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ORIGINAL PAPER

Carcinoid tumor arising in a horseshoe kidney

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Abstract Carcinoid tumors are common neoplasms developing in gastrointestinal and respiratory tract. They are rarely found in the kidney. To date, approximately 40 cases of primary renal carcinoid tumors have been reported, with less of a third of them occurring within a horseshoe kidney. These cases appear to have a better prognosis, even in the presence of distant metastases, compared to those arising in normal kidneys.

Keywords Carcinoid tumor · Horseshoe kidney

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Introduction

Carcinoid tumors are common neoplasms developing in gastrointestinal and respiratory tract. However, they are rarely found in the kidney. To date, approximately 40 cases have been reported [1, 2]. Of these, 11 were found in association with horseshoe kidney (HSK). Owing to the low incidence of this association, it is very difficult to define the best therapeutic method and predict the outcome. We present a 33-year-old woman who had a primary carcinoid tumor within a HSK and who has developed metastatic disease and progression after surgical treatment and adjuvant chemotherapy.

Case report

A 33-year-old woman presented with a 1-year medical history of constipation and lower back pain. At physical examination, a right flank abdominal mass was found. High serum creatinine levels were also found (1.8 ng/dl). Magnetic resonance imaging (MRI) showed a bilateral tumor arising in a HSK (Fig. 1). There was no evidence of metastatic disease. She underwent right radical nephrectomy and left partial nephrectomy with isthmectomy without complications.

The histopathologic examination showed a solid mass with trabecular pattern of growth.

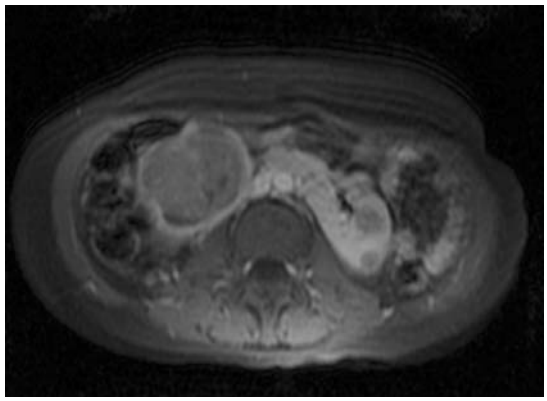

Fig. 1 MRI showing right renal tumor, isthmus without affection and left renal tumor at lower pole

Microscopically, tumor cells had eosinophilic, finely granular cytoplasm and nuclei with finely granular chromatin, the so-called ''salt and pepper'' pattern (Fig. 2A and B). Immunohistochemical staining was positive for Synaptophysin, Neuron-specific enolase (NSE) and Chromogranin A (Fig. 3A–C).

The final diagnosis was a bilateral primary carcinoid tumor arising in a HSK, stage II for the right kidney (T2 N0 M0) and stage I for the left kidney (T1 N0 M0) according to the TNM-AJCC classification [3].

After surgery the patient remained with steady renal function, without requiring dialysis and without any complication. Due to high serum creatinine levels, strict follow-up was carried with MRI. Liver metastases were detected 5 months after surgery and chemotherapy with etoposide and cisplatin was administered. After 3 cycles a new MRI showed liver metastases and tumor recurrence in the remaining left kidney. Due to the lack of response to the first chemotherapeutic regimen, second line 5-fluorouracil based chemotherapy was given. However, disease progression with new liver and lung metastases was demonstrated. A new chemotherapeutic regimen with etoposide and carboplatin was started. After 3 cycles of this combination, the patient decided to interrupt chemotherapy and she was followed-up with best supportive care. During the last follow-up visit, 33 months after liver metastases were diagnosed, the patient is alive with clinical and radiological evidence of progression.

Discussion

Primary carcinoid tumor of the kidney is a rare neoplasm. To date, approximately 40 cases have been reported. Of these, 11 were found in association with HSK. Krishnan [4] estimated that the relative risk for NET developing in a HSK is 62, which is greater than that reported for Wilms tumor and transitional cell carcinoma of the renal pelvis. Adding recent cases reported, Motta [1] suggested that the relative risk rises to 120.

The origin of renal carcinoid tumors is controversial because enterochromaffin cells are not found in normal renal parenchyma. It has been suggested that they might originate from neuroendocrine cells associated with intestinal metaplasia of the renal collecting system or neuroendocrine cells found within teratomatous intestinal or respiratory epithelium within the kidney [1, 5]. These theories could explain that renal carcinoid tumor is more frequent in HSK,

