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SARCOMATOID CHROMOPHOBΕ RENAL CELL CARCINOMΑ. A CASE REPORT AND REVIEW OF THE LITERATURE.

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Summary.- OBJECTIVES: We report herein the clinical, histological, and immunohistochemical features of a case of sarcomatoid chromophobe renal cell carcinoma.

METHODS/RESULTS: A 59-year-old woman referred a two-month history of constant right flank pain, and hematuria. A right radical nephrectomy was performed. Gross pathologic examination showed a tumor located in the lower part of the kidney with two different aspects. Histologically, the tumor was composed of two intermixed distinct morphologic components: a chromophobe renal cell carcinoma and a high-grade spindle cell sarcoma.

CONCLUSION: Our case represent a typical sarcomatoid chromophobe cell carcinoma. This unusual renal cancer has the potential to behave aggressively and to metastasize.

Keywords: Kidney. Sarcomatoid Carcinoma. Chromophobe carcinoma. Immunohistochemistry

INTRODUCTION

Chromophobe renal cell carcinoma is a rare variant of renal carcinoma, with distinct histochemical, ultrastructural, and genetic characteristics (1,2). They are relatively uncommon accounting for 5 % of renal neoplasm (3). This subtype of kidney cancer has been considered to show a better prognosis than conventional renal clear cell carcinoma. On the other hand, foci of high-grade spindle cells, often reminiscent of a malignant fibrous histiocytoma (sarcomatoid component), can occur in all histologic subtypes of renal cell carcinoma (RCC) and its presence is associated with poor prognosis, with a median survival following diagnosis of less than 1 year reported in most studies (4-12).
Histologically, the tumor was composed of two intermixed distinct morphologic components: a chromophobe renal cell carcinoma and a high-grade spindle cell sarcoma. The chromophobe renal cell carcinoma was composed of compact epithelial cells in solid sheets. The cells were of large size with well-defined borders and abundant, finely reticular, translucent cytoplasm (Figure 2 A,B). Characteristic perinuclear halos were also present, giving the cells a koilocytic appearance. The nuclei were centrally located and had irregular outlines with different degrees of hyperchromasia. These tumor cells were strongly positive for Hale’s colloidal iron satín. Admixed with the chromophobe renal cell carcinoma were areas of sarcomatoid component (Figure 2 A,B). The sarcomatoid cells were spindle, multinucleated and epithelioid. Some tumor cells showed deeply eosinophilic cytoplasm without cross-striation. Mitotic figures were frequently observed. The spindle cells were arranged in ill-defined fascicles with occasional storiform pattern. The sarcomatoid component showed an aggressive, dissecting growth pattern with invasion into the perirenal adipose tissue.

Immunohistochemical studies showed cytokeratin AE1/AE3, cytokeratin 7, epithelial membrane antigen and CD117 reactivity in chromophobe cells carcinoma, (Figures 2, C, D, E, F). The sarcomatoid cells were spindle, multinucleated and epithelioid. Some tumor cells showed deeply eosinophilic cytoplasm without cross-striation. Mitotic figures were frequently observed. The spindle cells were arranged in ill-defined fascicles with occasional storiform pattern. The sarcomatoid component showed an aggressive, dissecting growth pattern with invasion into the perirenal adipose tissue.

In this report we present a rare case of sarcomatoid chromophobe renal cell carcinoma showing an aggressive behavior. The histologic, histochemical and immunohistochemical features are presented as well as a review of the literature.

CASE REPORT

A 59-year-old woman referred a two-month history of constant right flank pain, and hematuria. She had a noncontributory medical history. Her physical examination was unremarkable. A cystoscopy was performed, showing no alterations. An abdominl computerized tomography revealed a non-homogeneous mass, which measured 7 cm, involving the lower pole of the right kidney. The working diagnosis was renal cell carcinoma. She underwent a right radical nephrectomy. The patient died of multiple metastases eight months after the surgical procedure.

Pathological findings

The resected right kidney weighed 188 g. The tumor was located in the lower part of the kidney and measured 6.8 x 3 x 2 cm. On the cut surface the tumor showed a biphasic appearance, with one area yellowish-white in color, and the other area showed homogeneous aspect with hemorrhage, tan in color (Figure 1, A,B). The tumor partly invaded the surrounding adipose tissue. The renal sinus, vascular and ureteral margins of resection were free of tumor. The adrenal gland showed no gross abnormalities.

