

Rare Isolated Bladder Metastasis in Breast Cancer

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Abstract

Breast cancer (BC) is the most common cancer in women, and approximately 317,000 new cases are expected to be diagnosed in the United States in 2025. Lymph nodes, bones, lungs, liver, and brain are common target organs for BC metastasis. Metastasis to the bladder is extremely rare, with approximately 70 cases reported in the literature. A 76-year-old female patient underwent a right total mastectomy by the general surgery team approximately 25 years ago for a mass in the right breast. The patient presented to the urology outpatient clinic with complaints of hematuria and dysuria. Imaging revealed a solid mass measuring approximately 6.5x3.5 cm, protruding into the bladder lumen from the left anterolateral wall, with a distinct soft-tissue component anteriorly extending into the perivesical fatty planes (possible bladder tumor). Based on this, we performed transurethral bladder tumor (TUR-MT). BC accounts for approximately 2.5% of all cases of metastatic bladder cancer in which the breast is the primary site of origin. Most secondary tumors arise by direct spread from another pelvic neoplasm, such as sigmoid colon, prostate, or cervical cancers. Metastases from distant organs are rarely reported in the literature; the most common are stomach, lung, and melanoma. Metastasis to the bladder after BC is rare and may occur many years later. Although the majority of cases are of the lobular subtype, metastasis can also occur in other subtypes. It may be asymptomatic or manifest as hematuria and voiding problems. Diagnosis involves imaging with ultrasound and magnetic resonance imaging, cystoscopic biopsy, and TUR-MT sampling.

Keywords: Bladder, breast cancer, metastasis

INTRODUCTION

Breast cancer (BC) is the most common cancer in women, and approximately 317,000 new cases are expected to be diagnosed in the United States in 2025.¹

BC can be classified into four molecular subtypes: luminal A, luminal B, human epidermal growth factor receptor 2 (HER2)-positive, and triple-negative BC. These subtypes have very different metastases, prognoses, and treatment methods.²

Lymph nodes, bone, lung, liver, and brain are common target organs for BC metastasis.³ Metastasis to the bladder is extremely rare, with approximately 70 cases reported in the literature. In an autopsy series conducted in 1950, Abrams et al.⁴ identified bladder metastasis in four

patients after examining 167 cases of metastatic BC. In this case, which we identified approximately 25 years after diagnosis, we aimed to contribute to the literature by conducting a literature review.

CASE REPORT

A 76-year-old female patient underwent right total mastectomy by general surgery approximately 25 years ago due to a mass in the right breast. Pathology showed a ductal carcinoma with neuroendocrine differentiation (ER+, T2 N0 M0). Tumor dimensions were reported as T: 16x15x15 mm. She received 4 cycles of combination therapy consisting of cyclophosphamide, methotrexate, and 5-fluorouracil. In addition to this treatment, the patient received tamoxifen therapy. The patient was monitored with annual follow-ups. In 2015, while under follow-

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up, the patient presented to the gynecology and obstetrics outpatient clinic with a complaint of vaginal bleeding. Ultrasound revealed a thick-walled cystic lesion with dense contents, measuring 5.5x3.5 cm, in the right ovarian bed. Based on these findings, the patient underwent a total hysterectomy with bilateral salpingo-oophorectomy in 2015.

Pathology: right adnexa: poorly differentiated malignant epithelial tumor (consistent with breast carcinoma/metastasis of high-grade ductal carcinoma). Uterus: poorly differentiated malignant epithelial tumor in the serosa/implant of high-grade breast ductal carcinoma. Left adnexa: reported as normal.

Following this surgery, she received 6 cycles of paclitaxel plus carboplatin in 2016. The patient was followed by medical oncology and had not received any additional treatment. The patient presented to the urology outpatient clinic with complaints of hematuria and dysuria. The imaging results revealed a solid mass measuring approximately 6.5x3.5 cm protruding from the bladder lumen on the left anterolateral wall of the bladder, with a distinct soft tissue component anteriorly extending into the perivesical fatty planes (bladder tumor?). Based on this, we performed a transurethral bladder tumor (TUR-MT) operation.

The TUR-MT pathology result was consistent with poorly differentiated breast carcinoma, with infiltration or metastasis and minimal malignant epithelial tumor involvement. Approximately 20-25% neuroendocrine differentiation in the carcinoma was observed.

Immunohistochemistry

1. In the TUR immunostaining, CK7 was patchy and variably positive; CK20 was negative (suboptimal technique, no external or internal

controls); uroplakin was negative; thrombomodulin was negative; p40 was negative; e-cadherin was positive; mammaglobulin was negative; gcdfp-15 was negative; progesterone receptor was moderately to strongly nuclear positive in approximately 40% of cells; estrogen receptor was diffusely and strongly nuclear positive; c-erb-b2 was negative (score 0/suboptimal technique, no external control); CD10 was negative; synaptophysin was negative; chromogranin-A was positive in approximately 20-25% of cells; Ki-67 proliferation index was 70% (nuclear positive) (Figure 1).

