

## Case Report

# Breast metastasis from clear cell renal carcinoma: a case report and literature review

Ketao Jin<sup>1</sup>, Ji Wang<sup>2</sup>, Chenyang Ye<sup>3</sup>, Hanchu Xiong<sup>2</sup>, Bojian Xie<sup>4</sup>, Wenmin Wang<sup>4</sup>, Jichun Zhou<sup>2</sup>, Jieqing Lv<sup>1</sup>, Binbin Cui<sup>4</sup>

<sup>1</sup>Department of Colorectal Surgery, Shaoxing People's Hospital, Shaoxing Hospital of Zhejiang University, Shaoxing, P. R. China; <sup>2</sup>Department of Surgical Oncology, Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, Hangzhou, P. R. China; <sup>3</sup>Department of Thoracic Surgery, The 2nd Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, P. R. China; <sup>4</sup>Department of Surgical Oncology, Taizhou Hospital, Wenzhou Medical University, Linhai, P. R. China

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**Abstract:** Breast metastasis from clear cell renal cell carcinoma is rare and usually correlates with poor prognosis. Thus far, only sporadic cases have been reported and no systematic standards for diagnosis and treatment have been reached. This present study not only reports a rare case of breast metastasis from renal malignancy but also reviews all related literature. A 56-year-old female with a history of clear cell renal cell carcinoma resection suffered from breast metastasis. She received lumpectomy and survived for 16 months after surgery. Improvements in prognosis, early detection, and surgical resection of metastatic lesions are necessary. Metastasis is prone to occur in the ipsilateral breast. Comprehensive consideration, including radiology, pathology, and individual medical history, is required for diagnosis.

**Keywords:** Breast neoplasms, renal cell carcinoma, metastasis, case report

### Introduction

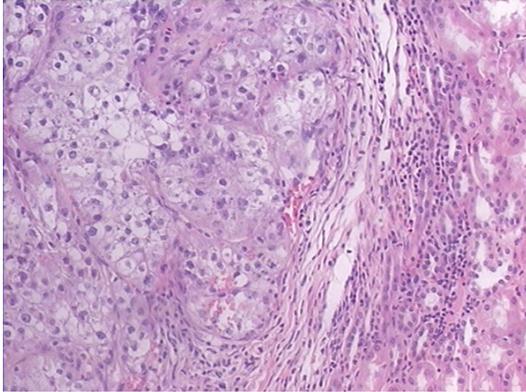
Breast metastasis from extramammary malignant neoplasms is rare, accounting for approximately 0.3-2.7% of all breast tumors [1]. Extramammary tumors mainly include hematological malignancies, lung cancer, and malignant melanomas, whereas metastasis from the kidneys is extremely rare. To the best of our knowledge, there are no published studies discussing breast metastasis from clear cell renal cell carcinoma (ccRCC). This study presents a rare case of breast metastasis from renal cell cancer (RCC). Relevant studies on this topic were reviewed with an aim of shedding light on diagnostic features and potential therapy strategies for this rare event.

### Case report

A 56-year-old woman received a right radical nephrectomy followed by interferon therapy, in 2012, with pathologically confirmed conventional clear cell carcinoma Fuhrman Grade 3

(**Figure 1**). The maximum diameter of the tumor was 4.5 cm. According to TNM classification, the tumor was T1bN1M0 and stage III. Three months after surgery, the patient developed lung metastasis and was treated by everolimus 10 mg q.d. After another 9 months, bone metastasis was identified and she was given zoledronic acid. In September 2013, she noticed a lump in her right breast. The lump was located in the lower outer quadrant and presented several mixed solid cystic masses with a lobulated shape (3.6 cm in maximal diameter), according to breast ultrasound imaging (**Figure 2A**) and hypervascularity Doppler imaging (**Figure 2B**). Mammogram images revealed a mass without microcalcification (**Figure 2C**). Image examination detected no signs of enlarge lymphnodes. The patient then received a lumpectomy. Histological examination confirmed a metastasis of renal clear cell carcinoma (**Figure 3A**), Fuhrman grade 2, with positive immunostaining for CK and vimentin (**Figure 3B, 3C**), but negative staining for CD10,

## Breast metastasis from clear cell renal carcinoma



**Figure 1.** Histological examination showed clear cell renal cell carcinoma (Original magnification H&E stain,  $\times 100$ ).

CK7, and GCDFP-15. After an overall survival of 36 months, the patient died in the beginning of 2015.

### Discussion

Frequency of tumor metastasis to breasts from extramammary lesions is very low and usually indicates a poor prognosis. One study of breast metastasis from non-breast solid neoplasms reported a median survival time since diagnosis of breast metastasis of 10 months [2]. The prognosis of patients not receiving surgery was poorer than those with surgery ( $P < 0.001$ ) [2]. Therefore, timely and effective diagnosis of breast lesions is critical. Breast malignancies should be differentiated according to the following possibilities. First, if the patient has a previous medical history of extramammary malignancies, the breast lesion could be either a metastasis or a new primary breast tumor called double/multiple primary cancers. It is also possible for concurrence of both situations mentioned above. An example of tumor-to-tumor metastasis, a patient that initially underwent nephrectomy for ccRCC happened to receive modified radical mastectomy for invasive ductal carcinoma 3 years later. Histological examination of the breast lesion, however, not only revealed a breast cell malignancy but also a small focus of metastatic clear cells [4]. Second, if the patient has no known cancer-related history, a primary breast malignancy should be initially considered. The possibility of simultaneous discovery of breast metastasis and primary cancer also needs to be considered when it comes to suspicious features [5].

