# Breast Metastasis from a Medullary Renal Cell Cancer

Amal Alrayes, MBBCh, MRCSI, CABS* Ali Alhawaj, MB BCh BAO**

**A twenty-seven-year-old female diagnosed with renal cell carcinoma presented post-radical nephrectomy with bilateral breast lesions. Clinically, the lesions appeared malignant. Core biopsy confirmed a metastatic secondary breast cancer from primary medullary renal cell carcinoma.**

**Metastatic breast cancer from renal cell carcinoma is extremely rare; very few cases were reported in the literature. There are no clear guidelines on the management of such cases. The prognosis is very poor and the treatment remains controversial.**

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Metastatic neoplasms to the breasts from extra-mammary tumors are extremely rare. The incidence ranges from 0.5% to 6.6% of all malignant tumors according to autopsy series[1]. Primary tumors that commonly metastasize to the breast include the contralateral breast, lymphoma, leukemia, malignant melanoma and lung cancer[2-5].

Primary medullary renal cell carcinoma (RCC) is an extremely rare and aggressive disease accounting for 3% of all neoplasms in adults[3]. At the time of diagnosis, 30% of patients have metastases to other organs, such as the lung, lymph nodes, bone, liver, adrenal gland and central nervous system. Therefore, breast involvement is considered extremely rare[3]. According to literature, only 25 cases were reported. Among them, 14 occurred after nephrectomy, as in our case[6]. This is the first documented case of RCC metastases to the breast in the Kingdom of Bahrain.

The aim of this presentation is to report a rare case of primary medullary renal cell carcinoma, which had metastasized to the breast following nephrectomy.

## THE CASE

A twenty-seven-year-old female, known case of sickle-cell trait was diagnosed with left kidney RCC in January 2015. She underwent left radical nephrectomy on 18 February 2015. Pathological examination demonstrated medullary RCC with free vascular and surgical margins, see figures 1 and 2.

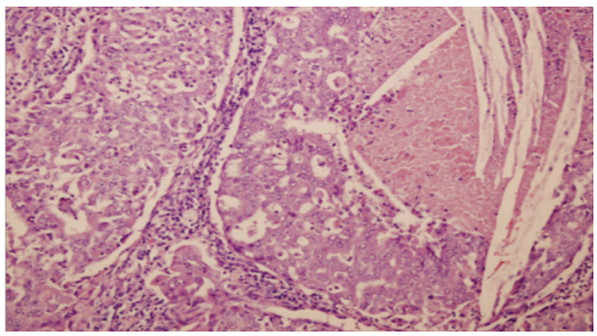

**Figure 1: Nephrectomy Specimen Showing an Ill-Circumscribed Tumor Measuring 5.5 x 5 x 3.5 cm in the Mid Pole of Left Kidney with Areas of Hemorrhage and Necrosis**

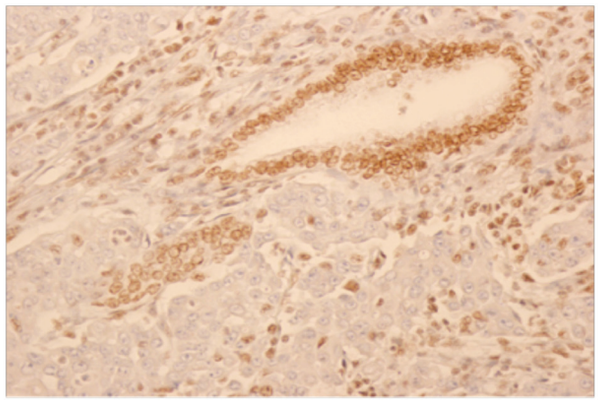

**Figure 2: Renal Tumor Showing Loss of INI Immunostaining Consistent with Medullary Renal Cell Carcinoma**

The immediate postoperative course was uneventful, and the patient was disease-free both clinically and radiologically. PET CT Scan three months postoperatively revealed active and significant abdominal lymphadenopathy at the left para-aortic and aortocaval region with high fluorodeoxyglucose (FDG) metabolism, which was highly suggestive of metastasis, and no apparent other uptake. The patient was started on molecular-targeted therapy: Pazopanib (systemic tyrosine kinase inhibitor).