The patient was subsequently scheduled by radiation oncology for definitive radiotherapy to the bladder and placed on follow-up.

DISCUSSION

BC accounts for approximately 2.5% of all metastatic bladder cancers as the primary site of origin.⁵ Most secondary tumors arise from direct spread from another pelvic neoplasm, such as sigmoid, prostate, or cervical cancer. Metastases from distant organs are rarely reported in the literature, the most common being stomach, lung, and melanoma.⁶

Metastasis initially involves the outer layer of the bladder wall and progresses toward the mucosa. Therefore, the symptoms of bladder involvement appear at a later stage when the mucosa is also affected.⁷

Metastases from the lobular subtype of BC are generally seen either as nodules that spread to parenchymal organs or as a diffuse, sclerotic-like thickening involving serosal surfaces, the retroperitoneal space, or the walls of hollow and internal genital organs. Moreover, this “diffuse” pattern of metastatic spread in the retroperitoneum may cause bilateral hydronephrosis and not be detected for some time

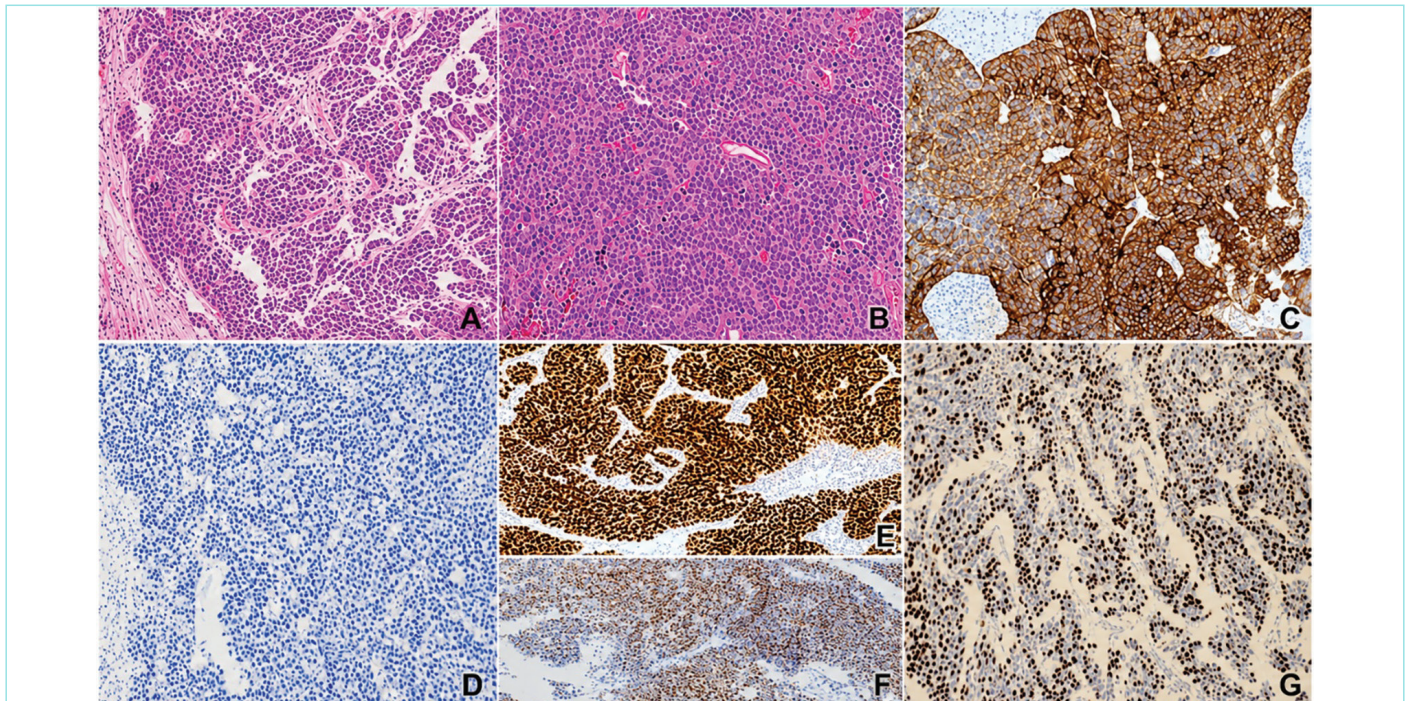


Figure 1. A) Tumor cells form solid layers and cords of varying sizes (H&E, 4x); B) Tumor lesion composed of cells with bizarrely shaped large vesicular/hyperchromatic nuclei in places and narrow eosinophilic cytoplasm (H&E, 100x); C) CK7 patchy, variable intensity positive; D) CK20 negative; E) Estrogen receptor diffusely strongly nuclear positive; F) Progesterone receptor moderately to strongly nuclear positive in approximately 40% of cells; G) Ki-67 proliferation index 70% nuclear positive (100x).

