

Triple-negative invasive lobular carcinoma presenting with synchronous gastric metastasis: A case report

LIANGXUE ZHU, YAJUN XING and MINGYUN WANG

Department of Oncology, Nanjing Gaochun People's Hospital, Jiangsu, Nanjing 211300, P.R. China

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Abstract. Triple-negative invasive lobular carcinoma (TN-ILC) is a rare and highly aggressive subtype of breast cancer. The development of gastric metastases in breast cancer is extremely rare and typically occurs several years after initial diagnosis. The present case report describes a 68-year-old postmenopausal female patient who presented with TN-ILC with gastric metastases at initial diagnosis. This metastatic pattern is very rare and is often mistaken for primary gastric cancer, which poses a notable diagnostic challenge. Imaging and histopathological analyses confirmed typical TN-ILC features (estrogen receptor negative, progesterone receptor negative and HER-2 1+ positive) and revealed diffuse metastases to the gastric wall, brain, bone, adrenal glands, pleura and lymph nodes. Gastric metastases from breast cancer were further confirmed by immunohistochemical studies, including for GATA binding protein 3, Villin and cytokeratin 7/20. It is noteworthy that the patient exhibited no gastrointestinal symptoms, which could have led to a missed diagnosis. The present case underscores the significance of a comprehensive evaluation in metastatic breast cancer.

Introduction

According to the Global Cancer Statistics Report 2022, breast cancer has become the second most common malignancy in the world and the leading cause of cancer incidence among women, posing a notable threat to women's health (1). Invasive lobular carcinoma (ILC) is the second most common histological type of breast cancer, accounting for ~15% of all cases (2). Triple-negative ILC (TN-ILC) accounts for 2-9% of ILC cases, with the majority of cases exhibiting androgen receptor (AR) positivity (3). Notably, ILC tends to metastasize to the gastrointestinal tract, peritoneum, soft meninges and ovaries more

often than invasive ductal carcinoma (4,5). However, gastric metastases are rare; the reported incidence is 0.06-0.6% (6,7). Reports in the literature of TN-ILC with gastric metastases at initial diagnosis are uncommon, and gastric metastases can have similarities to primary gastric cancer (5,8), posing a diagnostic challenge.

In the present case report, a rare case of TN-ILC with gastric metastasis upon initial presentation is described. The imaging findings and histopathological evidence provide novel insights into this uncommon metastatic pattern, contributing to the limited body of knowledge on this clinical scenario.

Case report

Case presentation. A 68-year-old postmenopausal woman presenting with 1 week of chest distress was admitted to Nanjing Gaochun People's Hospital (Nanjing, China) in February 2024. Initial CT imaging revealed a 4.0 cm irregular left breast mass (Breast Imaging Reporting and Data System 5) (9) with axillary lymphadenopathy, bilateral pleural effusions and pericardial effusion (Fig. 1A). Systemic evaluation including CTs and MRIs demonstrated extensive metastases including gastric wall thickening (Fig. 1B), a left adrenal nodule (Fig. 1C), cerebral enhancing lesions (Fig. 1D) and osteolytic bone lesions (Fig. 1E).

Peripheral blood tests showed elevated tumor markers: CEA 30.12 ng/ml (normal value, ≤ 5 ng/ml), CA125 321.1 U/ml (normal value, < 35 ng/ml) and CYFRA 21-1 117.5 ng/ml (normal value, < 3.3 ng/ml). Gastroscopy revealed superficial atrophic gastritis, gastric fundus polyp and infiltrative lesion of the gastric body, as shown in Fig. 2A. Immunohistochemical analysis of the left breast mass (Fig. 3) revealed estrogen receptor (ER)(-), progesterone receptor (PR)(-), HER-2(1+), E-cadherin(-), Ki-67(+ with local areas reaching 30%), β -catenin(+), cytokeratin (CK)5/6(-), CK14(-) and AR(++). Combined with the hematoxylin and eosin (HE) staining results (Fig. 2B), these findings confirmed classic ILC with a triple-negative molecular subtype. HE staining of the biopsy of the gastric lesions showed an adenoid structure and indicated adenocarcinoma (Fig. 2C). The gastric lesion (corpus ventriculi) exhibited ER(-), HER-2(1+), GATA binding protein 3 (GATA-3)(+), CK7(++), CK20(-) and Villin(-), confirming metastasis of the primary adenocarcinoma of the breast (Fig. 4). The final diagnosis was stage IV (cT2N3M1; TNM Staging System, the eighth AJCC staging edition) (10)

