Case Report
Breast metastases from renal cell carcinoma in a male patient: a rare case and review of the literature

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Abstract: Metastases to the breast from extra-mammary tumors are uncommon. Renal cell carcinoma (RCC) is considered to be an unusual source of such metastases, especially for a male, with only three previously reported cases. Here, we report a 40-year-old Asian male post nephrectomy for RCC diagnosed three years prior who presented with a breast mass. Ultrasound evaluation of the breast mass revealed a solid lesion that was concerning for malignancy. Given the relatively recent history of renal cell carcinoma, the possibility of a metastasis was considered. However, the extremely low incidence of RCC metastasis to the breast would lead pathologists and clinicians to consider a primary tumor such as male breast cancer as the first differential diagnosis. Ultimately, the histopathological evaluation showed that the neoplastic cells showed clear cell carcinoma features. Immunohistochemistry (IHC) showed that the neoplastic cells were positive for cytokeratin (CK), CD10, vimentin, and epithelial membrane antigen (EMA), but were negative for estrogen receptor (ER), progesterone receptor (PR), and GATA-3. Based on the medical history, morphology, and IHC study, the diagnosis of RCC metastatic to the breast was established. Due to the extremely low incidence of metastatic RCC to the breast, the risk of misdiagnosis is high and has the potential to negatively impact patient management. Here, we review the clinical, pathological, and prognostic information of RCC metastasis to the breast. When a male with a history of RCC presents with a suspicious breast mass, metastatic carcinoma should be taken into consideration, and pathologic examination is the most useful tool for the definitive diagnosis.

Keywords: Breast, renal cell carcinoma, histological, metastatic carcinoma, treatment

Introduction

Renal cell carcinoma (RCC) accounts for 2-3% of adult tumors, representing 90% of renal malignancies and is the most lethal neoplasm of the urologic system [1, 2]. Lung, lymph-node, bone, and liver present as the most common metastatic sites [3-6]. Metastases to the breast from extra-mammary malignancies are rare, particularly in males [7, 8]. Most frequently, these metastases are observed in melanoma, lymphoma, and leukemia, while metastasis from RCC is considered as an uncommon source [9]. Here we report a 40-year-old Asian male, with an isolated metastasis to the breast occurring three years after undergoing a nephrectomy for RCC. To our knowledge, there are only twenty-seven cases of RCC metastatic to the breast reported previously, and this is the third reported case in a male. Due to the extremely low incidence of the metastatic RCC to the breast, it is easily overlooked in favor of more likely diagnoses which may severely impact both treatment and prognosis.

Case presentation

A 40-year-old Asian male presented to our hospital with a mass in the left breast which had been discovered one month ago. The patient had no pain or any other symptoms. He had a history of RCC and underwent nephrectomy three years ago. During this period, the patient was closely followed-up by radiological examination, and no signs of recurrence or metastasis were detected.
Materials and methods

Ultrasound examination was performed to evaluate the mass. H&E staining was performed using the resected tissues according to the standard protocol. Immunohistochemistry was performed using the SP kit (Maixin Biotechnology, Fuzhou, Fujian, China) according to the manufacturer’s protocol. These sections were incubated overnight at 4°C with the following primary antibodies: CK (1:100, Dako, Carpinteria, CA), vimentin (1:200, Dako), CD10 (1:200, Dako), ER (1:100, Dako) PR (1:100, Dako), GATA-3 (1:200, Dako) and EMA (1:100, Dako). This study was prospectively performed and approved by the institutional Ethics Committees of China Medical University and conducted in accordance with the ethical guidelines of the Declaration of Helsinki. Written informed consent was obtained from the patient for the publication and accompanying images.