because of its appearance. By contrast, metastases of invasive ductal BC are seen almost exclusively as nodules and do not tend to involve the retroperitoneum or other organs.^{8,9} In contrast, in our case the patient's primary diagnosis was reported as ductal carcinoma showing neuroendocrine differentiation.

The presentation of lower urinary tract-like symptoms across a broad clinical spectrum poses challenges for diagnosing isolated bladder metastasis. Clinically, symptoms may range from painless hematuria to stress and urge urinary incontinence, and may also include frequent urination, nocturia, and rarer findings such as dysuria and back pain.¹⁰ That hematuria may be caused by factors such as cystitis, cyclophosphamide, stones, and bladder cancer contributes to diagnostic difficulty.¹¹ It is present in cases where hydronephrosis is reported as the initial reason for referral.^{12,13} The presenting symptoms of some cases reported in the literature are listed in Table 1.

One of the key factors complicating diagnosis is the duration of metastases, which can extend from early to much later stages. While cases ranging from 1 to 17 years have been reported (Table 1), metastasis can occur at much later stages, as seen in our case. Therefore, this must be considered even during long-term follow-up.

Feldman et al.¹⁴ described a patient who had negative cystoscopic findings despite significant evidence of bladder involvement based on symptoms, ultrasound, and CT scans; they stated that the evaluation should include further imaging studies. We supported our case by performing pelvic magnetic resonance imaging (MRI). (Figures 2 and 3). It has also been reported that positron emission tomography/computed tomography imaging is appropriate and contributes to the imaging evaluation of patients with bladder tumors (Figure 4).¹⁵

Immunohistochemical staining for various markers is routinely used in the diagnosis of undifferentiated tumors. Cytokeratins CK7, CK18, CK19, and CK20 are the main markers used in the diagnosis of epithelial differentiation. Other commonly used markers include estrogen

receptor/progesterone receptor for endometrial and breast carcinomas, CA 19-9 for pancreaticobiliary malignancy, prostate-specific antigen for prostate carcinoma, thyroglobulin for thyroid, uroplakin III for urothelium, and HepPar I for hepatocellular carcinoma.¹⁶ Although a review of the literature reveals reported cases of mammaglobin and GCDFP-15 positivity (Table 1), a study of 100 BC patients found Mammaglobin positivity in 57% of metastatic BC cases, compared with 27% for GCDFP-15.¹⁷ In our case, both markers were reported as negative.

CONCLUSION

Metastasis to the bladder after BC is rare and may occur many years later. Although the majority of cases are due to the lobular subtype, metastasis can also occur in other subtypes. It may present asymptotically or manifest with hematuria and voiding problems. Diagnosis involves imaging with ultrasound and MRI, biopsy with cystoscopy, and TUR-MT sampling. A definitive diagnosis is established by immunohistochemical examination. In patients with a history of BC, new urinary symptoms that appear years later should be evaluated for bladder metastasis.

MAIN POINTS

- Metastasis to the bladder from breast cancer (BC) is extremely rare and may mimic primary bladder tumors clinically and radiologically, leading to diagnostic delay.
- In patients with a history of BC, the development of hematuria and lower urinary tract symptoms, even many years after the initial diagnosis, should raise suspicion of metastasis to the bladder.
- Definitive diagnosis relies on immunohistochemical evaluation of cystoscopic and TUR-MT specimens in conjunction with imaging findings; and optimal management requires a multidisciplinary approach.

Table 1. Previously reported cases of bladder metastasis from breast cancer and comparison with the present case

