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Original contribution

Small cell carcinoma of the kidney: a clinicopathologic study of 14 cases☆

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Summary Small cell carcinoma of the kidney is distinctively rare. We searched pathology files in 2 institutions and found 14 cases of renal small cell carcinoma. The patients' mean age at diagnosis was 59 years (range, 22-75 years); 8 were women, and 6 were men. Patients usually presented with hematuria (n = 6) and abdominal pain (n = 5). The mean tumor size was 7.1 cm (range, 3.5-14.0 cm). The small cell carcinoma was pure in 9 cases and mixed with high-grade urothelial carcinoma in 5 cases. None was associated with any type of renal cell carcinoma. Tumor necrosis was present in all cases, and lymphovascular invasion was identified in 6 cases. The tumor invaded the perinephric adipose tissue in 13 cases and was confined to the kidney in only 1 case. Lymph node metastases were identified in all patients who underwent lymph node dissection (5/5). On immunostains, the small cell carcinoma cells were positive for pancytokeratin (11/12), chromogranin (6/9), and synaptophysin (8/9). Follow-up data were available for 13 patients, and 11 died of small cell carcinoma at a mean of 15 months (range, 4-31 months) after diagnosis. Of the 2 surviving patients, 1 was alive at 5 months after diagnosis, and the other, whose disease was confined to the kidney, was alive with no evidence of disease at 137 months. In summary, renal small cell carcinoma is a highly aggressive disease that often presents at an advanced stage with widespread metastases. Patients usually have a poor clinical outcome despite multimodal therapy. The frequent coexistence of small cell carcinoma with urothelial carcinoma suggests that renal small cell carcinomas may evolve from a preexisting urothelial carcinoma.

1. Introduction

Small cell carcinoma (SmCC) is a distinct histologic phenotype that can arise from a variety of organs [1-3]. SmCCs of various origins share similar histologic features: poorly differentiated carcinoma cells with finely granular nuclei, inconspicuous nucleoli, scant cytoplasm, nuclear molding, and poorly defined cellular borders. SmCCs also frequently express neuroendocrine markers such as synaptophysin, chromogranin, and CD56. In addition, SmCC is most commonly associated with paraneoplastic syndromes such as inappropriate antidiuretic hormone secretion, cerebellar degeneration, and Lambert-Eaton myasthenic syndrome [4]. Clinically, SmCC represents one of the most aggressive carcinomas. Most patients with SmCC present with widespread

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metastases, which makes it difficult to eradicate the disease by surgery. Although SmCC responds to chemotherapy and radiation treatments, patients usually die of the disease in a relatively short time after diagnosis.

More than 90% of SmCCs occur in the lungs, but the disease is also found in various extrapulmonary sites including the genitourinary tract, gastrointestinal tract, breast, cervix, skin, salivary glands, and larynx [5-16]. The genitourinary tract is the most common extrapulmonary site, with approximately 900 new cases diagnosed every year in the United States [15]. Most SmCCs in the genitourinary tract occur in the prostate and urinary bladder [9-13]. SmCC of the kidney is extremely rare, with only a few cases reported in the literature [17-21].

To better understand this rare disease, we studied the clinical and pathologic features of 14 cases of renal SmCC from 2 institutions. To our knowledge, the current study presents the largest series of patients with this extremely rare renal malignancy seen in the literature to date.

2. Materials and methods

With the approval of the institutional review board, we retrospectively reviewed the surgical pathology report databases for patients with SmCC of the kidney who were treated at The University of Texas MD Anderson Cancer Center or The Methodist Hospital in Houston, Texas, from 1987 through 2009. Eighteen patients with SmCC in the kidney, including the renal pelvis and renal parenchyma, were identified, but 4 of them were excluded from the study because they had lung SmCC and their renal lesions were considered to represent a metastasis from the primary lung disease.

All patients with renal SmCC underwent radical nephrectomy. For each radical nephrectomy specimen, the tumor was extensively sampled for histologic examination with at least 1 tissue section per centimeter of the largest tumor dimension, and 2 or more tissue sections were routinely submitted from the pelvicalyceal regions. The hematoxylin-eosin–stained slides from all patients were available for review in this study. The reviewed pathologic parameters included tumor size, location, stage, necrosis, lymphovascular invasion, non-SmCC tumor components, and other histologic changes. Demographic and clinical information, including patient age and sex, symptoms at presentation, treatment, follow-up time, and clinical outcome, was obtained from the patients' charts.

Immunohistochemistry was performed on formalin-fixed, paraffin-embedded sections using polymeric biotin-free horseradish peroxidase on a Leica Microsystems Bond Max stainer (Leica Microsystems, Bannock, IL). Sections were routinely heated for epitope retrieval, and commercially available antibodies were used as described in Table 1. Peroxidase activity was visualized by staining with 3,3′-diaminobenzidine. Optimal dilutions and incubation times were determined using standard techniques. In each staining series, positive and negative controls were included with the tumor samples.

Table 1 Primary antibodies used for immunohistochemical analyses

Antibody	Clone	Vendor	Dilution
Cytokeratin AE1/AE3	Polyclonal	Dako, Carpentaria, CA	1:100
Synaptophysin	Monoclonal (27G12)	Leica Microsystems	1:600
Chromogranin	Monoclonal (LK2H109-2)	Millipore, Billerica, MA	1:4000
CD56	Monoclonal (123C3)	Invitrogen Carlsbad, CA	1:100
CD99	Monoclonal (O-13)	Invitrogen	Prediluted
TTF-1	Monoclonal (8G763/1)	Dako	1:200

3. Results

3.1. Patient demographics and clinical findings

We identified a total of 14 cases of renal SmCC that accounted for less than 1% of all renal tumors treated at our hospitals during the period studied. Of the 14 patients, 8 were women and 6 were men (Table 2). Their mean age at diagnosis was 59 years (range, 22-75 years). Notably, 4 patients were younger than 40 years, ranging from 22 to 39 years. The most common symptoms at presentation were hematuria (n = 6) and abdominal pain (n = 5). In addition, 2 patients presented with a flank mass; 1 patient's renal mass was found on a computed tomography scan performed as a follow-up for bladder carcinoma. Eight tumors were found in the left kidney and 6 in the right. All patients were treated with radical nephrectomy.

3.2. Pathologic findings

On gross examination, the radical nephrectomy specimens showed a unifocal tumor in all cases. The tumor was located centrally around the renal pelvis in 5 cases and was located peripherally in renal parenchyma in 9 cases. The tumor usually had an ill-defined border, and the cut surfaces were soft and friable with areas of necrosis. The mean tumor size was 7.1 cm (range, 3.5-14.0 cm). Microscopically, the tumors showed sheets or large nests of small tumor cells infiltrating the renal parenchyma (Fig. 1A). The tumor cells were round or oval with scant cytoplasm and indistinct cell borders (Fig. 1B). The nuclei were hyperchromatic with evenly distributed chromatin, inconspicuous nucleoli, and abundant mitotic figures (Fig. 1C). Nuclear molding