



A case report of breast cancer metastasis to the bladder from invasive ductal carcinoma

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Introduction and importance: Breast cancer is the most common malignancy among women worldwide, predominantly manifesting as invasive ductal carcinoma (IDC), which usually metastasizes to the bones, lungs, and liver. However, metastasis to the bladder is exceedingly rare, with few documented cases and limited understanding in the existing literature.

Case presentation: A 57-year-old woman with a history of IDC presented with a lump in her left breast and was initially treated with chemotherapy and a modified radical mastectomy. Years later, she developed urinary symptoms, which upon investigation revealed multiple bladder tumors and right kidney hydronephrosis. Diagnostic imaging, including ultrasound and computed tomography (CT) scans, supported these findings.

Clinical discussion: The discovery of bladder metastasis from IDC highlights significant diagnostic challenges due to the atypical presentation. The case underscores the importance of considering unusual metastatic sites in patients with known breast cancer, especially when they present with non-specific urinary symptoms. This report explores the potential pathophysiological mechanisms of such rare metastatic occurrences and discusses the implications for clinical practice.

Conclusion: This case exemplifies the critical need for heightened awareness and thorough evaluation in patients with unusual symptoms and a history of breast cancer. It calls for more comprehensive diagnostic approaches and possibly adjusted treatment protocols to better manage atypical metastases, ultimately aiming to improve patient outcomes and contribute to a deeper understanding of metastatic breast cancer behavior.

Keywords: bladder, breast cancer, invasive ductal carcinoma, metastasis

Introduction

Breast cancer is the most common malignant tumor among women worldwide, encompassing various subtypes with distinct pathological and clinical characteristics. Invasive ductal carcinoma (IDC) is the most prevalent form of breast cancer, accounting for about 80% of all cases. Although breast cancer typically metastasizes to the bones, lungs, and liver, metastasis to the bladder is extremely rare and seldom reported in clinical practice.

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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Annals of Medicine & Surgery (2024) 86:5529–5534

Received 29 February 2024; Accepted 26 June 2024

Published online 11 July 2024

<https://dx.doi.org/10.1097/MS9.0000000000002352>

HIGHLIGHTS

- Documents a rare bladder metastasis case from breast cancer.
- Highlights the need for vigilance in atypical metastases.
- Advocates regular monitoring to improve patient outcomes.
- Contributes to global knowledge on rare cancer spread.

The pathophysiological mechanisms behind breast cancer metastasis to unconventional sites such as the bladder are not fully understood. Traditional pathways suggest dissemination via lymphatic or hematogenous routes; however, under the backdrop of different breast cancer subtypes, it may involve complex biological interactions and abnormal mechanisms of molecular signaling pathways that require further clarification.

This case report meticulously documents a rare instance of invasive ductal carcinoma of the breast metastasizing to the bladder, discussing the diagnostic challenges and treatment approaches. Through this report, we aim to contribute to the sparse literature on such atypical metastatic presentations and emphasize the need for vigilance in patients with known and treated primary tumors who present with unusual symptoms. Understanding these rare events can enhance our overall knowledge and facilitate more effective management strategies in similar future cases.

