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A unique case of hormone receptor-positive breast cancer metastasis to kidney responsive to endocrine therapy

Ami Patel, MD*; Rita Blanchard, MD

***Ami Patel, MD**

Department of Hematology/Oncology, Boston University Medical Center, USA
Email: ami_patel@dfci.harvard.edu

Abstract

Renal metastasis from breast cancer is very rare and often asymptomatic. It is generally noted as an incidental finding on imaging and may even mimic the appearance of primary renal tumors on radiographic imaging. It is often detected several years after the initial diagnosis. As only a handful of cases have been reported in the literature to date, the optimal therapy is unknown. Of the few cases that have been reported, surgical resection appears to be the treatment of choice in managing isolated metastatic renal lesions. However, outcomes of most cases managed in this fashion have not been reported. Percutaneous cryoablation is another treatment option for local control of isolated renal metastasis from breast cancer when surgery is not an option. Chemotherapy has generally been the therapy of choice in patients with multifocal renal lesions or poor-risk disease, but survival of >8-10 months has only been reported in 2 out of 8 cases treated with chemotherapy. While bony metastases tend to respond well to endocrine therapy, response is generally not as robust in the setting of visceral metastases which are a poor prognostic factor. Many tumors are intrinsically resistant or develop resistance to endocrine therapies. Although endocrine therapy is currently first-line therapy in the setting of visceral metastases because it can offer disease control with less adverse effects and improved quality of life compared to chemotherapy, there have been no case reports showing successful treatment of renal metastases specifically. We aim to present a unique case of hormone receptor-positive breast cancer with metastatic spread to the kidney that was detected approximately 10 years after the initial diagnosis and has been responsive to endocrine therapy. This case illustrates that endocrine therapy may be a viable option to treat breast cancer in the setting of rarely identified renal metastasis not amenable to surgical resection.

Keywords

hormone receptor-positive breast cancer; metastasis; kidney; endocrine therapy

Abbreviations

AC-T: Adriamycin/Cyclophosphamide + Paclitaxel; XRT: Radiation therapy; RCC: Renal Cell Carcinoma; CT: Computed tomography; CAP=Chest/Abdomen/Pelvis; H/H: Hemoglobin(g/dl)/Hematocrit(%); BMI: Body mass index; IVC=Inferior vena cava

Introduction

Distant metastatic spread is the major cause of death from breast cancer [1]. Breast cancer metastasis can occur via direct invasion, lymphangitic spread, and/or hematogenous spread. Common sites of breast cancer metastasis include bone, lungs, liver, and brain. While bone is the most common site of metastasis, approximately 60% of metastatic breast cancer cases have lung involvement. The liver is generally involved in 50% of metastatic breast cancer cases and the brain is involved in about 15% of cases [2-3]. Liver and brain metastases usually occur late in the disease course and are suggestive of poor prognosis [1]. In contrast, breast cancer metastasis to the kidney is very rare and often asymptomatic. Only a few such cases have been sporadically reported in the literature to date. It is thought that metastatic spread to the kidney in these cases is primarily hematogenous [4]. Additionally, the interval between initial breast cancer diagnosis and detection of renal metastasis is often several years and longer disease-free intervals are associated with better prognosis [5]. It is notable that renal metastases from breast cancer can mimic the radiographic appearance of primary renal tumors and approximately 9-14% of renal tumors found at the time of autopsy are from breast origin [6-7].

Case Presentation

Our patient is a 43 year-old woman with past medical history significant for hypertension, hyperlipidemia, obesity, open-angle glaucoma, and stage IIIA (T3N2AM0) invasive ductal carcinoma of the left breast initially diagnosed in June 2003. She denied any smoking history or family history of breast cancer at the time of diagnosis. Patient underwent left modified radical mastectomy and axillary lymph node dissection in July 2003. This was sequentially followed by 4 cycles of adjuvant chemotherapy with dose-dense AC-T, adjuvant XRT to the left chest and axilla completed in April 2004, and endocrine therapy for 4 years which she self-discontinued in March 2008 (initially anastrozole which was later switched to exemestane/triptorelin due to palpitations and then to tamoxifen to simplify her regimen prior to moving to Florida). Patient underwent left breast reconstruction with TRAM flap in October 2005 and remained without evidence of disease until May 2012 when she sustained a pathological left hip fracture in the setting of a mechanical fall. Imaging at that time revealed metastatic disease in the left hip and knee for which she underwent left hip replacement followed by XRT to the left hip and tibial plateau in August 2012.