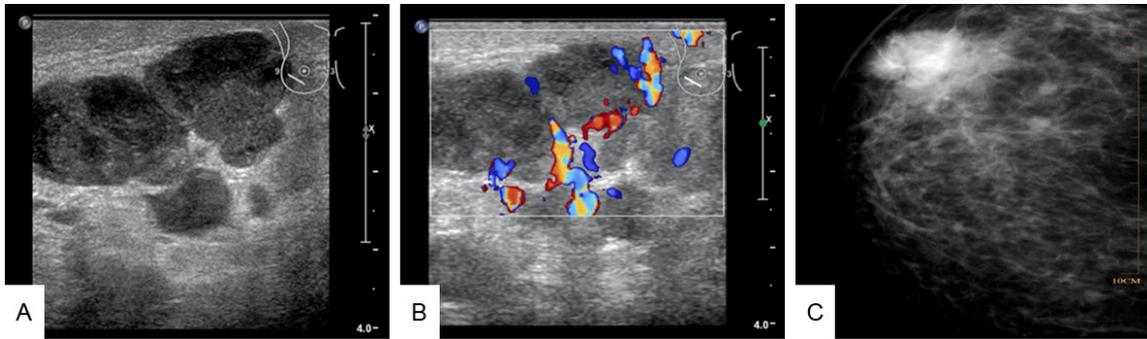
To find common characteristics of breast metastasis from ccRCC, this study used keywords such as “clear cell” OR “renal”, “breast”, and “metasta\*”, finding 8 related cases [4-11] in English with full text available. Their features are summarized in **Table 1**.

Most patients were over 60 years old, except one young woman of 44. Two cases were diagnosed with both primary renal cancer and breast metastasis at the same time, while six of the eight cases took more than 3 years from primary diagnosis to breast metastasis. There are two possible reasons to explain this: (1) Slow development of the disease or (2) Late discovery of the breast mass. The present case is the second youngest patient reported with an onset age of 56. It only took 19 months to diagnose breast metastasis.

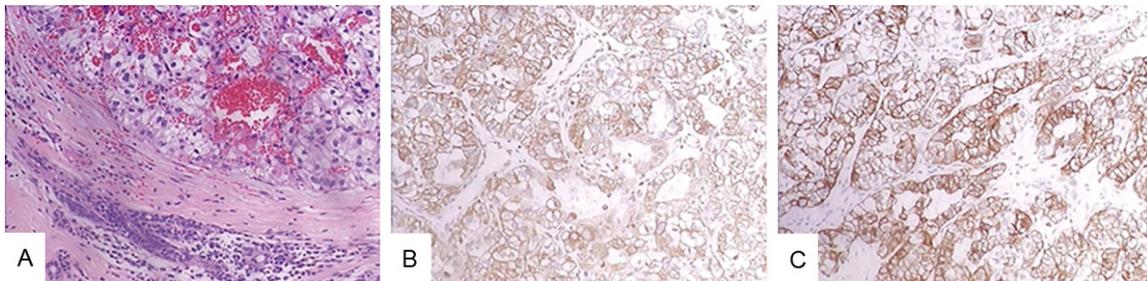
Seven of nine cases (six cases in **Table 1** and one case we presented) had an ipsilateral metastasis in the breast with renal lesions while only one patient happened to form a contralateral metastasis. Another patient with contralateral metastasis had a history of ipsilateral mastectomy for breast cancer. This was hard to classify [11]. These significant preferences indicated that more attention should be paid to ipsilateral metastasis.

Screening by radiological examination is a necessary method for discovery and differentiation of the breast lesions. Surov et al. [3] discussed features of radiological appearance in patients with breast metastases from non-mammary malignancies. 1) In mammography, the most common pattern of metastasis is a round oval mass with well circumscribed margins, while 10% have microcalcifications; 2) Ultrasound images are frequently characterized by hypoechoic, round or oval shape, and microlobulated or circumscribed margins, with posterior acoustic enhancement. Hypervascularity appearing in Doppler imaging accounts for 39% of breast metastasis; 3) Regarding magnetic resonance imaging, most lesions exhibit homogenous contrast enhancement with 18% of type 1, 52% of type 2, and 30% of type 3 kinetic curve. The cases listed for this study were in accordance with these characteristics. However, their appearances did not seem specific compared to primary breast cancer. Biopsy is a sensitive and specific approach for identifying metastases to the breasts. It helps to prevent

## Breast metastasis from clear cell renal carcinoma



**Figure 2.** A. Ultrasonography showed hypoechoic, lobulated mass in the right breast. B. Color Doppler sonogram showed intralesional vascularization. C. Craniocaudal mammogram presented a large mass without microcalcification in the lower-outer quadrant.