Case report

A 57-year-old female underwent a core needle biopsy in June 2016 due to a lump in the left breast. She was diagnosed with IDC. Immunohistochemistry results: ER (+,80%), PR (+,50%), HER2(-), Ki67 (+,70%) (Stage: cT2N1M0; Type: Luminal B). After six cycles of preoperative neoadjuvant chemotherapy with Epirubicin 90 mg and Paclitaxel 315 mg, she underwent a modified radical mastectomy for left breast cancer in November of the same year. The postoperative pathology report indicated IDC, tumor size: 5.0×4.5×1.5 cm; axillary lymph nodes 4/16. Immunohistochemistry: ER (+,80%), PR (+,50%), HER2 (-), Ki67(+,10%). Stage: ypT2N1M0, Type: Luminal B. The post-operative pathology suggested non-pCR, and it was recommended that the patient undergo radiation therapy combined with endocrine therapy. However, she chose not to undergo radiation therapy but to receive regular endocrine therapy with tamoxifen (10 mg, bid). In December 2020, she sought medical attention for a nodule with rupture in the left chest wall. A biopsy revealed cancer cell infiltration originating from the breast. Immunohistochemistry results: ER (+,80%), PR (+,50%), HER2 (-), Ki67 (+,50%). A positron emission tomography-computed tomography (PET-CT) scan showed multiple bone metastases throughout the body, with no clear abnormalities in the urinary system or other areas. To control local rupture symptoms and seek palliative surgical opportunities to prevent further tumor spread, a plan for chemotherapy, endocrine therapy, and surgical treatment was developed. The patient received first-line rescue chemotherapy (vinorelbine, 40 mg; carboplatin, 0.2 g; 6 cycles) and endocrine therapy (anastrozole 1 mg, qd). The patient refused treatment with zoledronic acid. In January 2022, the rupture of the chest wall mass was alleviated, and surgery was performed to excise recurrent lesions, followed by a skin flap transfer. From February 2022, regular treatments with fulvestrant(500 g, every 28 days) and zoledronic acid(4 mg, every 28 days) were initiated.

In March 2023, the patient experienced frequent urination and a sensation of incomplete bladder emptying. Further examinations: ultrasound examination revealed low echogenicity at the posterior wall of the bladder (Fig. 1); venous pyelography revealed the presence of an intracavitary filling defect (Fig. 2A, B); enhanced CT scan confirmed hydronephrosis of the right kidney (Fig. 3). These examination results collectively indicate the possibility of malignant tumors in the bladder and the lower segment of the right ureter. It was suggested that the patient undergo further cystoscopic testing and subsequent treatment, but the patient refused further treatment. Fifteen days later, the patient's symptoms gradually worsened, and she was hospitalized to complete cystoscopic examination, during which multiple papillary round tumors were seen in the trigone area of the bladder (Fig. 4A), the posterior wall of the bladder (Fig. 4B), and the right sidewall of the bladder (Fig. 4C). The examination results further indicated multiple tumors in the bladder. Considering the patient's condition (tumors in the bladder and the lower segment of the right ureter, severe hydronephrosis of the right kidney, non-functional right kidney) and the possible uncontrollable bleeding risk associated with bladder biopsy, a bladder biopsy was not performed. After multi-disciplinary consultation and thorough communication with the patient and her family, it was decided to proceed with surgery as soon as possible. One day later, the patient underwent a right nephrectomy, right ureterectomy, and cystectomy, as well as a left

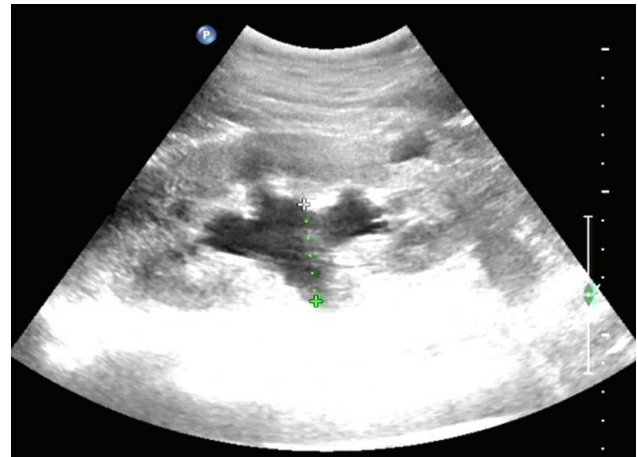


Figure 1. Ultrasound indicates hypoechogenicity of the posterior bladder wall.

ureterostomy at our hospital. The pathological diagnosis from both our hospital and the high-level hospital confirmed metastatic breast cancer. Immunohistochemistry results showed ER(-), PR(-), HER2 (-), Ki67(10%) (Fig. 5A-F). Postoperatively, the patient continued symptomatic treatment and regular follow-ups. The last follow-up for this case was conducted in December 2023. Unfortunately, the patient passed away in November 2023 due to complications from the disease.