Author/year	Age	Histologic subtype	Interval from primary breast cancer	Presenting symptoms	IHC findings	Other metastatic sites	Notes
Kase et al., ¹⁸ 2018	NR	Invasive ductal carcinoma	8 years	Urinary incontinence	ER (+), PR (-), GCDFP-15 (+)	Bone metastasis	Secondary bladder metastasis
Hanley et al., ¹⁹ 2022	64	Not reported	13 years	Hematuria, urinary incontinence	ER (-), PR (-), HER2 (-), GATA3 (+), GCDFP-15 (+)	None	Isolated bladder metastasis
Oshiro et al., ¹³ 2024	61	Invasive lobular carcinoma	7 years	Nocturia, bilateral hydronephrosis	CK7 (+), GCDFP-15 (+), GATA3 (+), CK20 (-), ER (-), PR (-), E-cadherin (-), HER2 (-)	Bone metastasis	Lobular pattern with urinary tract obstruction
Caputo et al., ²⁰ 2022	70	Invasive ductal carcinoma	1 year	Hematuria	AE1/AE3 (+), CK8/18 (+), ER (+), PR (+), chromogranin (+), focal synaptophysin (+), CK20 (-), HER2 (-), p63 (-)	Bone metastasis	Ductal carcinoma with neuroendocrine marker expression
Khan et al., ²¹ 2021	63	Invasive ductal carcinoma	17 years	Hematuria	Hormone receptor positive (HR+)	None	Isolated bladder metastasis
Kleinmann et al., ²² 2005	65	Invasive ductal carcinoma	2.5 years	Hematuria	CA15-3 (+), CK18 (+?)	None	Isolated bladder metastasis
Ahmet Çamtosun, 2026	76	Invasive ductal carcinoma with neuroendocrine differentiation	25 years	Hematuria, dysuria	CK7 (+, patchy), CK20 (-), ER (+), PR (+), mammaglobulin (-), GCDFP-15 (-), uroplakin (-), p40 (-), chromogranin-A (+), synaptophysin (-), E-cadherin (+), HER2 (-)	Prior ovarian/uterine metastasis	One of the longest latency periods reported; neuroendocrine differentiation

IHC: Immunohistochemistry, ER: Estrogen receptor, PR: Progesterone receptor, HER2: Human epidermal growth factor receptor 2.

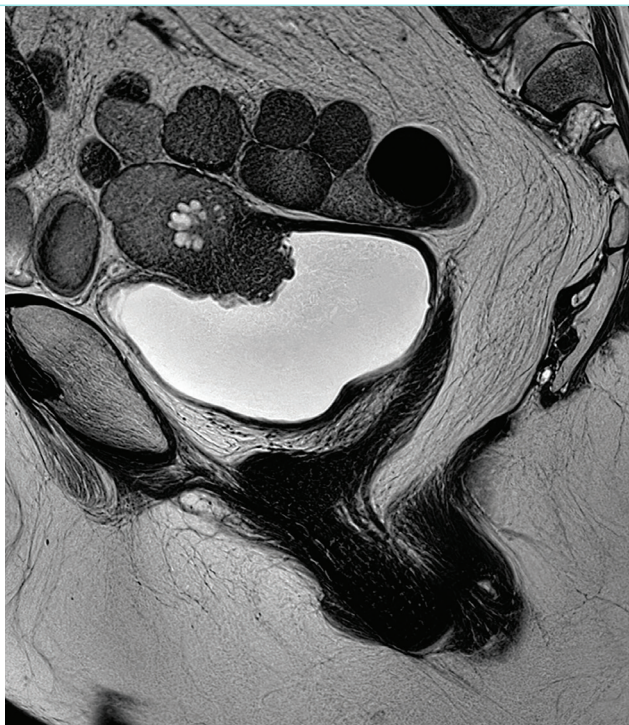


Figure 2. Pelvic MRI sagittal section showing a tumor invading the bladder.

MRI: Magnetic resonance imaging.



Figure 3. Pelvic MRI axial section showing a tumor invading the bladder.

MRI: Magnetic resonance imaging.

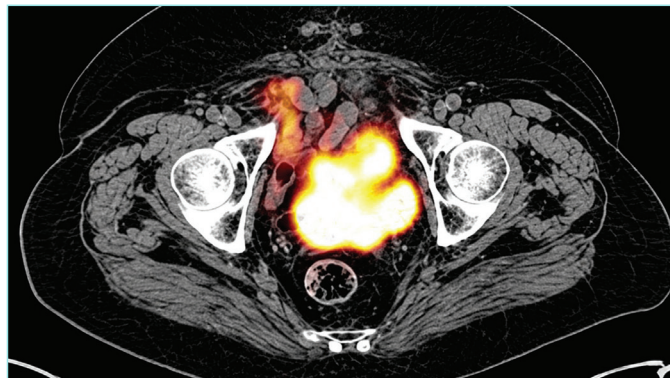


Figure 4. Bladder tumor image on PET/CT.

PET/CT: Positron emission tomography/computed tomography.

ETHICS

Informed Consent: Written informed consent was obtained from the patient for publication of this report and accompanying images.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.Ç., Design: H.B., Data Collection and/or Processing: H.G., Analysis and/or Interpretation: Ö.D., Literature Search: M.Y., Writing: Ö.F.Y.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

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