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ABSTRACT - We report two rare cases of Bellini duct carcinoma, a rare variant of renal cell carcinoma. Case 1: The patient, a 73-year-old female, was admitted to the hospital for macroscopic hematuria and right flank pain. She was diagnosed to have a stage IV Bellini duct carcinoma. There was a progression of the disease despite chemotherapy. She died 21 months later. Case 2: The patient, an 81-year-old male, was admitted to the hospital for generalized fatigue, weight loss and left flank pain. He was diagnosed to have a stage IV Bellini duct carcinoma. The patient was treated with chemotherapy; he died six months later. We report the clinicopathological features of two cases of Bellini duct carcinoma in order to contribute to the related literature of this rare disease.

Keywords: Bellini duct carcinoma, renal cell carcinoma, tumor

INTRODUCTION

Renal cell carcinoma (RCC) is a kidney cancer that originates in the lining of the proximal convoluted tubules, the very small tubes in the kidney that transport glomerular filtrate (GF) from the glomerulus to the descending limb of the nephron. Recently developed techniques of histochemistry have revealed a rare variant of renal cell carcinoma occurring in 1-3% of cases that originated from the collecting ducts of Bellini [1]. Its resistance to chemotherapy drugs used for renal cell carcinoma characterizes it. Here we present two rare cases of Bellini duct carcinoma.

CASE REPORTS

Case 1

A 73-year-old female admitted to our hospital in August 2011 for macroscopic hematuria and right flank pain. On physical exam, the patient had a palpable, mildly tender right flank mass. Laboratory examinations, including urine analysis, confirmed the presence of hematuria. Abdominal ultrasonography and CT scan revealed a tumor originating from the right kidney. On CT scan, this tumor appeared hypodense, heterogeneously enhancing with necrotic foci and measuring 11 x 8 cm. It invaded the right renal sinus, the inferior vena cava and the right psoas muscle. Systemic evaluation (including CT scan of the chest, abdomen and pelvis) revealed no distant metastases. CT-guided biopsy was done and the microscopic examination revealed poorly differentiated adenocarcinomatous proliferation and presence of multiple microabcesses in the tumoral tissue. Histochemistry revealed intense expression of CK7 by epithelial tumor cells. The final diagnosis was stage IV Bellini duct carcinoma.

The patient received multiple cycles of chemotherapy (Gemcitabine 1600 mg + Carboplatin 450 mg, Paclitaxel 100mg + Gemcitabine 1600 mg, Carboplatin 300 mg and Paclitaxel 100 mg). As the therapeutic effect was negative, she had progression of her disease with the apparition of liver, lung and mediastinal lymph nodes metastases, and she died in June 2013.

Case 2

An 81-year-old male admitted to our hospital in December 2011, for generalized fatigue, weight loss and left flank pain. On physical exam, the patient had left flank tenderness. Laboratory examinations, including urine analysis, revealed the presence of microscopic hematuria. CT scan revealed a heterogeneous left kidney with irregular borders and a tumor in its upper pole invading the perinephric fat tissue. Systemic evaluation including brain, chest, abdomen and pelvic CT scan revealed bilateral lung metastasis, diffuse mediastinal and retroperitoneal lymphadenopathy. CT-guided biopsy of the tumor was done, and the pathology report revealed poorly dif-
differentiated adenocarcinoma of papillary type. Histochemistry revealed CK7 positivity, diffuse positivity for vimentine and HMW (high molecular weight) cytokeratin. The final diagnosis was stage IV Bellini duct carcinoma.

The patient was treated with chemotherapy (Gemcitabine 1400 mg + Carboplatin 150 mg). He had progression of his disease and died after six months.

DISCUSSION

Bellini duct carcinoma (BDC), also known as low-grade collecting duct carcinoma and tubulocystic carcinoma [2] is a recently described type of kidney cancer that originates in the duct of Bellini of the kidney (Fig. 1). It was commonly diagnosed previously as renal cell carcinoma or a subtype of renal cell carcinoma [3]. However, it does not respond well to chemotherapy drugs used for renal cell carcinoma, and progresses and spreads more quickly. It is rare and accounts for 1-3% of all kidney cancers [1]. Only 40 cases were reported worldwide in 2002 [4]. Rumpelt et al. found six BDCs (0.4%) among 1400 consecutive renal cell carcinomas [5]. Fleming and Lewi defined the diagnostic criteria and established collecting duct carcinoma of the kidney as a separate histological entity arising in the renal medulla [6]. The World Health Organization reported these findings in their international classification of tumors, and grouped it with renal cell carcinoma with the sub-designation ‘Bellini duct carcinoma’ [7].