Correspondence to: Dr Mingyun Wang, Department of Oncology, Nanjing Gaochun People's Hospital, 53 Maoshan Road, Jiangsu, Nanjing 211300, P.R. China
E-mail: 872618281@qq.com

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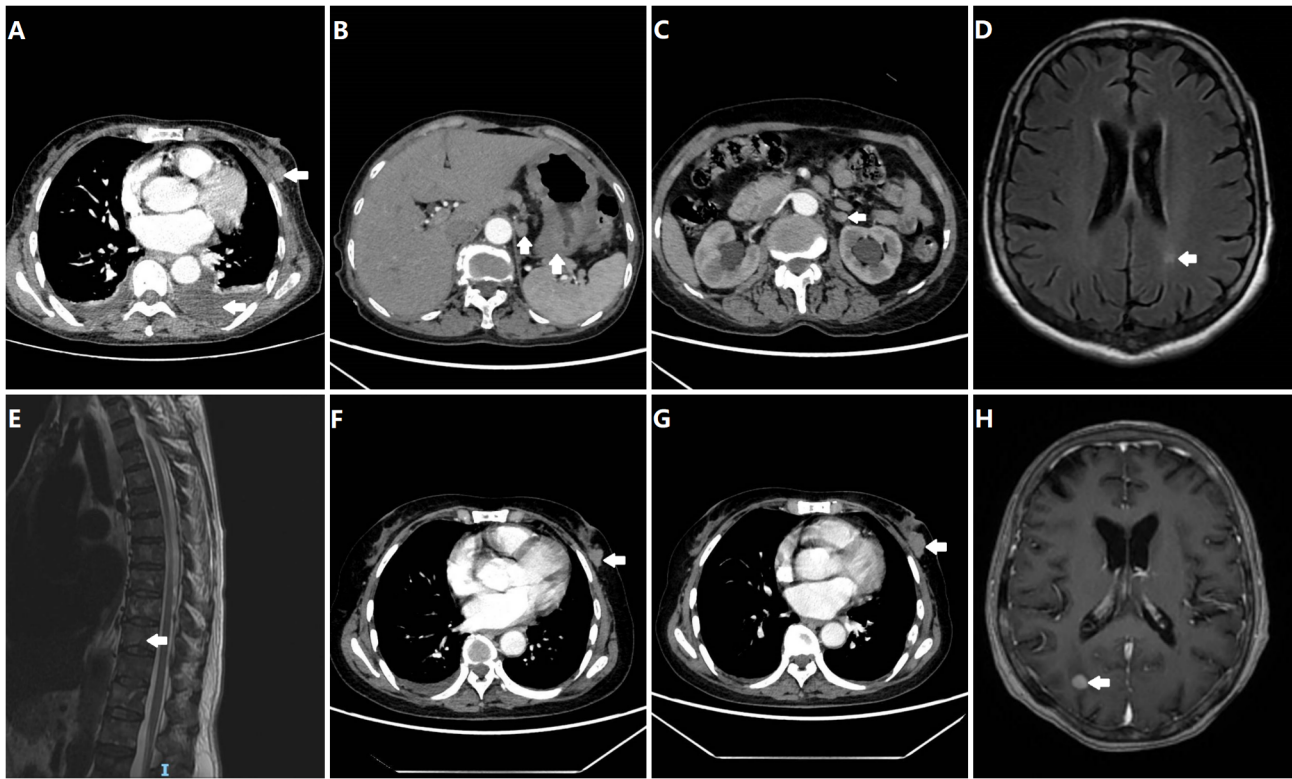