FIGURE 1A y B (Detail), Macroscopic finding showing tumor with biphasic appearance, with one area yellowish-white in color, and the other area showed homogeneous aspect with hemorrhage, tan in color.
FIGURE 2. Microscopic and immunohistochemical findings. A, Histologically, the tumor was composed of chromophobe renal cell carcinoma and a high-grade spindle cell sarcoma. The chromophobe renal cell carcinoma was composed of compact epithelial cells in a solid sheets (H&E 100x). B, Sarcomatoid cells intermixed with chromophobe cell carcinoma (Detail) (H&E 100x, 400x). C, Sarcomatoid cells with intense positivity for vimentin (DAB 100x, 400x) D, Cytokeratin 7 with reactivity in chromophobe cell carcinoma (DAB 100x, 400x). E, Cytokeratin 7 showing focal immunoreactivity in pleomorphic cell (DAB 400x). F, Citoplasmatic reactivity for CD117 (C-Kit) in neoplastic cells (DAB 400x).
TABLE I. ANTIBODIES USED FOR IMMUNOHISTOCHEMICAL STUDIES.

<table>
<thead>
<tr>
<th>Antigen</th>
<th>Clone</th>
<th>Source</th>
<th>Dilution</th>
<th>Pretreatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>CK AE1/AE3</td>
<td>AE1/AE3</td>
<td>Dako,Glostrup,Denmark</td>
<td>1:50</td>
<td>Steamer</td>
</tr>
<tr>
<td>CK 7</td>
<td>OV-TL 12/30</td>
<td>Dako,Glostrup,Denmark</td>
<td>1:50</td>
<td>Steamer</td>
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<tr>
<td>CK 20</td>
<td>Ks 20.8</td>
<td>Dako,Glostrup,Denmark</td>
<td>1:50</td>
<td>Steamer</td>
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<tr>
<td>EMA</td>
<td>E29</td>
<td>Dako,Glostrup,Denmark</td>
<td>1:100</td>
<td>Steamer</td>
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<tr>
<td>SMA</td>
<td>1A4</td>
<td>Dako,Glostrup,Denmark</td>
<td>1:100</td>
<td>None</td>
</tr>
<tr>
<td>Desmin</td>
<td>DE-R-11</td>
<td>Dako,Glostrup,Denmark</td>
<td>Prediluted</td>
<td>None</td>
</tr>
<tr>
<td>Anti-Myo D1</td>
<td>5.8 A</td>
<td>Dako,Glostrup,Denmark</td>
<td>1:50</td>
<td>Steamer</td>
</tr>
<tr>
<td>S100</td>
<td>Polyclonal</td>
<td>Dako,Glostrup,Denmark</td>
<td>1:200</td>
<td>Steamer</td>
</tr>
<tr>
<td>CD34</td>
<td>QBEnd10</td>
<td>Dako,Glostrup,Denmark</td>
<td>1:50</td>
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<tr>
<td>Vimentin</td>
<td>V9</td>
<td>Dako,Glostrup,Denmark</td>
<td>1:100</td>
<td>Steamer</td>
</tr>
<tr>
<td>CD117</td>
<td>Polyclonal</td>
<td>Dako,Glostrup,Denmark</td>
<td>1:200</td>
<td>Steamer</td>
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DISCUSSION

Sarcomatoid transformation in chromophobe renal cell carcinoma is extremely rare, with only, to our knowledge, sixteen similar cases reported in the English literature (Table II). We reviewed these together with our case. There was an apparent female preponderance. Of the sixteen cases, five occurred in men and eleven in women (M:F=1:2.2). The age of the patients ranged from 49 to 77 years (average: 60.31). In the largest series reported to date, of six cases of sarcomatoid renal cell carcinoma with foci of chromophobe renal cell carcinoma (CRCC), Akthar et al (5) found, similar relation between sex and the average age was 56.83. Probably, these findings suggest a presentation age older than conventional chromophobe renal cell carcinoma and appear that sarcomatoid chromophobe RCCs are more frequent in female patients. In regard to clinical symptoms, most patients had noted flank pain and hematuria. These clinical symptoms are similar to the other renal cell carcinomas.

Macroscopically, twelve carcinomas were located in the right kidney (75%) and four were located in the left side (25%). The tumor size ranged between 3 and 18 cm (average 9.97). Similar findings have been reported in CRCCs, although average size tumor was major in sarcomatoid chromophobe RCCs compared with the classical form (21). The lesion were widespread. In the sixteen patients, twelve have local spread (73.33%) and five cases showed distant metastases (33.33%). By contrast, in a recent analysis of 61 cases of chromophobe renal cell carcinoma Peryomaure et al. (21) found that the most common pathologic stage tumor was T1 in 65.6% of cases, and T2 in 31.1% patients. It is suggested that sarcomatoid chromophobe RRC is a more aggressive neoplasm compared with classic chromophobe carcinoma. Similar findings were obtained in the study by Cheville et al. (4). They demonstrated a very poor prognosis in the sarcomatoid chromophobe cell carcinoma compared with classic chromophobe cell carcinoma. Additionally, some reports indicate that sarcomatoid change is more common among patients with chromophobe cell carcinoma (5,22).