FIGURE 1. Position of the duct of Bellini in the kidney.
**Clinical features**

BDCs commonly present with gross hematuria. They tend to occur in younger patients. The average age of the patients was 55 years (range 37-76), and the male/female ratio was 4.4/1. Most cases had a tendency for early dissemination and a fatal clinical course [5]. Méjean et al. reported 20% survival at two years in a study on 10 patients with Bellini duct carcinoma. Mean patient age was 66 and the stage was pT3 in 8 out of 10 patients [3]. A study of 160 collecting duct renal cell carcinomas showed that collecting duct renal cell carcinoma was more common in black than in white patients (23% vs 9%, \( p < 0.001 \)), and the staging was more commonly T3+ than T2/T1 (33% vs 18%, \( p < 0.001 \)) and metastatic than regional/local (28% vs 17%, \( p = 0.001 \)) [8].

Because of these characteristics of Bellini duct carcinoma (early dissemination, fatal clinical course), the two cases we are reporting presented with an already metastatic disease, and survived for a very short period of time (21 vs 6 months for the first and second case respectively). A more important finding is that the second case had two unusual features of the disease: the age of presentation (81 years old) and the clinical presentation (no hematuria) (Table 1).

**Histologic diagnosis**

BDC can be identified based on gross, microscopic, histochemical, and immunohistochemical features. Macroscopically, BDC is often located at the confluence of the medulla and renal pelvis as a nodular mass if the tumor is small. It has a distinctive “bubble wrap” appearance [2] and shows a characteristic gray-white-tan color, with absence of foci of necrosis and hemorrhage [9]. Two histological types were described, the papillary type and the mixed type. The papillary type resembles the distal collecting duct and demonstrates an eosinophilic cytoplasm, nuclear polymorphism, and distinct nuclei with a papillary or tubulopapillary structure. On the other hand, the mixed type shows features of tubulopapillary adenocarcinoma and areas of transitional cell differentiation [10].

BDCs are positive by immunohistochemical staining with proteins typically expressed in the epithelium of the distal tubules like high-molecular-weight keratin and lectin [11]. Although little is known about the genetic profile of BDCs, a DNA flow cytometry study has demonstrated aneuploidy in 90% of these tumors [12], and cytogenetics has shown frequent monosomy of chromosomes 1, 6, 8, 14, 15, and 22 [13].

To improve the understanding of the biology of Bellini duct carcinoma, and to explore the possibility that different genes may be involved in the etiology and prognosis of this neoplasm, eleven cases of Bellini duct carcinoma were analyzed. The results showed that 64% of the cases showed absence or reduction of fasciulation and elongation protein zeta 1 (Fez1) expression. Loss and reduction of Fez1 were correlated with a higher prevalence of lymph node metastases (71% vs. 0%, \( p = 0.061 \)). Fez1-negative tumors also tended to have higher mortality than Fez1-positive tumors.

Median survival time was estimated to be 17 months for the former group, while median survival was not reached for the latter group during the course of the study (i.e., fewer than half of the patients died) (\( p = 0.078 \)). This corresponds to an estimated 5-fold increase in mortality risk for the Fez1-negative CDCs (hazard ratio of 5.5) [14].

Clinical trial investigation is urgently needed because of the aggressive and refractory nature of BDC. Several studies done to compare different treatment options like immunoreactive agents such as interferon or interleukin, and combination chemotherapy for relapsed disease or metastatic lesions, but generally proved to be ineffective [5]. Also, Staehler et al. showed that nephrectomy, adjuvant gemcitabine/cisplatin, and sunitinib therapy did not alter the course of disease, and gross resection of disease was rapidly followed by local recurrence and, subsequently, widespread dissemination of disease [15].

**CONCLUSION**

BDC is a rare tumor with tendency for early dissemination and fatal clinical course. This has pushed the investigators to determine the origin of all renal tumors and to distinguish rare forms such as BDC from common types of renal cell carcinoma. Besides, its resistance to different therapeutic agents makes establishing a modality of treatment highly desirable. Detailed, long-term follow-up to detect local recurrence or distant metastasis is also necessary.

**REFERENCES**


<table>
<thead>
<tr>
<th>TABLE I</th>
<th>PRESENTING SIGNS, HISTOLOGIC FEATURES AND HISTOCHEMICAL FEATURES OF THE TWO REPORTED CASES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Presenting signs</strong></td>
<td><strong>Histologic features</strong></td>
</tr>
<tr>
<td><strong>CASE 1</strong></td>
<td>Macroscopic hematuria</td>
</tr>
<tr>
<td></td>
<td>Right flank pain</td>
</tr>
<tr>
<td><strong>CASE 2</strong></td>
<td>Generalized fatigue</td>
</tr>
<tr>
<td></td>
<td>Weight loss</td>
</tr>
<tr>
<td></td>
<td>Left flank pain</td>
</tr>
</tbody>
</table>

R. JABBOUR et al. – Bellini duct carcinoma

Lebanese Medical Journal 2014 • Volume 62 (4) 243