Figure 1. (A) Chest CT demonstrating a left breast mass (arrow) with localized skin thickening and left pleural effusion. (B) The gastric wall was thickened with enlarged perigastric lymph nodes. (C) Metastatic nodules of the adrenal gland. (D) Cerebral metastases in the left occipital lobes. (E) Multiple metastases in the spine and vertebral body attachments. (F) Stable disease of breast cancer after two cycles of first-line chemotherapy. (G) Disease progression of breast cancer. (H) New intracranial metastases on the right side of the brain. White arrows indicate tumor location in all images.

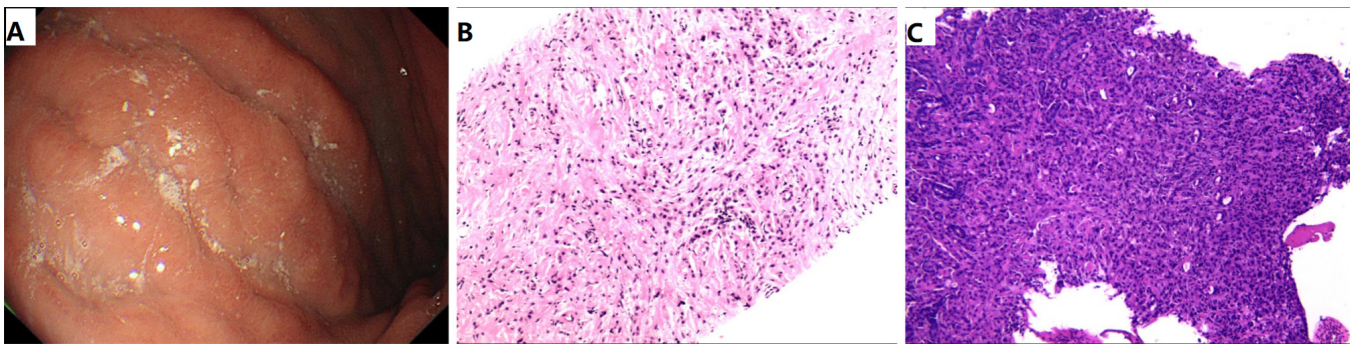


Figure 2. (A) Endoscopic view revealing congested, edematous gastric mucosa with infiltrative lesions, characterized by rigid folds and surface erosions. (B) HE staining of breast biopsy tissue showing characteristic invasive lobular carcinoma morphology (magnification, x10). (C) HE staining of gastric biopsy tissue showing adenocarcinoma (magnification, x10). HE, hematoxylin and eosin.

TN-ILC with multisystem metastases involving gastric, cerebral, osseous, adrenal, pleural and extensive lymph node sites. Unfortunately, due to financial reasons, the patient did not undergo further BRCA1/2, programmed death-ligand 1 and partner and localizer of BRCA2 gene testing.

Following the confirmed diagnosis, the patient underwent first-line chemotherapy with a TX regimen (paclitaxel 175 mg/m² day 1 plus capecitabine 1,000 mg/m² twice daily on days 1-14, every 21 days). The patient's disease was stable after two cycles as assessed by the RECIST 1.1 criteria (10) (Fig. 1F). After completing six cycles of treatment, the patient started maintenance therapy with single-agent capecitabine

(1,000 mg/m² twice daily for 14 consecutive days, repeated every 21 days) with regular imaging monitoring.