**Figure 3.** A. Histological examination showed metastatic cells with clear cytoplasm separated by a prominent vascular network in breast. (Original magnification H&E stain,  $\times 100$ ). B, C. Immunohistochemistry of metastatic cells showed CK (+), and Vimentin (+), respectively. (Original magnification H&E stain,  $\times 100$ ).

unnecessarily over-enlarged surgery due to misdiagnosis of primary breast cancer. In nine cases, five patients were diagnosed successfully by biopsy including core biopsy or fine-needle aspiration cytology (FNAC). One failed because of insufficient tissue. There have been several controversies regarding the accuracy of FNAC, not only concerning inadequate tissue but also the limitation of cytomorphology and lack of histology [7]. Thus, needle-core biopsies have been widely used. Biopsies combined with immunological technology will enhance accuracy [12].

For immunohistochemistry examinations, metastatic cells from ccRCC are stained positive for almost 90% of RCC markers, but only 15% positive for breast cancer markers [13]. For example, CD10, an antibody against proximal tubular brush border antigen, shows high sensitivity and specificity in indicating metastatic cells from ccRCC, but is uncommon for breast cancer (5%) [14]. In the case of simultaneously existing primary invasive ductal carcinoma of breast tissue and metastasis of clear cell carcinoma, a cluster of clear cell RCC could be

encased by typical IDC [4]. Immunostaining was shown positive for CD10 and vimentin in the focus of clear cell, while the surrounding IDC was negative for both markers and positive for Her2/neu. Additionally, co-expression of CK and vimentin helps to detect a focus of clear cell RCC [15]. In contrast to these positive markers, estrogen receptors GDFP-15 and CK7 are rarely expressed in ccRCC. Although immunostaining facilitates to differentiate diagnosis, a comprehensive decision should be noticed because most markers do not have a specificity of 100%.

Eight of nine patients underwent surgery treatment, with one even receiving further interferon treatment. Surgery treatment brought higher survival advantages than non-surgery treatment [2]. However, considering the limited sample number and selection bias for this study, more data are needed to evaluate the advantages of surgical resection of breast metastases.

Breast metastasis from ccRCC is rare and has been associated with poor prognosis.

## Breast metastasis from clear cell renal carcinoma

**Table 1.** Clinical characteristics and treatment outcomes in eight cases with breast metastasis from ccRCC

Author	Age (years)	Disease progression	Treatment for renal mass (maximal diameter)	Time from diagnosis to breast metastasis (years)	Breast metastasis				Axillary lymph nodes	Survival time after breast treatment (months)
					Location (quadrant)	Size (mm)	Biopsy	Treatment		
Carr, B. I (1983) [11]	64	Right breast cancer→right kidney→left breast metastasis from kidney	Excision	5	Upper outer	NR	Yes	NR	NR	NR
Chen, T. D et al. (2014) [4]	74	Right kidney→lung and right breast metastasis with concurrency of breast cancer	Excision	4	Upper outer	35*35*20	Yes	Excision	Negative	NR
Solaini, L et al. (2014) [5]	44	Simultaneous discoveries of left kidney primary cancer and metastatic site including left breast, liver and lymphadenopathies etc.	Palliative care (80 mm)	Simultaneously	Upper inner	15*10	Yes	Palliative care	Negative	4
Alzaraa, A et al. (2007) [6]	81	Right kidney→right breast metastasis	Excision	5.5	Upper outer	17*13*9	Yes	Excision	Negative	17+
Botticelli, A et al. (2013) [7]	60	Right kidney→right adrenal→left breast metastasis	Excision (54 mm)	4	Lower inner	5*6	Yes, but invalid due to insufficient tissue	Excision	NR	NR
Forte, A et al. (1999) [8]	71	Left kidney→right breast metastasis	Excision	6	Superior internal and inferior internal	100*80	No	Excision	Negative	NR
Gacci, M et al. (2005) [9]	79	Right kidney→right breast metastasis	Excision (45 mm)	3	NR	NR	NR	Excision + interferon	NR	10+
Lee, W. K et al. (2007) [10]	71	Simultaneous discoveries of right kidney primary cancer and breast metastasis→brain metastasis	Interleukin-2 immunotherapy (160 mm)	Simultaneously	Lower outer	About 40	Yes	Interleukin-2 immunotherapy	NR	5+

Abbreviations: NR, not report; ccRCC, clear cell renal cell carcinoma.

## Breast metastasis from clear cell renal carcinoma

Currently, there are no established therapies. However, timely discovery and surgical interference are necessary to achieve good prognosis. Ipsilateral metastasis of the breast is more frequent. Final diagnosis requires comprehensive consideration, including radiology, pathology, and individual medical history.

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### Disclosure of conflict of interest

None.

**Address correspondence to:** Dr. Binbin Cui, Department of Surgical Oncology, Taizhou Hospital, Wenzhou Medical University, 150 Ximen Street, Linhai, P. R. China. E-mail: cuiibb@enzemed.com

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