An unusual location for metastasis – Breast cancer in the bladder

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ABSTRACT

Metastatic breast cancer is the second most common cancer related death amongst women in the United States. The common locations for metastases—lymph nodes, bone, lung, liver, brain—are well reported. Rarely, breast cancer metastasizes to the bladder. We present a case of primary hormone positive, HER2 unamplified breast cancer, thirteen years in remission, with triple negative metastases to the bladder. Urologists should consider breast metastases in patients with even a remote history of breast cancer who present with gross hematuria to avoid delays in treatment.

1. Introduction

Secondary cancers of the bladder are less common than primary urothelial cell carcinoma. When spread to the bladder occurs, it is typically from regional sites—prostate, colorectal, and cervical being the most common sites of origin. Less common culprits include common cancers: lung, skin, and breast. We report on a case of breast metastases to the bladder. Breast cancer is the most common cancer diagnosed in women in the United States. 1 Mortality in breast cancer is associated with metastatic disease rather than a primary disease. 2 The most common locations for metastases include bone, lung, liver, and brain. In total, 55 incidents of breast cancer metastases to the bladder have been reported, most found post-mortem. 2,2 We present the case of a 64-year-old woman status post simple mastectomy with node-negative ER+/PR+/HER2-breast cancer who underwent adjuvant chemotherapy and completed 10 years of aromatase inhibition for a total cancer-free period of 13 years prior to diagnosis with metastatic disease to the bladder.

2. Case description

A 64-year-old woman with a past medical history of breast cancer status post simple mastectomy, adjuvant chemotherapy, graduated from ten years of aromatase inhibition therapy and cancer-free for 13 years presented to urology clinic with a 3-month history of urinary incontinence, frequency, and urgency. A dipstick urine was unremarkable, cultures negative. She was diagnosed with overactive bladder (OAB) and started on solifenacin 5mg daily. One month later, the patient experienced gross hematuria, suprapubic pain, worsening of frequency. She was treated for suspected urinary tract infection (UTI) with cephalaxin and phenazopyridine. Her symptoms of hematuria and suprapubic pain resolved. Two weeks later, the patient experienced gross hematuria, dysuria, flank pain, and nausea. She presented to the emergency department. Computed tomography (CT) showed bladder wall thickening and ureteral dilation with abnormal enhancement concerning for malignancy vs cystitis (image 1). She was again treated with cephalaxin for suspected UTI with resolution of hematuria, dysuria, and persistence of urgency, frequency, and incontinence. She followed-up in clinic and reported an 11 pound weight loss, anorexia, and continued lower urinary tract symptoms (LUTS). On physical exam, a mass was palpable along the anterior vaginal wall. Cystoscopy revealed bulbous changes under the trigone and posterior bladder wall. She was taken to the operating room three weeks later. An exam under anesthesia noted palpable bladder mass without visual extension into the anterior vagina or rectum. The previously visualized bulbous, nodular bladder mucosa extended through the trigone, lateral walls, and circumferentially around the bladder neck. The ureteral orifices could not be located. The bulbous bladder mucosa was resected with a bipolar loop; approximately 6 cm was resected. The bladder dome and urethra were without visible

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The pathology findings were remarkable for infiltrating carcinoma invading the muscularis, GATA3 and BRST2 positive and therefore compatible with breast cancer (Image 2). While the patient’s primary breast cancer was ER+, PR+, HER2-, the metastases to her bladder were triple negative. Since diagnosis with metastatic breast cancer to the bladder, the patient has received pembrolizumab and paclitaxel therapies, complicated by obstruction necessitating bilateral nephrostomy tubes, two UTIs, constipation and peripheral neuropathy.

In this case, metastatic breast cancer masqueraded as OAB and hemorrhagic cystitis; the time from symptom onset to transurethral bladder resection of tumor (TURBT) was 6 months. Other case reports of breast cancer metastases to the bladder consider incidence, treatment, and congruity of primary and metastatic immunohistochemistry. Our case is one of incongruent primary and metastatic immunohistochemistry and our discussion focuses on detection and consideration from the field of urology, rather than oncological management.

3. Discussion

This case described an uncommon location of breast cancer metastases—the bladder. Prior autopsy studies have shown that breast cancer invades bladders “outside-in”—invoking the outer bladder wall with inward invasion through the detrusor muscle. The mucosa is involved last. Irritative symptoms, including incontinence, and frequency typically arise first and are indicative of detrusor involvement. Involvement of the mucosa, and the associated symptom of hematuria, is often a late finding and explains why cytology is often benign.

Our patient presented with frequency, urgency, incontinence, gross hematuria, flank pain and a rising creatinine; symptoms in line with those of other case reports. Creatinine changes are associated with obstruction rather than indicative of the presence of metastases. These presenting symptoms are non-specific within the field of urology. As such, our patient’s presentation was treated first as overactive bladder, and subsequently as UTI.

Similarly, primary bladder cancer is often a delayed diagnosis in women as they are often treated for more benign causes of LUTS before cancer is considered. Persistence and/or worsening of urgency, despite treatment for urinary tract infection, should flag consideration of less common causes of LUTS such as primary urothelial cell carcinoma and secondary metastatic disease.

CT is the most used imaging method leading to initial suspicion of bladder malignancy. Characteristic findings include bladder wall thickening, enhancing lesions, hydronephrosis and presence of spine metastases in a patient with LUTS. Cystoscopy typically notes inflammatory changes, wall thickening, granulation tissue and a general suspicion that visualized tissue is abnormal and not classical for bladder cancer. Breast cancer metastases to the bladder typically occur ≥5 years after primary breast cancer diagnosis and are reported as late as 17 years later. Our patient’s bladder metastases appeared 13 years after initial breast cancer diagnosis. Not all metastases showed congruent immunohistochemistry with their respective primary tumors; however, our patient’s triple-negative metastasis in the setting of a hormone-positive primary breast cancer is currently the only such incongruity reported.

While breast cancer is an unusual culprit to metastasize to the bladder.
bladder, other uncommon metastases exist, too. Reports of primary melanoma, cholangiocarcinoma, nasopharyngeal carcinoma and pheochromocytoma with metastases to the bladder have been documented. Notably, all presented with lower urinary tract symptoms.

4. Conclusion

This case report highlights the importance of considering metastatic disease—even in instances of remote cancer history—in patients with lower urinary tract symptoms and a history of primary breast cancer.

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