Subsequent evaluation in February 2025 revealed disease progression (Fig. 1G), which led to a switch to second-line therapy. After initiation of second-line utidelone monotherapy (30 mg/m² on days 1-5, every 3 weeks) in February 2025, follow-up imaging in May 2025 revealed new intracranial metastases accompanied by clinical manifestations of dizziness. Following disease progression in May 2025 (Fig. 1H), the patient underwent systemic therapy with toripalimab (240 mg on day 1, every 3 weeks) plus eribulin (1.4 mg/m² on day 1-8, every 3 weeks), concurrent with local radiotherapy

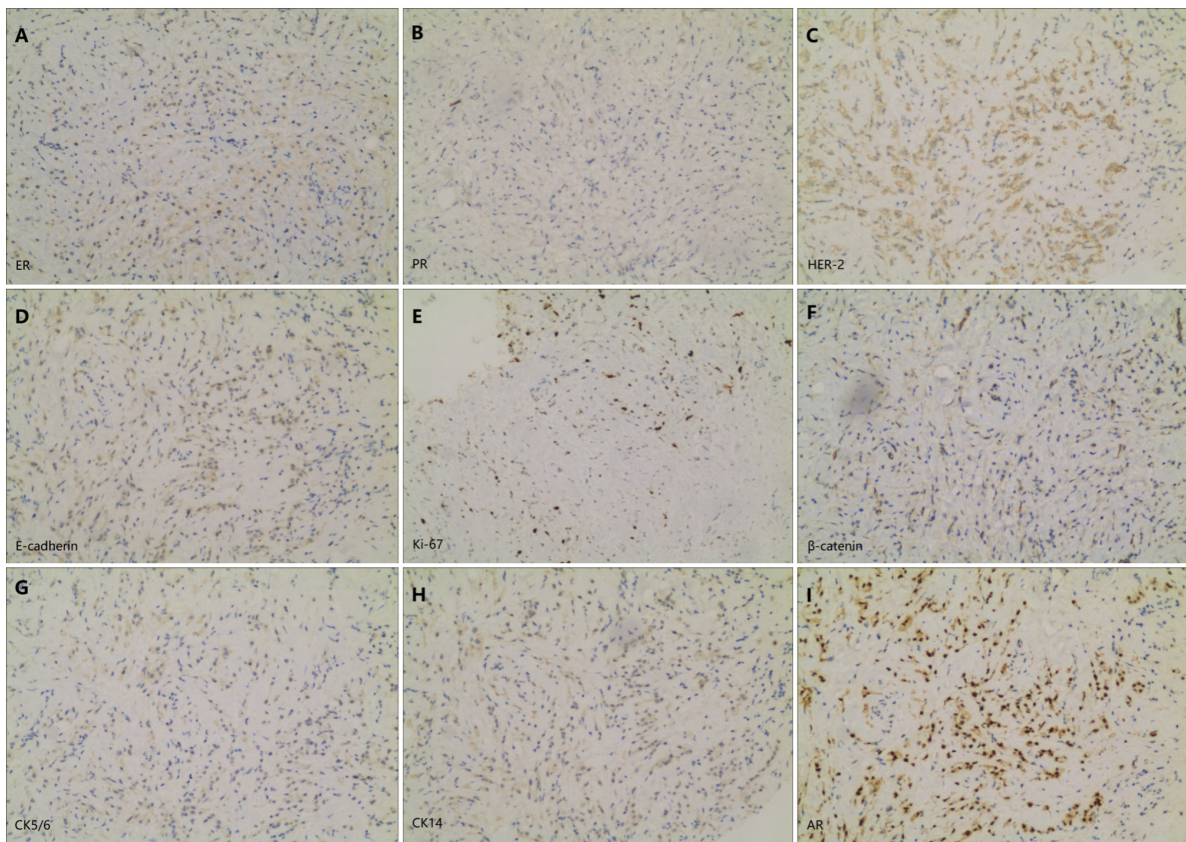


Figure 3. Immunohistochemistry results of the breast biopsy specimen (magnification, x100). Staining for (A) ER, (B) PR, (C) HER-2, (D) E-cadherin, (E) Ki-67, (F) β -catenin, (G) CK5/6, (H) CK14 and (I) AR. ER, estrogen receptor; PR, progesterone receptor; CK, cytokeratin; AR, androgen receptor.