Discussion

Breast cancer metastasis to the bladder is extremely rare^[1]. Globally, there have been only 54 reported cases of breast cancer metastasizing to the bladder, most of which were discovered post-mortem, with very few clinical diagnoses^[2]. When bladder metastasis is confined to the serosal or muscular layers, patients usually exhibit no significant symptoms. Clinical symptoms appear only after the tumor invades the mucosal layer^[3]. Symptoms are varied and include frequent urination, painless hematuria, nocturia, difficulty in urination, urinary tract obstruction, urinary incontinence, and back pain^[4–7]. Severe cases can lead to hydronephrosis and renal failure^[8]. The patient in this case sought medical attention due to frequent urination, which led to the discovery of right kidney hydronephrosis. Breast cancer metastasis to the bladder often occurs in the late stages, accompanied by widespread metastasis to other organs^[9].

The most common type of breast cancer is IDC, accounting for about 90% of all breast cancers, followed by invasive lobular carcinoma (ILC), which accounts for about 10%^[10–13]. Although IDC is more common than ILC, studies by Feldman and others have found that ILC has a significantly higher incidence of bladder metastasis compared to IDC^[14]. This may be related to the different metastatic mechanisms of IDC and ILC. ILC, due to the loss of E-cadherin, exhibits a more dispersed growth pattern. This leads it to metastasize to more varied and atypical locations such as the gastrointestinal tract, peritoneum, and ovaries. Meanwhile, IDC typically has a more cohesive growth pattern, tending to metastasize to common areas such as lymph nodes, lungs, and liver. The ability of ILC to spread in a wide tissue area without typical structural boundaries may be one of the reasons why its bladder metastasis rate is significantly higher than that of

