Bellini's duct carcinoma: A report of two cases and a review of the literature

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Abstract. Bellini's duct carcinoma (BDC) is a rare and aggressive variant of renal cell carcinoma that possesses an extremely poor prognosis. The greater the grade or stage of disease, the poorer the prognosis tends to be. This study presents two cases of BDC; one case of low grade BDC and one case of high grade BDC in a 47-year-old male and 74-year-old female, respectively. The 47-year-old male patient presented with painless gross hematuria, which had lasted for 3 weeks and subsequently underwent purely laparoscopic nephroureterectomy. After 4-years of follow-up, the patient remained disease-free. By contrast, a right renal tumor was identified in the 74-year-old female patient during a routine examination. Radical right nephrectomy and lymph node dissection were performed, however, 10 months after surgery the patient succumbed due to wide-spread metastasis. The two cases reported in the present study not only represent excellent examples of the disease spectrum, but also act as a reminder of the possibility of detecting BDC in an early stage of disease. Therefore, the epidemiology of BDC has been discussed, and the aggressive growth pattern of BDC has been presented in terms of signs, symptoms and imaging examinations, including ultrasonography, computed tomography (CT), angiography and single photon emission CT, in the early stage of disease.

Introduction

Bellini's duct carcinoma (BDC), which arises from the distal segment of the collecting duct, is a rare and aggressive malignant tumor with a poor prognosis. BDC comprises <1% of all renal tumors (1), but it is extremely aggressive and is accompanied by metastatic diseases in the majority of reported cases. The prognosis of BDC is poor, with ~70% patients succumbing due to disease progression within 2 years of diagnosis (2). The only favorable prognosis factor is low-grade and low-stage disease (3-5). If BDC could be detected in the early stage of disease, the poor prognosis of BDC may be changed. However, due to the rarity of BDC, the similarities of the symptoms, signs and imaging examination findings with other variants of renal cell carcinoma (RCC), and the poor prognosis of BDC, it is challenging and crucial to differentiate other RCC variants from BDC. The RCC database of Peking University Shenzhen Hospital (Shenzhen, China) was reviewed, and out of a total of 311 RCC cases, two cases of BDC with different grades of disease and prognoses were identified.

Case report

Case one. In December 2010, a 47-year-old man presented to the Department of Urology, Peking University Shenzhen Hospital, with a complaint of painless gross hematuria during urination that had lasted 3 weeks. Physical examination revealed percussion pain over the left kidney region. The laboratory examinations revealed no extrarenal manifestations. The blood routine examination revealed no anemia and polycythemia; electrolyte examination revealed no hypercalcemia; erythrocyte sedimentation rate (ESR) examination revealed no fast ESR; and alkaline phosphatase examination revealed no elevated alkaline phosphatase. A kidney tumor was suspected based on the ultrasonography of the urinary system, which revealed a hypechoic solid lesion in the left pelvis, measuring 3.76x3.06 cm in size, which was heterogeneous inside and demonstrated a blood flow signal. Therefore, a contrast-enhanced computerized axial tomography (CT) scan was performed, which revealed a slightly contrasted, 2 cm in diameter, ill-defined mass with a complete capsule,
in the middle and lower pole of the of the kidney. The CT scan confirmed that there was no tumor thrombus and no metastasis to the lymph nodes, liver, pancreas, spleen and other organs. The patient underwent purely laparoscopic nephroureterectomy.

The final pathological diagnosis was left renal BDC, with grade IV Fuhrman nuclear malignancy. According to the 2009 American Joint Committee on Cancer (AJCC) tumor-node-metastasis (TNM) classification of malignant tumors (6), the patient was diagnosed with stage T1aN0M0 disease, indicating low-grade BDC. Cytokeratin-7 (CK7) was not expressed in the tumor, but immunostaining for vimentin (Vim), epithelial membrane antigen (EMA), pan cytokeratin (AE1/AE3) and common acute lymphocytic leukemia antigen (CD10) was positive in the tumor. The patient rejected any type of chemotherapy when he was informed of the possible side effects. At the 4-year follow-up, the patient remained disease-free.