Patient was then maintained on leuprolide (eventually changed to triptorelin per formulary) and monthly pamidronate which was changed to denosumab in January 2013 after PET CT confirmed progression of disease with multiple bony metastases in the right scapula, left iliac bone, and possibly the left distal femur. She remained clinically stable over the next year but restaging contrast-enhanced CT CAP showed a 2.2 cm lesion in the interpolar region of the right kidney suspicious for RCC with enlarging prominent adjacent lymph nodes measuring up to 11 mm along the right renal vein and upper IVC, in addition to stable bony metastases. Patient remained asymptomatic, denying any flank pain or gross hematuria. Physical exam at that time did not reveal any breast masses or related adenopathy in either breast. Vital signs were notable only for hypertension to 177/111 and BMI elevated in the obese range (33.78). Basic labs were unremarkable except for mild normocytic anemia (H/H=11/35.6) and hyperglycemia to 304 mg/dL. Renal function, liver function, and alkaline phosphatase were all noted to be within normal limits. Findings on MRI Abdomen with and without contrast done in March 2014 were

felt to be consistent withright renal cell carcinoma measuring 2.6 cm in greatest dimension with enlarged right retrocaval lymph nodes measuring up to 1.0 cm. No evidence of the right renal vein or IVC invasion was noted.

To confirm the diagnosis, the right renal lesion was biopsied in April 2014. Pathology surprisingly revealed metastatic carcinoma involving renal parenchyma but favoring breast primary. Surgical RO resection was not felt to be an option given significant adjacent lymphadenopathy in addition to the presence of extensive bony metastases. Since patient had already received adjuvant chemotherapy in the past, we decided to initiate treatment with endocrine therapy that she had not previously received given strong ER positivity of her tumor. Our hope was that this would decrease the tumor burden of her visceral and bony metastatic disease or at least stabilize it. Thus, letrozole 2.5 mg PO q daily was started in May 2014, while monthly triptorelin and denosumab were continued for her extensive metastatic bony disease. Fortunately, her disease has remained stable for over 2.5 years on this regimen which she continues to tolerate well. Her most recent restaging contrast-enhanced CT CAP in July 2016 showed stable right renal lesion still measuring approximately 2 cm (slightly decreased in size from 2.6 cm at initial presentation) and significant decrease in the size of the lytic lesion in the left ilium (now 3.0 cm from 3.5 cm previously).

Discussion

Generally, treatment options for renal metastases from breast cancer depend on the patient's functional status and the extent of metastatic disease (number of organs involved, number of metastases, ability to achieve R0 resection, and disease-free interval) [1,4]. Given that the incidence of renal metastasis from breast cancer is very rare, the optimal management is unknown. When isolated metastatic disease is present, surgical resection appears to be the most appropriate treatment. However, survival >24 months was reported in only 1 such case treated with nephrectomy. Furthermore, there is no data regarding need for adjuvant chemotherapy after R0 resection. While 6 out of 8 cases initially reported in the literature were treated with nephrectomy, outcomes were not reported in most of these cases [1,4]. Percutaneous cryoablation is another effective and well-tolerated option for local control in patients with isolated metastatic lesions in the kidney and other organs who are not candidates for surgery [8]. In contrast, chemotherapy has generally been believed to be the best option to treat patients with poor-risk disease or multifocal renal metastases. Survival of >8-10 months was reported in the remaining 2 such cases treated with chemotherapy [1,4]. In the setting of visceral metastases, endocrine therapy is currently considered first-line therapy and our case illustrates that this concept is still applicable when the metastatic visceral disease is rarely present in the kidney.

Although bony metastases respond well to endocrine therapy, this is not true to the same degree for all other metastatic sites including visceral disease[1]. Tumors can be intrinsically resistant or develop resistance to endocrine therapies [9]. The presence of visceral metastases is a poor prognostic factor. Response of metastatic breast cancer lesions in the kidney to endocrine therapy has not yet been documented specifically based on our review of literature, although visceral metastases in general are known to be responsive to endocrine therapy. Endocrine therapy is therefore currently regarded as first-line therapy in the setting of visceral metastases since it is associated with less toxicity and improved quality of life compared to chemotherapy, while offering disease control and delaying need to use

chemotherapy [10]. From our patient's experience, it appears that endocrine therapy can be a viable and well-tolerated option to treat renal metastasis from breast cancer when surgical resection is not an option. Her case is like most other reported cases of renal metastasis from breast cancer in that she remained disease-free for a long interval of about 10 years after initial treatment of her breast cancer before asymptomatic metastatic disease was incidentally detected in her right kidney on restaging scans. However, her case is unique in that her metastatic renal lesion has remained stable for over 2.5 years on endocrine therapy alone.