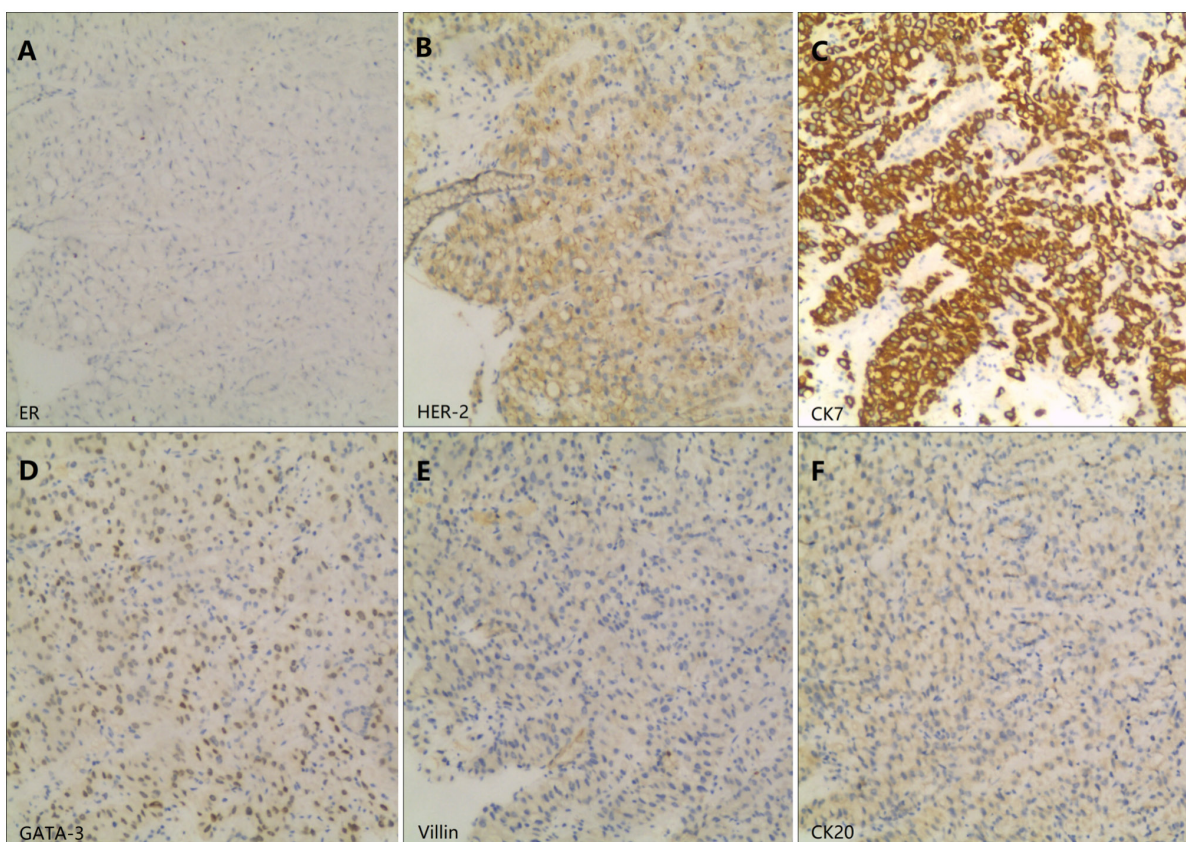


Figure 4. Immunohistochemistry results of the gastric biopsy specimen (magnification, x100). (A) ER, (B) HER-2, (C) CK7, (D) GATA-3, (E) Villin and (F) CK20. ER, estrogen receptor; PR, progesterone receptor; CK, cytokeratin; GATA-3, GATA binding protein 3.

(stereotactic radiotherapy of 27 Gy in 9 Gy fractions) for brain metastases. This regimen remains ongoing as of July 2025.