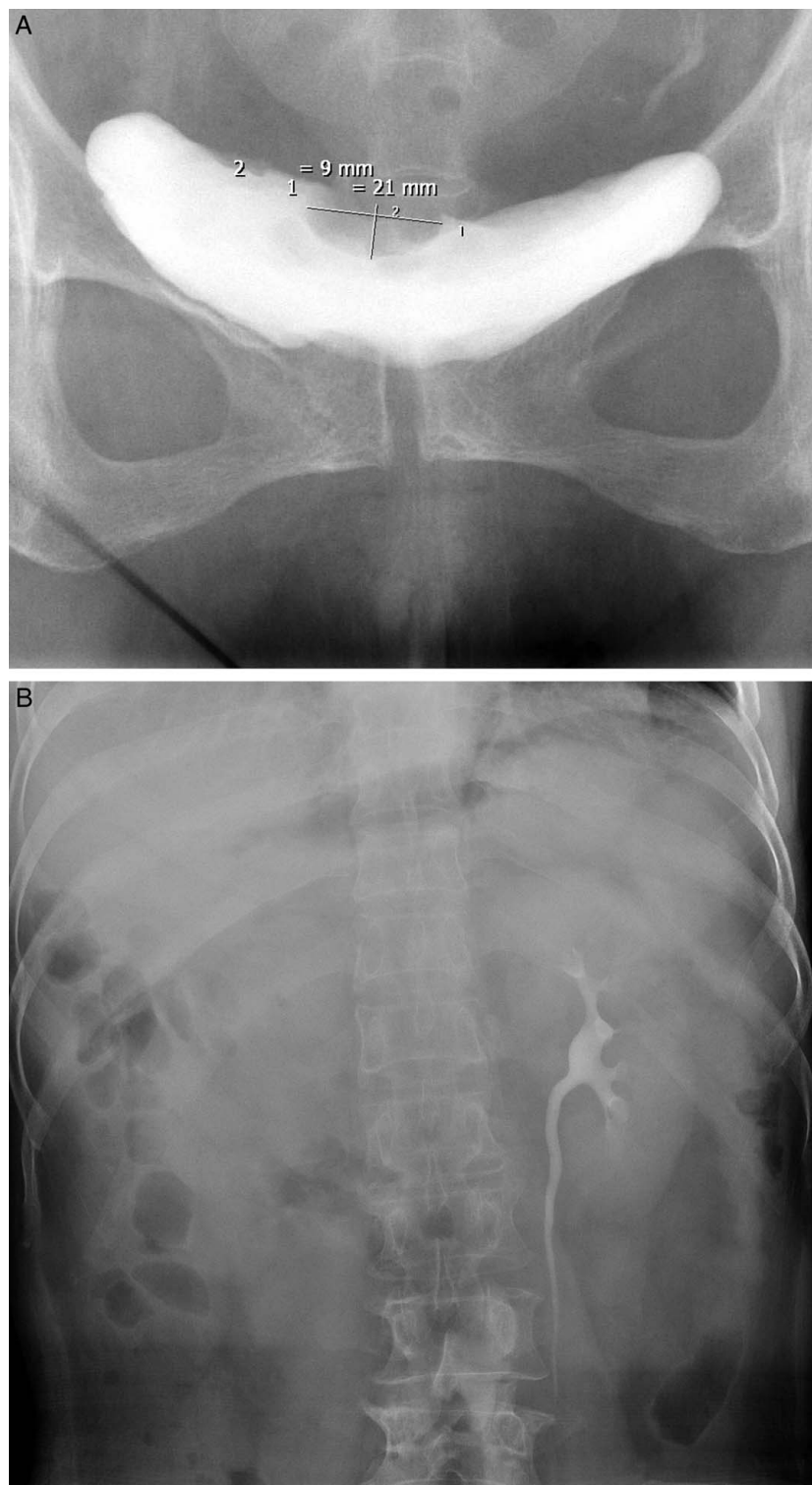


Figure 2. (A) Venous pyelography suggests a filling defect in the cavity. (B) Venous pyelography indicates severe hydronephrosis of the right kidney.

IDC^[15]. The mechanism of bladder metastasis from IDC in this case report is not yet clear. Some studies suggest that steroid immunosuppression may lead to atypical metastasis^[1]. Currently, the mechanism behind bladder metastasis of IDC following hormone therapy is not well understood.

When considering bladder lesions in breast cancer patients, initial evaluation should involve a combination of bladder ultrasound and CT scan. High-resolution soft tissue imaging provided by MRI is crucial for accurate tumor staging and assessing the involvement of surrounding tissues. PET-CT is helpful for a whole-body assessment



Figure 3. Enhanced computed tomography scan indicates right kidney hydronephrosis.

to detect other potential metastatic sites. During breast cancer follow-up, serum CA15-3, as one of the most sensitive tumor markers, its continuous elevation strongly suggests breast cancer recurrence^[16,17]. Cystoscopy allows direct observation of the bladder mucosa, and bladder biopsy followed by histological examination is crucial for determining the tumor's origin. However, for this patient, considering that the patient had reached the surgical indication and needed surgery as soon as possible, and that the pathology would require several days of waiting time, coupled with the uncontrollable risk of bleeding associated with bladder biopsy that might affect subsequent treatment, it was decided after discussion to proceed directly with surgery instead of waiting for the pathology results after a bladder biopsy. Immunohistochemical staining is vital for differentiating between primary bladder tumors and metastatic breast cancer^[18]. Immunohistochemistry results also provide important information for developing treatment plans and predicting patient prognosis^[19].

In treating patients with breast cancer metastasis to the bladder, systemic treatment plans should be developed in addition to local

treatment, based on the immunohistochemistry of the bladder metastasis. The main goals of local treatment (such as surgical resection or radiation therapy) and systemic treatment (including chemotherapy, endocrine therapy, and targeted therapy) for patients with advanced breast cancer that has metastasized to the bladder are to prolong life, alleviate symptoms, and improve quality of life^[20]. There may be changes in phenotypic markers between the primary and metastatic sites in breast cancer patients. Research by Lindström *et al.*^[21] shows that 31% of patients who underwent endocrine therapy experienced loss of ER in metastatic sites. In this case, after a series of treatments, the hormonal status of the bladder metastasis changed from positive to negative. The American Society of Clinical Oncology recommends that treatment decisions should be based on the ER, PR, and HER2 status of the metastatic site when there is a change in receptor status^[22]. The 2015 clinical practice guidelines for breast cancer by the National Comprehensive Cancer Network suggest re-biopsy of metastatic breast cancer for confirmation of diagnosis^[23].