Figures

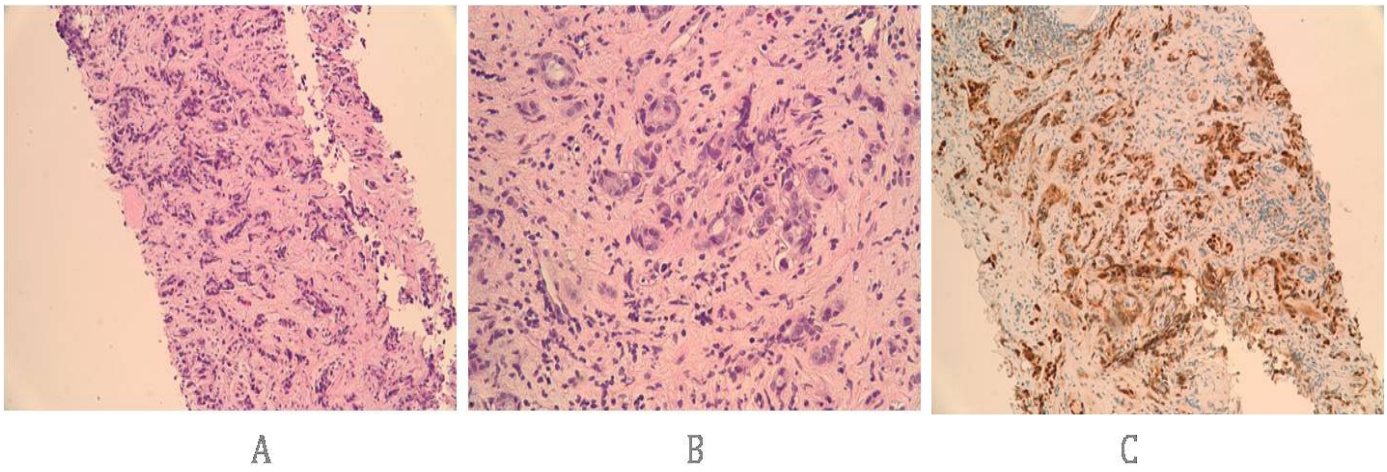
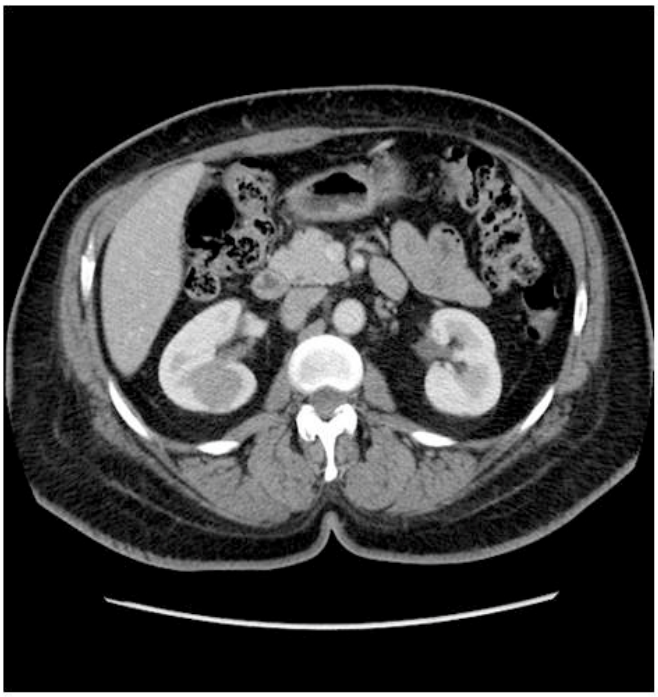
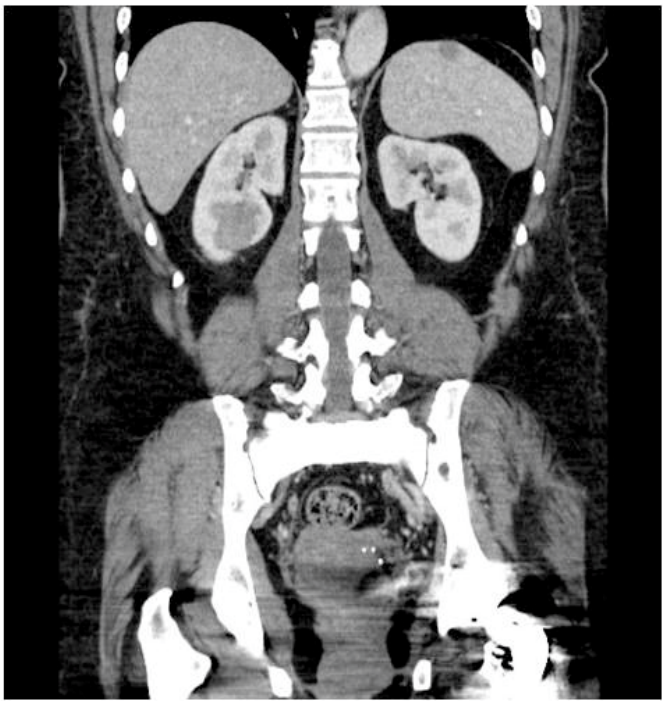