Materials and methods. Gastroscopy and breast tissue biopsy specimens were routinely fixed in 3.7% neutral formalin at room temperature for 6–24 h, followed by conventional procedures including dehydration and paraffin embedding. The specimens were then cut into 3- μ m-thick sections and stained with HE for light microscopy examination. Hematoxylin staining was performed for 5 min and eosin staining for 3 min at room temperature. Immunohistochemistry was performed using the EnVision method. The staining process included dewaxing and hydration of the paraffin sections which involved a descending alcohol series, then PBS washing for 5 min for three times. Antigen retrieval was performed using citrate buffer (pH 6.0; cat. no. G1202; Wuhan Servicebio Technology Co., Ltd.) at 95°C for 20 min. Endogenous peroxidase blocking was achieved by incubating with 0.3% H₂O₂ for 15 min. Non-specific binding was blocked with 5% normal goat serum (cat. no. ab7481; Abcam) for 30 min at room temperature. The primary antibodies used included: ER (cat. no. ZA0102), PR (cat. no. ZA-0255), HER-2 (cat. no. ZM-0065), E-cadherin (cat. no. ZA-0565), Ki-67 (cat. no. ZM-0166), CK5/6 (cat. no. ZM-0313), CK14 (cat. no. ZA-0540), AR (cat. no. ZA-0554), GATA-3 (cat. no. ZA-0661), CK7 (cat. no. ZM-0071), CK20 (cat. no. ZA-0574) and Villin (cat. no. ZM-0261), all from Beijing Zhongshan Golden Bridge Biotechnology Co., Ltd. (OriGene Technologies, Inc.) and supplied at a ready to use dilution. The primary antibodies were applied at 37°C for 1 h. Following this, secondary universal antibodies (rabbit/mouse IgG; 1:200; cat. no. SAP-9100; Beijing Zhongshan Golden Bridge Biotechnology Co., Ltd.; OriGene Technologies, Inc.) combined with diluted biotin (100 μ l) were applied at 37°C for an additional 30 min. The specimens underwent chromogenic reactions and re-staining before being sealed. Diaminobenzidine (DAB) served as the chromogenic substrate. Following DAB visualization, nuclei were counterstained with hematoxylin for 5 min at room temperature. A BX53 Olympus standard light microscope equipped with an image acquisition system was used to analyze the sections.

Discussion

ILC represents the predominant breast cancer histological subtype that metastasizes to the gastrointestinal tract (4). Existing literature reports gastric metastasis incidence rates of 0.06% among patients with breast cancer, but some studies suggest that this percentage may be slightly higher, at ~6% (6,7). Of note, gastric metastases typically appear several years after the diagnosis of the primary breast tumor (11,12). Notably, >90% of breast cancer cases with gastric metastases are documented to be ER positive (13). The present case represents a rare clinical presentation of TN-ILC with synchronous gastric metastasis at initial diagnosis.

Gastric metastases typically present with non-specific gastrointestinal symptoms including abdominal pain (the most common symptom), nausea, dyspepsia, anorexia and bleeding (14). Notably, 20–30% of cases remain asymptomatic

and are incidentally detected during evaluations, which significantly increases the diagnostic difficulty (15). Endoscopic features of gastric metastases typically show poor specificity, with the classic ‘linitis plastica’ pattern being the most commonly observed (16). Other endoscopic findings may include localized ulcerative or polypoid lesions, submucosal nodularity or mass formation, increased mucosal fragility, fold thickening, diffuse infiltration patterns and external compression deformities. The diagnostic sensitivity of superficial biopsies remains suboptimal due to the characteristic submucosal and muscular infiltrative pattern, similar to that of primary gastric malignancies. Current evidence suggests that ~30% of gastric metastases may be missed during initial endoscopic evaluation, primarily due to inadequate sampling depth (17). This diagnostic challenge is further corroborated by autopsy studies revealing an 11.6% incidence of gastric metastases among patients with breast cancer (18), strongly suggesting clinical under-detection of this metastatic pattern. In the present study, the complete absence of gastrointestinal symptoms and the non-specific radiological finding of gastric wall thickening in the patient posed significant diagnostic difficulties. The endoscopic appearance of infiltrative lesions in the gastric body was indistinguishable from primary gastric carcinoma. Ultimately, a comprehensive histopathological evaluation by immunohistochemical analysis was required to confirm the diagnosis.