This study reports a rare case of breast cancer metastasizing to the bladder. The analysis of this particular case has deepened our understanding of the multi-organ metastasis characteristics of breast cancer. This case highlights the differences in metastatic behavior between invasive ductal and lobular carcinoma, as well as the potential impact of endocrine therapy on the metastatic pathway. In this case, the metastasis of breast cancer occurred not in common organs such as the lung or bones but in the bladder, challenging our traditional understanding of breast cancer metastasis patterns. It emphasizes the need in clinical practice to be vigilant for atypical metastatic sites when urinary system symptoms appear in breast cancer patients with distant metastases. Furthermore, this case underscores the importance of regular systemic examinations in the management of breast cancer, particularly in the advanced stages of the disease. Early identification and treatment of atypical metastases can significantly improve the patient's quality of life and prognosis. In summary, this case report provides important clinical insights for the diagnosis, treatment, and management of breast cancer. It highlights the diversity and unpredictability of breast cancer metastasis and offers new directions for future research, especially in exploring the mechanisms of breast cancer metastasis and optimizing treatment strategies. We anticipate that future research will further reveal the biological basis of metastasis in different types of

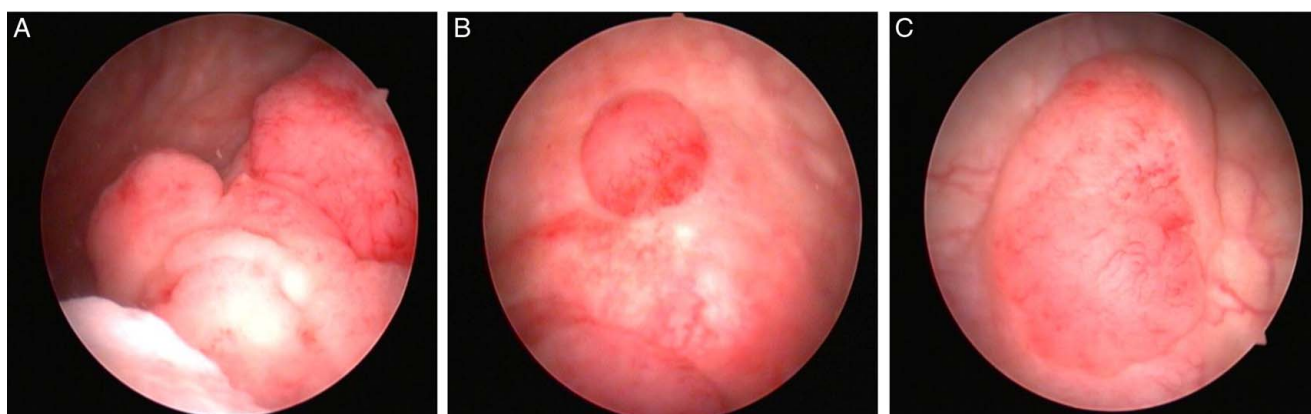


Figure 4. (A) Multiple tumors in the trigone area of the bladder. (B) Tumor on the posterior wall of the bladder. (C) Tumor on the right sidewall of the bladder.