Figure: Pathology: Core fragment of dense fibrous tissue with an infiltrate of partially crushed tubular glands. A: Low power, B: High power, C: Positive ER stain supporting breast origin.

Positive Markers	Negative Markers
ER, AE1/3, Vimentin	PR, Her2-Neu, GCDFP, PAX-8, RCC, CD10, CD117, Ck7



January 2014



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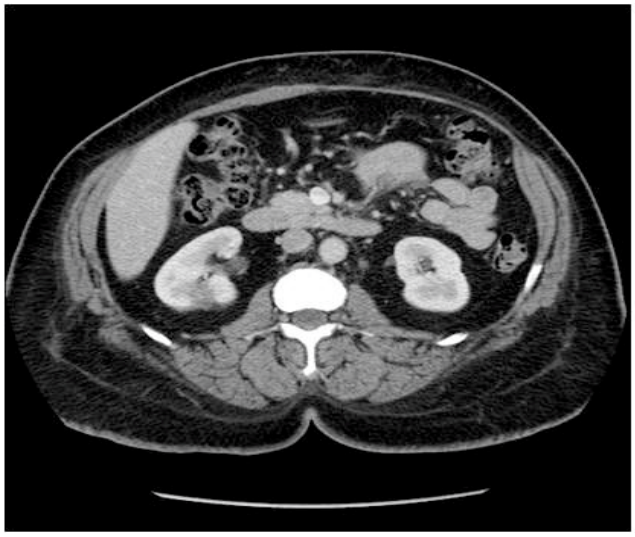

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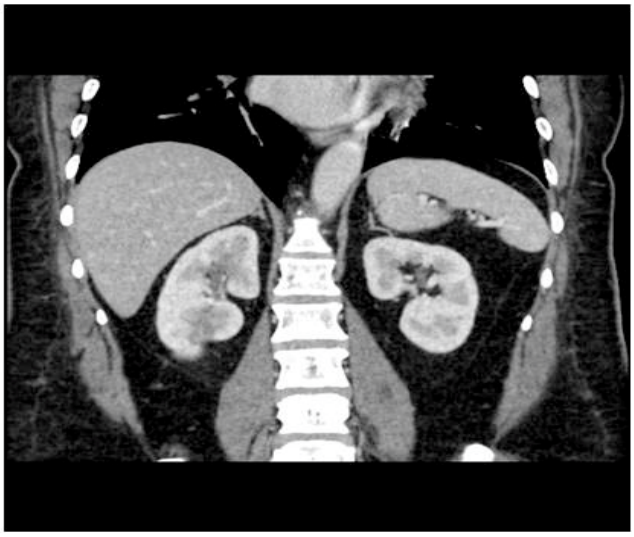

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Conclusion

Endocrine therapy can be a viable and well-tolerated option to treat renal metastasis from breast cancer when surgical resection or other therapies for local control are not an option due to extent of disease. Our case demonstrates that it may be an equally effective and less toxic treatment option compared to chemotherapy which has generally been the treatment of choice in this setting when surgery is not an option.

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Authors Information: Ami Patel, MD*; Rita Blanchard, MD

Department of Hematology/Oncology, Boston University Medical Center, USA

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