Case two. In addition, in September 2012, a 74-year-old woman presented to the Department of Urology, Peking University Shenzhen Hospital, with a hypoechoic solid lesion, 7 cm in diameter, on the right kidney, which was indicated during sonography. Urinary sonography indicated that the mass, which protruded outside the right kidney, was irregular in shape and heterogeneous inside, with an abundant blood flow signal. However, the physical examination was not notable and the laboratory examinations, which included routine blood and urine tests, blood electrolyte tests and ESR tests, as well as calcium and alkaline phosphatase tests, were normal. In order to further define the right renal mass, a contrast-enhanced CT was performed. The result confirmed a circular low-density shadow on the right kidney, which demonstrated contrast-enhancement in the early phase and was considered to mostly consist of renal cancer cells. According to the imaging findings and the patient’s request, radical right nephrectomy and lymph node dissection was performed with a tentative diagnosis of renal cancer.

The tumor was morphologically consistent with BDC, measuring 7.8x5.5x5 cm in size, infiltrating perinephric fat and formatting satellite nodules in the kidney. One metastatic tumor was indicated in the right renal hilar lymph node. The final pathological diagnosis was right renal BDC, with grade IV Fuhrman nuclear malignancy. According to the 2009 AJCC TNM classification, the patient was diagnosed with stage T3aN1M0 disease, indicating high-grade BDC. Immunohistochemically, the tumor exhibited weak positive staining for Vim and CD10 and strong positive staining for AE1/AE3, CK7 and EMA. The findings were compatible with a diagnosis of BDC. The patient succumbed 10 months post-surgery due to widespread metastasis.

Discussion

The results demonstrated that the occurrence of BDC is 0.64%, which is similar to other cases of BDC reported in Mexico, Japan and Italy (5,7,8). The present two cases, which presented with different grades and prognoses of BDC, were in stark contrast. The TNM classifications of the low- and high-grade cases were T1aN0M0 and T3aN1M0, respectively. The high-grade case demonstrated a slight high stage with an infiltration of perinephric fat and only one regional lymph node metastasis; however, the patient with low-grade BDC survived for ~5 times the post-surgery lifespan of the patient with high-grade BDC. To the best of our knowledge, a lower grade and stage of disease is the only favorable prognosis factor for BDC.

Although BDC is a rare variant of RCC, BDC demonstrates the poorest prognosis and grows in a highly aggressive pattern, with early distant metastasis (9). Therefore, if BDC is detected at an early stage and intervention is prompt, the prognosis of BDC may be improved.

BDC is most common in older men (>40 years old), with a mean age of diagnosis of 58.2 years; however, the majority of BDC patients are younger than classical RCC patients, which occurs predominantly in the seventh and eighth decades of life (7,10,11). Auguet et al reported a case of BDC and highlighted the possibility of a strong family history of associated malignancy in BDC patients; however, this theory is controversial, as there is little supporting published data (10,12). In the two cases reported in the present study, there was no family history of BDC. In one study, the majority of patients with BDC were symptomatic, with regional lymph node metastasis or distant metastasis at presentation (7). The majority of the complaints reported by patients with BDC, including flank pain, hematuria, palpable abdominal mass and weight loss, are similar to those reported by patients with conventional RCC. However, patients with BDC may also present with back pain (12), paraplegia (13), hemodialysis for chronic renal failure (14) and other symptoms associated with distant metastasis. BDC not only demonstrates an aggressive nature in the signs and symptoms of the disease, but also in imaging findings.

Clinically, B-scan ultrasonography is the first method selected to examine patients with renal cancer, and even for the census of renal tumors, due to its non-invasiveness, convenience and speed. In the two cases reported in the present study, ultrasonography of the patient with high-grade BDC revealed a more invasive tumor compared with the patient with low-grade BDC, with the mass being irregular in shape, protruding outside the right kidney and having an abundant blood flow signal. CT provides fundamental evidence for the diagnosis of renal cancer. Medullary involvement and an infiltrative appearance are common findings on CT scans and may indicate the diagnosis of collecting duct carcinoma. In large tumors, however, these features are frequently overshadowed by an exophytic or expansile component that may not be distinguished from the more common cortical renal cell carcinoma (15). In reported cases that used angiography, the BDCs were all hypovascular (15,16), whereas 90% of clear cell RCCs were hypervascular (17). Wang et al first reported a BDC patient with deteriorated renal function, revealed by single photon emission CT, which is unusual in RCC (16). Wang et al (16) hypothesized that the infiltrative growth pattern of BDC impaired the nephrons. This is a hypothesis that requires additional studies.

In conclusion, BDC is a rare and aggressive variant of RCC. The two present low- and high-grade cases with favorable and poor prognoses, respectively, are examples of the disease spectrum and act as a reminder that certain invasive imaging evidence, including infiltrative appearance, medullary involvement and hypervascularity, may result in a poor prognosis.
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