropriate negative and positive controls were included.

3. Results

3.1. Clinicopathologic features

The clinical presentation, tumor location, treatment, and clinical follow-up on the 6 cases with available information are summarized in Table 1. All patients were men (age, 53-86 years) and presented with hematuria (n = 5) or recurrent urinary tract infections secondary to urethral stricture (n = 1). One of the patients had a prior history of prostatic adenocarcinoma and was treated for Lupron for 10 years before presentation with the bladder carcinoma.

3.2. Histological features

All 6 cases had in common the presence of prominent rhabdoid features. The rhabdoid component ranged from 40% to 80%. Characteristic rhabdoid cells were large and

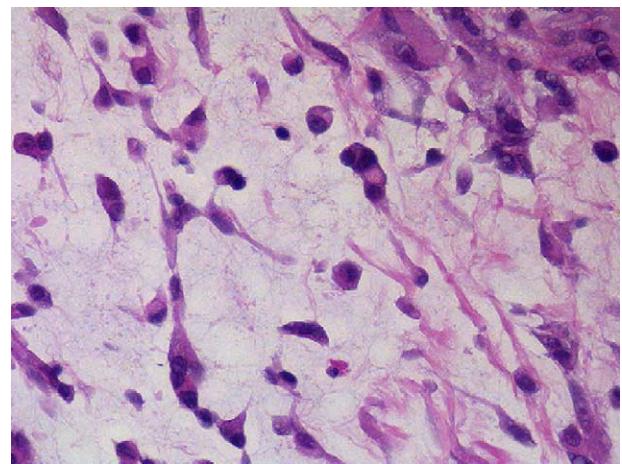


Fig. 1 Case 2: characteristic large rhabdoid cells with abundant cytoplasm containing a brightly eosinophilic body, vesicular nuclei, and a prominent nucleolus in a myxoid background.

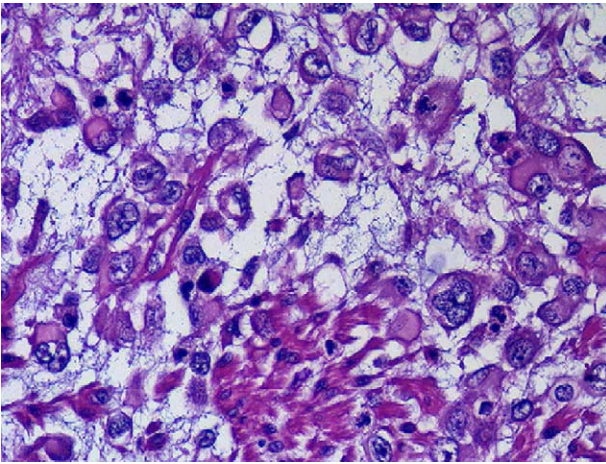


Fig. 2 Case 4: large round and oval rhabdoid cells with prominent nucleoli.

round or oval with abundant cytoplasm containing a brightly eosinophilic body, vesicular nuclei, and a prominent nucleolus (Fig. 1 and 2). Rhabdoid cells were discohesive and were present singly, in clusters, and/or in large sheets (Fig. 3). Macroscopic features were nonspecific with the exception that case 1 was polypoid and case 6 had a papillary configuration.

The first case was a poorly differentiated carcinoma of the bladder with rhabdoid and small-cell features (4.0 cm). The small-cell component was less predominant than the rhabdoid component (Fig. 4), with the rhabdoid component comprising approximately 80% of the total tumor. Characteristic rhabdoid cells intermixed with the small-cell component were observed (Fig. 5). The carcinoma arose in association with flat carcinoma in situ and extended through the bladder muscularis and into the perivesical fat. The same patient also had a small focus of prostatic adenocarcinoma (Gleason grade 3 + 3 = 6).

The second case was a poorly differentiated malignant tumor of the bladder with multiple histological patterns

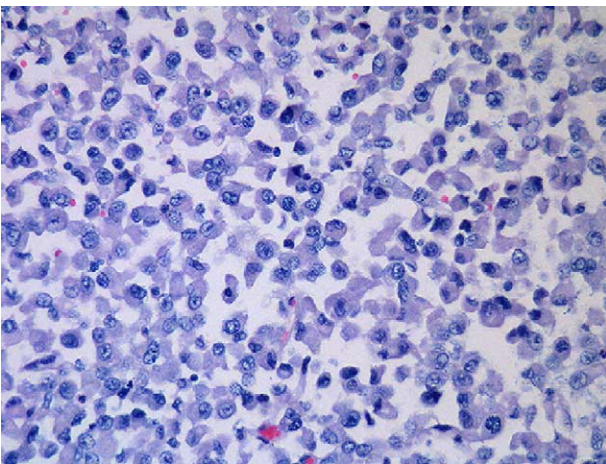


Fig. 3 Case 3: rhabdoid cells, some of which were discohesive, present either singly, in clusters, and/or in large sheets.