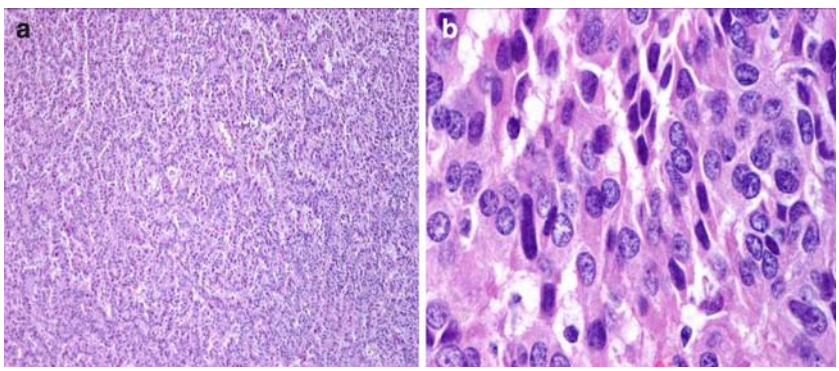

Fig. 2 (**A**) Trabecular pattern of growth (H&E 10x). (**B**) High-power view showing the cytologic appearance of a carcinoid tumor. The tumor cells have uniform features with eosinophilic, granular cytoplasm and nuclei with granular chromatin, the so called ''salt and pepper'' pattern (H&E 40×)

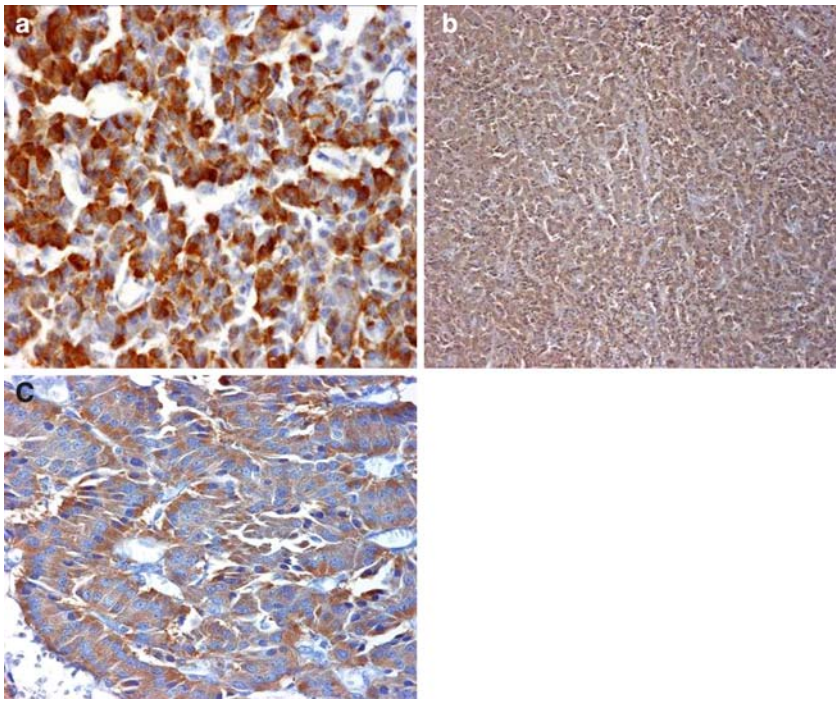

Fig. 3 This primary carcinoid tumor of the kidney showed immunoreactivity for (**A**) Synaptophysin, (**B**) Neuron-specific enolase and (**C**) Chromogranin A

possibly because abnormalities or teratomatous elements in epithelium are more common in these kidneys [6].

The most common symptoms at the time of diagnosis are abdominal or lower back pain and weight loss. Hematuria and pyuria may be present [1]. Carcinoid syndrome is rarely associated with primary renal carcinoid tumor, even in case of metastatic disease [1, 4, 7]. The classical Carcinoid syndrome occurs in less than 10% of patients with gastrointestinal carcinoid and in less than 5% of patients with pulmonary carcinoid [8, 9]. This is characterized by cutaneous flushing most commonly on the face, neck and upper chest, and diarrhea in almost 75% of cases. Other less common manifestations include cardiac valvular abnormalities (carcinoid heart disease), bronchoconstriction and pellagra. These clinical manifestations are caused by the release of 5-hydroxytryptophan (5-HTP), 5-hydroxytryptamine, histamine, polypeptide hormones (corticotrophin), prostaglandins, kinins and substance P from carcinoid tumor [8, 9].

Microscopically, the tumor cells are well differentiated. The architecture is often trabecular-cordonal, and therefore, similar to that seen in rectal carcinoid and stromal carcinoid of the ovary. The cytoplasm of tumor cells may have an oncocytic appearance. The diagnosis is based on immunohistochemical features. These include staining for chromogranin A, NSE, synaptophysin and protein S-100 [1, 4].

The prognosis of patients with renal carcinoid tumors is difficult to predict, and the stage at the time of diagnosis seems to be the most important factor [1, 10]. Published data suggest a better prognosis for primary renal carcinoid tumors arising in HSK than those arising in normal kidneys [1, 4]. Outcome appears not to be directly related to the presence of nodal metastases or type of surgery. The development of distant metastases after surgery seems not to worsen prognosis [1]. However, even though our patient has a 33-month survival after metastases were initially detected, the disease has showed progression and the disease-free period after surgery was as short as 5 months. For that reason, we believe that, for localized tumors, an aggressive surgical approach should be the treatment of choice, given that the use of chemotherapy as adjuvant or palliation has been unsuccessful and radiotherapy is only palliative [8].

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