Immunohistochemical analysis is the most important method for distinguishing primary gastric cancer from metastatic gastric cancer. While ~80% of breast cancer metastases to the stomach retain ER and PR expression, it is noteworthy that 32 and 12% of primary gastric carcinomas may demonstrate ER and PR positivity, respectively, which limits the specificity of these markers when used alone (19,20). HER-2, an established oncogenic driver in breast cancer, typically shows negative expression in ILC (21) and exhibits marked heterogeneity in gastric cancer, thereby diminishing its diagnostic utility for identifying metastatic lesions (14). CK7/20 provides a clearer distinction, with CK7(+)/CK20(-) expression strongly suggesting a breast, lung, thyroid or gynecological origin, whereas primary gastric malignancies often show a CK7(+)/CK20(+) co-expression pattern (22). Of particular value is GATA-3, a zinc finger transcription factor that plays a key role in breast epithelial differentiation. GATA-3 is expressed in all ILC cases (23), whereas its expression in primary gastric adenocarcinoma is <5% (24). In addition, Villin, a cytoskeletal protein that is consistently expressed in the gastrointestinal epithelium but is absent in breast tissue, further improves diagnostic specificity (25). In the present case of triple-negative breast cancer [ER(-)/PR(-)/HER-2(-)], the combined immunohistochemical profile of CK7(+)/CK20(-)/GATA-3(+)/Villin(-) provided conclusive evidence for metastatic breast carcinoma, resolving the initial diagnostic challenge posed by morphological similarities to primary gastric cancer.

The discovery of gastric metastasis typically implies advanced disease. Notably, 90–94% of patients with breast cancer diagnosed with gastric metastasis also have other distant metastases (26). This aggressive clinical presentation portends a poor prognosis, with a median survival time of ~10 months (17) and 3-year survival rates of 79.1% (6). Current evidence suggests

that while a mastectomy may confer survival benefits in carefully selected patients with solitary metastases, the majority of cases derive no significant survival advantage from surgical intervention compared with systemic therapy alone (27). Based on these considerations, we recommend that treatment strategies for patients with breast cancer and gastric metastases should prioritize systemic therapies, with individualized regimens incorporating tumor burden, biomarker profiles (including hormone receptor and HER-2 status) and patient performance status. Local interventions should be reserved for two specific clinical scenarios: i) As consolidative therapy following favorable response to systemic treatment; or ii) for palliation of refractory local symptoms including pain or obstructive complications.

In the present study, the simultaneous discovery of the primary TN-ILC and its gastric metastasis serves as a notable clinical alert, emphasizing the need for heightened suspicion of unusual metastatic sites even at initial presentation in patients with this aggressive subtype. Multiple biopsies of the suspicious area and immunohistochemistry can improve the diagnostic accuracy of gastric metastases in breast cancer.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

LZ conceptualized the case report, wrote the manuscript and performed additional data analysis. YX and MW were involved in the treatment and follow-up in this case. MW critically revised the manuscript, provided supervision and approved the final manuscript for publication. All authors have read and approved the final version of the manuscript. LZ and MW confirm the authenticity of all the raw data.

Ethics approval and consent to participate

Ethics approval was not required for the present study in accordance with our local and institutional requirements. The present study was conducted in accordance with local legislation and institutional requirements. The participant provided written informed consent to participate in the present study.

Patient consent for publication

Written informed consent for publication of this article was obtained from the participant.

Competing interests

The authors declare that they have no competing interests.

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