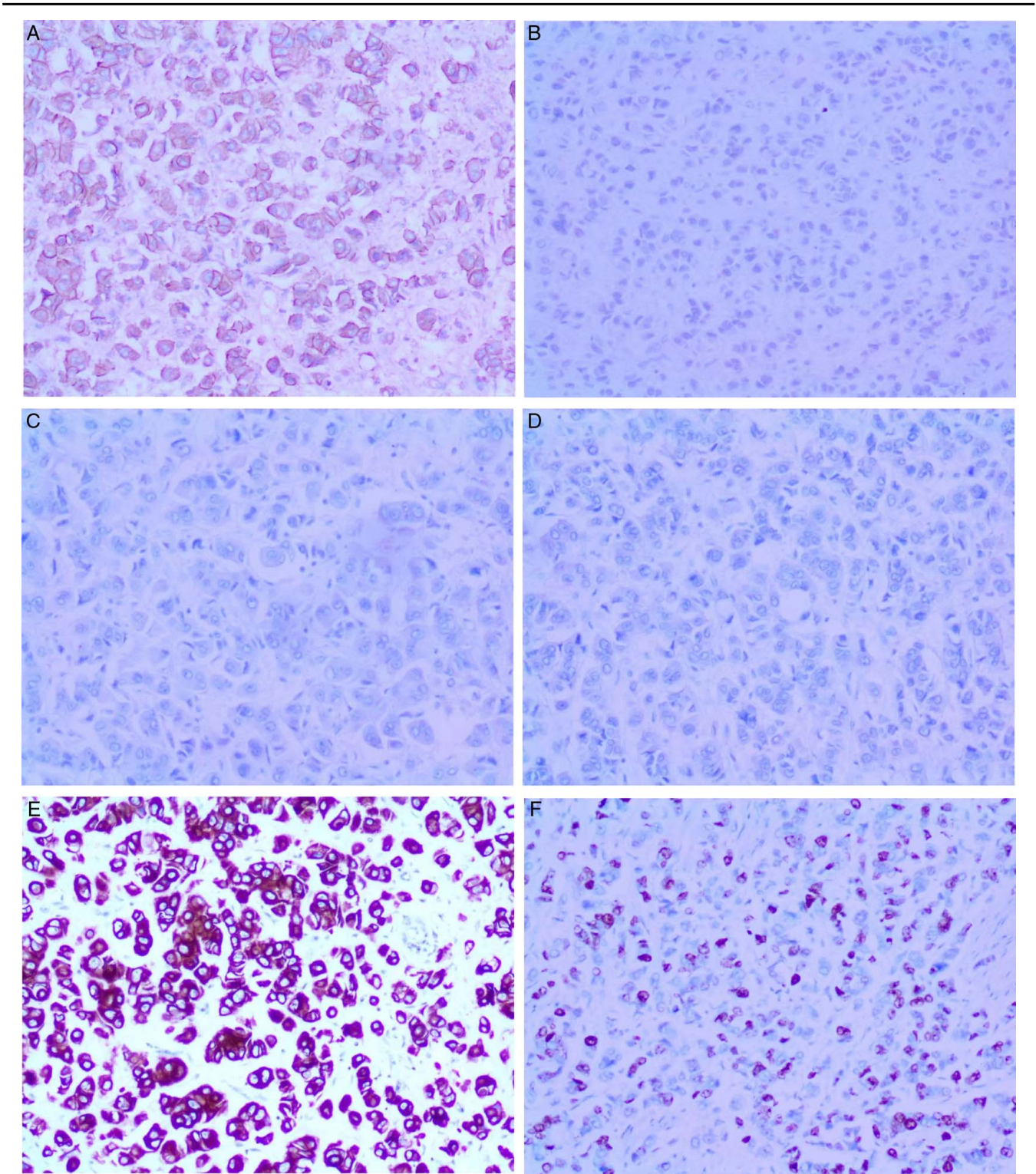


Figure 5. (A) E-Cadherin positive in tumor cells. (B) ER tumor cells negative. (C) PR tumor cells negative. (D) HER2 tumor cells negative. (F) Ki67 positive in 10% of tumor cells. (E) CK7 tumor cells positive.

breast cancer, providing more precise guidance for clinical treatment.

Ethical approval

Not applicable.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Source of funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Author contribution

T.H.: conceptualization; funding acquisition; writing—original draft. G.S.: project administration. X.H.: investigation. T.B.: conceptualization. H.H.: conceptualization. Z.Z.: conceptualization. W.B.: conceptualization. R.T.: conceptualization. X.Y.: supervision. T.S.: supervision. X.D.: supervision. X.W.: conceptualization; supervision; writing—review and editing. Y.Z.: conceptualization; writing—review and editing.

Conflicts of interest disclosure

The authors declare no conflicts of interest.

Research registration unique identifying number (UIN)

Not applicable.

Guarantor

Yuhai Zhang.

Data availability statement

The research findings reported in this article do not involve the generation or analysis of any datasets; therefore, data sharing is not applicable to this study.

Provenance and peer review

Not applicable.

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