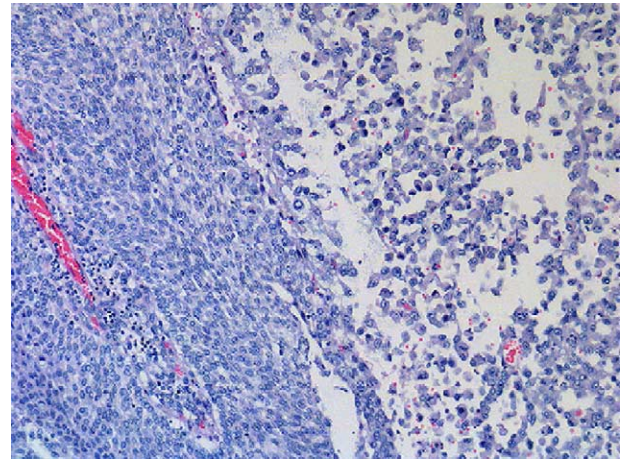


Fig. 4 Case 3: in situ and infiltrating high-grade papillary urothelial carcinoma of the renal pelvis. Urothelial components (left) intermixed with the rhabdoid components (right).

including rhabdoid, sarcomatoid, and myxoid, with invasion of the muscularis propria. Large, pleomorphic rhabdoid cells were abundant, comprising approximately 70% of the tumor (Fig. 1).

The third case was in situ and infiltrating high-grade papillary urothelial carcinoma of the renal pelvis, with prominent rhabdoid and myxoid features (Fig. 3). Although the urothelial components were intermixed with the rhabdoid components, in other areas, 2 distinct populations were seen. The rhabdoid components made up approximately 50% of the tumor. The carcinoma involved the renal pelvis and extended into perinephric fat.

The fourth and fifth cases were urothelial carcinomas originating in the bladder with prominent rhabdoid features, occupying 60% of each tumor. The tumor from the fourth case also had focal myxoid features. In the fourth case, characteristic rhabdoid cells were intermixed with more pleomorphic cells (Fig. 2).

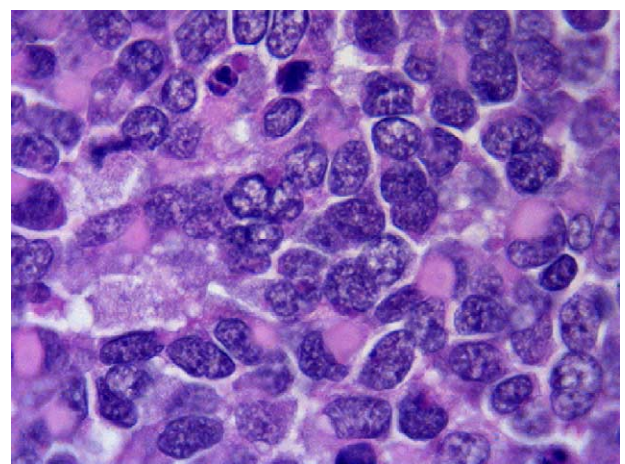


Fig. 5 Case 1: characteristic rhabdoid cells intermixed with the small-cell component.

Table 2 Immunohistochemical staining results of the rhabdoid component

Antibody	Case 1 ^a	Case 2 ^b	Case 3	Case 4 ^c	Case 5	Case 6 ^d
Cytokeratin CAM 5.2	+	–	+	ND	+	–
Cytokeratin AE1/AE3	ND	–	+	–	ND	+
EMA	+	+	+	+	+	–
Smooth muscle actin	–	ND	–	ND	–	–
S-100	ND	+	–	ND	ND	ND

Abbreviation: ND, not done.

^a The first case had mixed rhabdoid and small-cell and showed strong positivity for chromogranin and NSE in the small-cell component.

^b The second case was also negative for HMB45 and Melan A.

^c The fourth case was also negative for CK7, thrombomodulin, and desmin.

^d The urothelial component of the sixth case was also positive CAM 5.2 and EMA.

The sixth case was in situ and infiltrating high-grade papillary urothelial carcinoma of the renal pelvis, with prominent rhabdoid and sarcomatoid features. The rhabdoid component comprised approximately 40% of the total tumor. The carcinoma extended into perinephric fat and adrenal gland. Multiple positive lymph nodes were present with extranodal tumor extension.