A repeat PET-CT four months later revealed recurrence in the tumor bed with disease progression and newly developed FDG uptake in the left supraclavicular, retrocrural, common iliac lymph nodes and bilateral breast lesions with high suspicion of malignancy, see figure 3. MRI breast and biopsy were scheduled; however, the patient was lost to follow-up.

* Consultant General Surgical Oncologist
** Surgical Resident
Department of General Surgery
Salmaniya Medical Complex
The Kingdom of Bahrain
E-mail: dr.ali.alhawaj@gmail.com; alrayes.amal@gmail.com; arayes@health.gov.bh

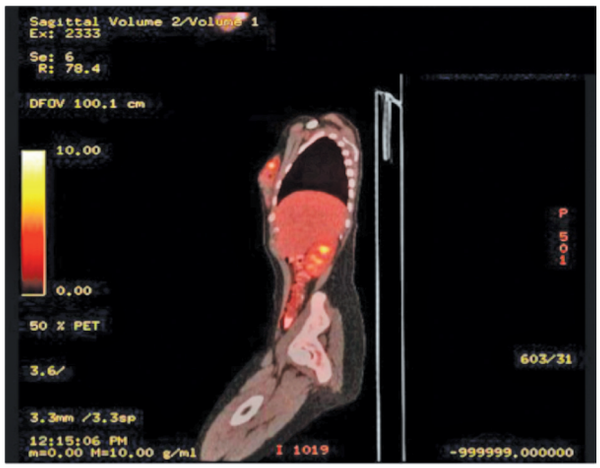


**Figure 3: PET CT Scan Showing High FDG Re-uptake in the Breast**

The case was presented at a multidisciplinary conference. Treatment options were discussed thoroughly regarding surgical approach compared to conservative approach for the abdominal disease recurrence. However, surgery for the breast secondary was not considered given her systemic disease. Due to the rare presentation of such cases and the lack of guidelines, the optimum management remains controversial. However, the patient was reluctant to go for surgery with a notable deterioration in her general condition.

Two months later, the patient was noted to have progressively enlarging bilateral breast lesions. A core biopsy was performed and demonstrated features compatible with metastatic carcinoma originating from a primary medullary RCC, see figure 4. During the same admission, the patient started experiencing diffuse abdominal pain and distension. CT abdomen revealed bowel dilatation with transitional zone at the splenic flexure consistent with bowel obstruction. Her clinical condition and abdominal findings were deteriorating. An emergency laparotomy was performed. Intra-operatively, a tumor recurrence was found in the tumor bed, which was unresectable, very large and adherent to the retroperitoneum with invasion of the colonic splenic flexure. An extended right hemicolectomy with ileostomy and mucous fistula was performed. The postoperative course was uneventful. Palliative chemotherapy was decided. However, the patient deteriorated systemically and expired of the disease progression twelve months following her initial diagnosis.

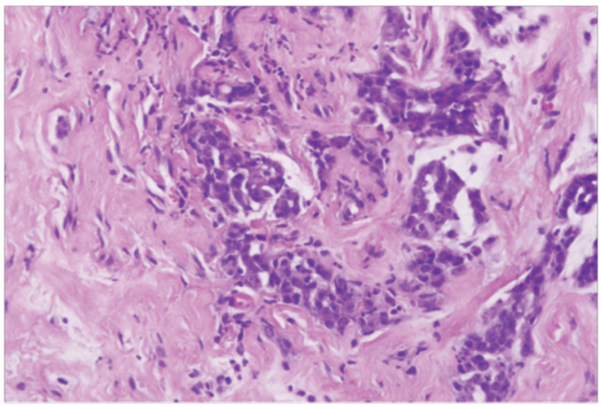

**Figure 4: Breast Core Biopsy Showing Linear Fragments of Breast Parenchyma Revealed Foci of Neoplastic Medullary Carcinoma**