Result

Currently, an ultrasound examination showed a solid mass measuring 1.23 × 0.97 × 1.17 cm³ with a regular margin at 8 o’clock, 4 cm from the left nipple, without lymph node enlargement (Figure 1A). Moreover, it showed that the nodule contained rich blood flow (Figure 1B), classifying the lesion as BI-RADS 4C. Both the radiologist and clinician became suspicious of this lesion. However, it was felt that this mass more likely represented a primary breast malignancy given that the incidence of metastatic RCC to the breast is so low. The patient opted to have the mass removed, which was completed under...
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Figure 3. Immunohistochemistry findings show that the tumor cells were strongly positive for CD10 (A), CK (B), EMA (C) and vimentin (D). Magnification 100 ×, Magnification 400 × in the lower right corner with black square.

local anesthesia. Gross examination revealed a white to pink, circumscribed, $1.3 \times 1.2 \times 1.2$ cm$^3$ mass. H&E and immunohistochemistry (IHC) staining was subsequently performed. Microscopically, the tumor was well circumscribed (Figure 2A), with a nest or gland-like architecture (Figure 2B) and small to medium size tumor cells with clear or eosinophilic cytoplasm showed atypical nuclei on low magnification (Figure 2C). Nucleoli were occasionally observed in some tumor cells on high magnification (Figure 2D). IHC showed that the tumor cells were strongly positive for CK, CD10, vimentin, and EMA (Figure 3), but negative for ER, PR, and GATA-3. Based on the medical history, morphology, and IHC, the diagnosis of metastatic RCC to the breast was confirmed (Furhman grade I).

Discussion

Breast is an uncommon site for metastatic disease, especially RCC, with only twenty-seven cases previously reported. Among these, there are fifteen cases of breast metastases discovered years after nephrectomy. In twelve of these cases, including two male patients, the initial presenting symptom was that of a palpable breast mass. To the best of our knowledge, patients with RCC metastasis to the breast after nephrectomy are listed in Table 1. The table shows that the age of the patients ranges from 14 to 88 years (average 66.5 years). Unlike our case involving a male patient, all fifteen cases of breast metastasis after nephrectomy were female patients. Interestingly, the histopathological type of all the metastatic RCC to breast reported have been cases of clear cell carcinoma. Furhman grade ranged from 1 to 3, but no classification of grade 4 cases were reported. Recurrence intervals ranged from 1 to 12 years, with the average recurrence interval being 5.6 years. Unlike a primary breast malignancy, the margins and axillary lymph nodes to be removed are more limited for a secondary metastasis. The prognosis is more favorable with a better functional status and single versus multiple metastases, disease-free survival from the first nephrectomy being greater than one year and having a low grade RCC [10]. According to the results of follow-up, those who develop secondary symptoms after nephrectomy in a short period tend to have a poor prognosis. Compared to the incidence of metastatic disease to the breast, primary breast malignancy is much more common, and clinicians will usually favor this as the top differential. So in this case, male breast carcinoma is the most important differential diagnosis.

During initial consultation, detailed examination should be performed to confirm whether the patient has any underlying malignant tumor. At present, fine needle aspiration cytology (FNAC) is the most usual method for breast lesion diagnosis, but it may increase the possibility of false negative rates for the vascular network that characterizes metastases from RCC [13]. Histopathologic examination is the most important tool in evaluating the differential diagnosis. Neoplastic cells from a malignant tumor will most often have a different morphology and immunohistochemical profile from
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Table 1. The clinical features and prognosis of patients with RCC metastasis to breast after nephrectomy