3.3. Immunohistochemistry

The immunohistochemical staining patterns of the 6 cases are presented in Table 2. The first case with mixed rhabdoid and small-cell components showed prominent dotlike positivity for cytokeratin (CAM 5.2) and EMA in the rhabdoid component and strong positivity for chromogranin and NSE in the small-cell component (Table 2). Immunohistochemical stains for cytokeratin showed either dotlike positivity or diffuse cytoplasmic staining in the rhabdoid component of the tumors (Table 2).

3.4. Follow-up

Of 5 patients, 2 died within 1 month, whereas a third patient died within 4 months. The remaining 3 patients were alive at 3, 3, and 9 months after diagnosis, respectively (Table 1). Of the 6 patients, 4 were treated initially with surgery (radical cystoprostatectomy, n = 2; radical nephrectomy, n = 2).

4. Discussion

Rhabdoid tumor was first described in the kidneys and was initially thought to be a sarcomatous variant of Wilms tumor by Beckwith and Palmer [7] in 1978 because of the resemblance of the cells to rhabdomyoblasts. Subsequently, Harris et al [4] coined the term “rhabdoid tumor.” Additional studies did not confirm the myogenic differentiation in these tumors. Rhabdoid tumors were later considered to be a distinct type of malignant renal tumor [8]. Renal rhabdoid tumor has been described as a solid tumor that is seen only in childhood, with most cases occurring in the first 2 years of life [5,9,10].

Malignant tumors with rhabdoid features in adults in extrarenal locations are considered to be phenotypic variants. Tumors with rhabdoid morphology have been described in all age groups and from multiple sites, including the extremities, brain, liver, mediastinum, orbit, heart, and others, and is now accepted as a discrete entity [3,10,11]. The rhabdoid phenotype has characteristic histological, ultrastructural, immunohistochemical, and cytogenetic findings [10]. Tumor cells are discohesive and are present either singly, in clusters, and/or in large sheets [1]. This neoplasm demonstrates a characteristic morphology with large pleomorphic cells with large nuclei and nucleoli. There is abundant cytoplasm containing eosinophilic inclusions that are composed of intermediate filaments. The tumors generally have a histological appearance similar to that of renal rhabdoid tumors. Ultrastructural studies have confirmed that the eosinophilic body corresponds to whorls of intermediate filaments. Immunohistochemical analysis usually demonstrates reactivity to vimentin, desmin, and keratin. Extrarenal rhabdoid tumors do not demonstrate skeletal muscle components by immunohistochemical analysis or electron microscopy. Cytogenetic analyses of rhabdoid tumors in children have shown a balanced translocation involving the short arm of chromosome 6 (6p12) and the long arm of chromosome 22 (22q11) [10]. More recently, a candidate tumor suppressor gene for malignant rhabdoid tumors in children, *INI1*, has been described in the same location (22q11) [12,13]. The cytogenetic and molecular changes in our cases would not necessarily be expected to show similar changes.

In the present report, we describe 6 cases of urothelial carcinoma with prominent rhabdoid features. Of the 6 cases in our series, 4 involved the bladder, whereas 2 cases originated in the renal pelvis. There have been only rare case reports of urothelial carcinomas with rhabdoid features in the literature [2-4,6,14]. Patients have ranged in age from 2 to 84 years. Rhabdoid differentiation is most commonly associated with urothelial carcinoma, as seen in the 6 cases described in this report. Duvdevani et al [2] and Kumar et al [6] have described cases of pure rhabdoid tumor of the bladder with no additional histological components. Rhabdoid component has also been described as a focal finding in a case of malignant fibrous histiocytoma of the bladder [14]. Harris

et al [4] described a rhabdoid tumor of the bladder with a distinct sarcomatoid component. Similarly, Inagaki et al [3] have also described a urothelial sarcomatoid carcinoma with rhabdoid differentiation from a 2-year-old female patient.

Rhabdoid tumors with myxoid areas may focally mimic inflammatory myofibroblastic tumors. Three of the cases in the present series had focal myxoid features but otherwise lacked more typical features of an inflammatory myofibroblastic tumor. In particular, the tumor cells in our cases lacked the tissue culture-like fibroblast cells and showed a greater degree of pleomorphism. The lesions also lacked the diffuse infiltration of inflammatory cells associated with inflammatory myofibroblastic tumor.

Tumors with a rhabdoid phenotype are associated with an aggressive clinical course. In one series of both renal and extrarenal rhabdoid tumors in children, patients died at a median period of 5 months (range, 0.5-30 months) after diagnosis [10]. Extrarenal adult rhabdoid tumors are considered to have an aggressive outcome [3,15]. In the 6 patients described in this study, the survival was also poor. Of the 6 patients, 3 died within 4 months. The remaining 3 patients were alive yet only at 3, 3, and 9 months after diagnosis. The histological findings in this study serve to broaden the morphological spectrum of urothelial carcinomas to include cases with prominent rhabdoid features and add further evidence as to their poor prognosis.

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