## DISCUSSION

Secondary breast cancer is rare; the incidence ranges from 0.5% to 6.6% according to autopsy series[1]. Metastases from the contralateral breast, lymphoma, leukemia, malignant melanoma and lung cancer have been reported in literature[2-5]. Metastases from Primary RCC are extremely rare and very few cases were reported in the literature.

The average age for a diagnosis of breast metastases from an extra-mammary primary malignancy is 47 years old; our patient presented at a much younger age[1]. Patients can either present with a breast lesion initially from a primary RCC or with breast metastases following nephrectomy. The majority of breast metastases from primary RCC occur 1 to 18 years after nephrectomy[2]. In our case, the patient presented five months after radical nephrectomy for RCC. Most of the reported cases were older females and were disease-free after the initial resection of primary RCC. Our case had rapid progression of the disease, which indicated aggressive tumor biology.

A metastatic breast lesion presents as a rapidly enlarging painless mass, usually not involving the skin with variable axillary lymph node involvement[1,3,6]. Radiologically, the lesions lack the usual microcalcifications on mammography but may show prominent vascularity suggestive of malignant disease[1,3,4,6]. CT scan should be included in the workup for disease staging[6]. Studies suggested that breast lesions presenting in patients with RCC should be investigated with a higher index of suspicion and a confirmatory histopathological biopsy is warranted[6].

It has been postulated that the mechanism of the spread of the tumor cells from RCC to the breast is hematogenous. It begins from the renal vein to the inferior vena cava, ending up in the arterial circulation and to the breast. Hence, it is likely to metastasize to multiple organs[2,6].

Studies have suggested a correlation between medullary RCC and sickle cell trait. Medullary RCC is a very aggressive disease that is usually metastatic at the time of presentation. The mechanism of malignant proliferation is thought to be triggered by the hypoxic acidotic environment in the medulla. This further promotes sickling of Hemoglobin S (Hgb S) leading to malignant growth[5].

There are no clear guidelines on the management of secondary breast lesions that metastasized from RCC. Several studies concluded that palliative radiotherapy or chemotherapy is preferred in diffusely metastatic diseases[1,3]. Other studies suggested surgical resection of the breast tumor bloc if the disease is localized to the breast, followed by adjuvant therapy; especially in patients who were cancer-free for a long period[4,8]. However, our patient presented with a rapid disease progression; hence, there was a very limited role for surgery in her case. The role of sentinel lymph node biopsy is limited in such cases, as the suggested mechanism of spread is hematogenous rather than lymphatic[6]. Moreover, most cases described in literature presented with breast tumor devoid of axillary lymph node involvement. Therefore, mastectomy and lymph node dissection add no benefit to the patient with metastatic disease from RCC[3].

The prognosis of metastatic RCC is very poor, and the survival rate ranges from 10 months to one year[1,2]. According to the Memorial Sloan-Kettering Cancer Center (MSKCC) study, the average survival of patients post-nephrectomy followed by metastasectomy is approximately 30 months[7].

## CONCLUSION

**A twenty-seven-year-old female was diagnosed with renal cell carcinoma post-radical nephrectomy who developed bilateral breast lesions and eventually multi-organs involvement which led to her demise.**

**Breast lesions presenting in patients with RCC should be investigated with higher index of suspicion. In cases of confirmed local recurrence, the role of surgery should only be considered if the recurrence was resectable with clear margins. The role of surgical management should be individualized. Surgical management of breast secondary malignancy would be recommended in case of absence of any other systemic disease. Prognosis remains guarded in view of the status of systemic disease and there is a lack of strong options of adjuvant treatment.**

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