<table>
<thead>
<tr>
<th>NO.</th>
<th>Source</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Tumor Type</th>
<th>Fuhrman grade</th>
<th>Recurrence interval (yr)</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A. Botticelli, et al [10]</td>
<td>60</td>
<td>F</td>
<td>CCC</td>
<td>II</td>
<td>4</td>
<td>NM</td>
</tr>
<tr>
<td>2</td>
<td>Mervat Mahrous, et al [5]</td>
<td>58</td>
<td>F</td>
<td>CCC</td>
<td>II</td>
<td>5 Died at 14 months</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>S Ganapathi, et al [11]</td>
<td>88</td>
<td>F</td>
<td>CCC</td>
<td>NM</td>
<td>4 At 1 and 6 months, no evidence of recurrence</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Ahmed Alzaraa, et al [8]</td>
<td>81</td>
<td>F</td>
<td>NM</td>
<td>NM</td>
<td>6</td>
<td>NM</td>
</tr>
<tr>
<td>6</td>
<td>Mark E O'Donnell, et al [12]</td>
<td>63</td>
<td>F</td>
<td>NM</td>
<td>NM</td>
<td>4 Died at 3 yrs</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>McLaughlin SA, et al [9]</td>
<td>76</td>
<td>F</td>
<td>CCC</td>
<td>II</td>
<td>12 At 3 months, no evidence of recurrence</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Svetana Bortnik [14]</td>
<td>57</td>
<td>F</td>
<td>CCC</td>
<td>NM</td>
<td>2.8 At 2 yrs, no evidence of recurrence</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Mauro Gacci [15]</td>
<td>82</td>
<td>F</td>
<td>CCC</td>
<td>II</td>
<td>3 Died at 7 months</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Marlena Pursner [16]</td>
<td>14</td>
<td>F</td>
<td>NM</td>
<td>III</td>
<td>1</td>
<td>NM</td>
</tr>
<tr>
<td>12</td>
<td>Lucia Vassali [17]</td>
<td>72</td>
<td>F</td>
<td>NM</td>
<td>II</td>
<td>9 At 1 yr, no evidence of recurrence</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>Neeta Pathe [18]</td>
<td>64</td>
<td>F</td>
<td>CCC</td>
<td>II</td>
<td>10 At 4 months, no evidence of recurrence</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>A. Forte [19]</td>
<td>71</td>
<td>F</td>
<td>CCC</td>
<td>NM</td>
<td>6</td>
<td>NM</td>
</tr>
<tr>
<td>15</td>
<td>Tai-Di Chen [20]</td>
<td>74</td>
<td>F</td>
<td>NM</td>
<td>III</td>
<td>3</td>
<td>NM</td>
</tr>
</tbody>
</table>

Notes: Abbreviations: F, female; CCC, clear cell carcinoma; NM, not mentioned.

that of a primary breast carcinoma. As in our case presentation, the tumor cells showed clear cell features which would lead the pathologist to consider a diagnosis of RCC. IHC also plays an important role, and in our case the tumor cells were positive for CK, CD10, vimentin, and EMA, and were negative for ER, PR, and GATA-3. The treatment of metastatic RCC and primary carcinoma of the male breast is quite different. The principle treatment for male breast carcinoma is a modified radical mastectomy. Based on the high rate of expression of estrogen and progesterone receptors (80-90%), endocrine therapy is utilized and is extremely effective in improving the prognosis, especially in patients with advanced disease [21]. Previous studies have shown that adjuvant radiotherapy and chemotherapy are effective in improving prognosis, but in some cases of older male patients, radiotherapy could cause severe cardiovascular and lung injury which leads to a worse clinical result [22]. Chemotherapy could be performed for patients with endocrine therapy resistance or positive lymph node status [23]. Due to the limited amount of the cases of solitary RCC metastasis to the breast, no standard treatment plan has been widely accepted. Lumpectomy is the main treatment, whether adjuvant radiotherapy and chemotherapy is necessary still needs further study. However, breast involvement may be a signal of rapid widespread dissemination of the neoplasm, and in that situation, the cancer cells are usually not sensitive to classical chemotherapy and radiotherapy. Targeted therapy against vascular endothelial growth factor (VEGF) and mammalian target of rapamycin (mTOR) are more effective in improving prognosis in that setting [24].

Conclusion

Establishing the correct diagnosis is crucial due to the differences in treatment and prognosis of male breast carcinoma and RCC metastatic to the breast. The correct diagnosis will aid the clinicians in choosing the most suitable medical plan for the patient and will hopefully translate to better patient outcomes. The possibility of metastatic carcinoma should not be ruled out for a lesion that does not show the typical characteristics of breast cancer.

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Disclosure of conflict of interest

None

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References