The coexistence of both histopathologic neoplasias, chromophobe cell carcinoma and sarcomatoid carcinoma, may be due to either dedifferentiation of the more differentiated chromophobe cell tumor or to the collision of two synchronous tumors. Actually, the dedifferentiation theory seems more accepted based on the evolution of renal carcinoma into a spindle cell morphology. This sarcomatoid change probably is the result of extensive chromosomal rearrangement, leading to an identical spindle cell morphology. Recently, an oncogene, KIT, has been shown to be involved specifically in the development of CRCC (23). Our findings confirmed the expression of KIT in classical CRCC carcinoma and probably support the hypothesis that KIT protein could be involve in the origin of CRCC. Additionally, in our case we could show no reactivity for CD117 in to the sarcomatoid component and this
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In conclusion, our case represents a typical sarcomatoid chromophobe cell carcinoma. These tumors are not frequent and in contrast with the classical form of chromophobe cell carcinoma, the diagnosis carries a worse prognosis, because this unusual renal cancer has the potential to behave aggressively and

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TABLE II. PREVIOUSLY REPORTED SARCOMATOID CHROMOPHOBE RENAL CELL CARCINOMA.

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of patients</th>
<th>Age/Sex</th>
<th>Location in kidney (size, cm)</th>
<th>Local spread</th>
<th>Distant metastases</th>
<th>Diagnostic term use</th>
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<tr>
<td>Akhtar et al, 1997 (5)</td>
<td>6</td>
<td>57/F</td>
<td>Right (in 3) (11.0)</td>
<td>Yes (in 3 pts)</td>
<td>Yes</td>
<td>Sarcomatoid renal cell carcinoma with chromophobe carcinoma</td>
</tr>
<tr>
<td>Gomez-Roman et al, 1997 (13)</td>
<td>1</td>
<td>61/M</td>
<td>Right lower (11.2)</td>
<td>Yes</td>
<td>No</td>
<td>Sarcomatoid chromophobe carcinoma</td>
</tr>
<tr>
<td>Hirowaka et al, 1998 (14)</td>
<td>1</td>
<td>57/F</td>
<td>Right upper (12.0)</td>
<td>-</td>
<td>No</td>
<td>Sarcomatoid renal cell carcinoma with chromophobe carcinoma</td>
</tr>
<tr>
<td>Kuroda et al, 1998 (15)</td>
<td>1</td>
<td>49/F</td>
<td>Right upper (3.0)</td>
<td>Yes</td>
<td>No</td>
<td>Chromophobe renal cell carcinoma with sarcomatoid foci</td>
</tr>
<tr>
<td>Mai et al, 1999 (16)</td>
<td>1</td>
<td>65/M</td>
<td>Right lower (10.0)</td>
<td>Yes</td>
<td>No</td>
<td>Sarcomatoid transformation of chromophobe renal cell carcinoma</td>
</tr>
<tr>
<td>Nagashima et al, 2000 (17)</td>
<td>1</td>
<td>72/F</td>
<td>Right lower (9.5)</td>
<td>Yes</td>
<td>No</td>
<td>Chromophobe renal cell carcinoma with sarcomatoid change</td>
</tr>
<tr>
<td>Tardio, 2000 (18)</td>
<td>2</td>
<td>77/F</td>
<td>Left mid (5.5)</td>
<td>Yes (in 1 pt)</td>
<td>No (in 2 pts)</td>
<td>Chromophobe renal cell carcinoma with sarcomatoid areas</td>
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<tr>
<td>Cserni et al, 2002 (19)</td>
<td>1</td>
<td>52/F</td>
<td>Right mid and lower (14.5)</td>
<td>Yes</td>
<td>No</td>
<td>Sarcomatoid renal cell carcinoma with foci of chromophobe cell carcinoma</td>
</tr>
<tr>
<td>Abrahams et al, 2003 (20)</td>
<td>1</td>
<td>55/M</td>
<td>Right lower (13.5)</td>
<td>Yes</td>
<td>Yes</td>
<td>Chromophobe renal cell carcinoma with sarcomatoid transformation</td>
</tr>
<tr>
<td>Current study</td>
<td>1</td>
<td>59/F</td>
<td>Right lower (6.8)</td>
<td>Yes</td>
<td>No</td>
<td>Sarcomatoid chromophobe carcinoma</td>
</tr>
</tbody>
</table>

could be interpreted as wide chromosomal change in CRCC producing spindle cell morphology. Finally, the collision theory seems unlikely because the close intermixing of the two patterns in some neoplasm, including the present one, and the rarity of each of the tumors.
to metastasize. Larger studies are needed to elucidate the clinical behavior of sarcomatoid chromophobe cell carcinoma.

REFERENCES AND RECOMMENDED READING
(*of special interest, **of outstanding interest)