

Linitis plastica-like metastasis of invasive lobular carcinoma: a diagnostically challenging case report and literature review

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Abstract

A 64-year-old woman with a history of bilateral recurrent breast cancer (intraductal carcinoma in the right breast and invasive lobular carcinoma in the left breast) had an FDG-PET-CT scan since her tumor markers were high. The FDG-PET-CT scan showed a moderate increase in FDG avidity in the diffuse thickened stomach wall. Endoscopic and endosonographic examinations revealed no malignancy. After two negative biopsies, suspicious imaging led to exploratory laparoscopy, and a trucut biopsy confirmed linitis plastica-like lobular breast cancer metastasis. Our aim with this case report and the review of the literature is to emphasize the importance of optimal deep tissue acquisition in establishing the correct diagnosis in light of radiological suspicion to inform a proper treatment plan in a multidisciplinary tumor board. (*Acta gastroenterol belg.*, 2026, 89, 499-502).

Keywords: Invasive lobular carcinoma, Linitis plastica, FDG-PET, Biopsy.

Introduction

Invasive lobular carcinoma (ILC) is the second most common subtype of breast cancer (15%). The predilection of the distribution of the first sites of metastases of ILC compared to IDC is the bones (61.7% vs. 49.7%), followed by the liver (25.7% vs. 31.2%), and then followed by the gastrointestinal organs, peritoneum, and pleura (19.5% vs 8.4%) (1). This distribution pattern draws our attention to the diverse follow-up examinations. Our patient presented with an elevated tumor marker and weight loss. Besides these important elements, it remained challenging to prove the malignancy in the stomach and its pathological characteristics. In this case report, we emphasize the importance of achieving a complete consensus in the tumor board, resulting in a concordance among imaging, histological, and laboratory results, and leading to a correct diagnosis, appropriate treatment, and support for quality of life.

Case Presentation

A 64-year-old female patient underwent segmentectomy and sentinel lymph node biopsy (SLNB) with the diagnosis of IDC in the left breast 11 years ago. The lesion was grade II IDC, ER+, PgR-, HER2-, pT1cN0(i-)(sn) and subsequently treated by radiotherapy. The patient subsequently received

adjuvant tamoxifen therapy for 6 years. About 2 years after discontinuation of tamoxifen, another mass lesion was detected in the right breast on follow-up ultrasonography, and the pathological diagnosis was ILC. (Grade II, ER 81-90%, PgR <1, HER2 0, Ki67 60%). CT and scintigraphy indicated no metastases; the tumor was staged cT1cN0M0. Breast-conserving surgery and SLNB were performed on the right breast, followed by radiotherapy. Treatment with letrozole was continued. In the 10th month of treatment, the patient underwent mammography and breast ultrasound because of an increase in the CA15.3 tumor marker to 79.9 KU/L. However, no tumoral lesion was detected. The patient, who had no complaints other than losing 10 kilograms in recent months, underwent an FDG-PET/CT scan. FDG-PET/CT revealed a slight increase in FDG uptake in a diffuse thickening of the gastric wall, particularly in the antrum region (Fig. 1A and 1B). Gastroscopy revealed thickened gastric rugae (Fig. 2), and biopsy was nonspecific with no atypia, which suggests mild chronic antral gastritis and excludes cancer by immunohistochemistry.

Two weeks later, an endoscopic ultrasonographic examination revealed that the stomach wall had thickened to 9.6 mm, showing a broad hypo-intense outer wall of the stomach, as seen in linitis plastica (LP) (Fig. 3). At this level, a deep jumbo biopsy was performed, suspecting possible GLP. Histopathological results were consistent with chemical gastropathy and were interpreted as favoring chronic gastritis. Immunohistochemistry (GATA3-, localized CDX2+) revealed the absence of malignancy.

Imaging findings were highly suggestive of LP; however, histological confirmation could not be obtained from the endoscopic biopsies. Following extensive discussion at our multidisciplinary oncology board, the decision was made to proceed with an exploratory laparoscopy and a full-thickness gastric biopsy.

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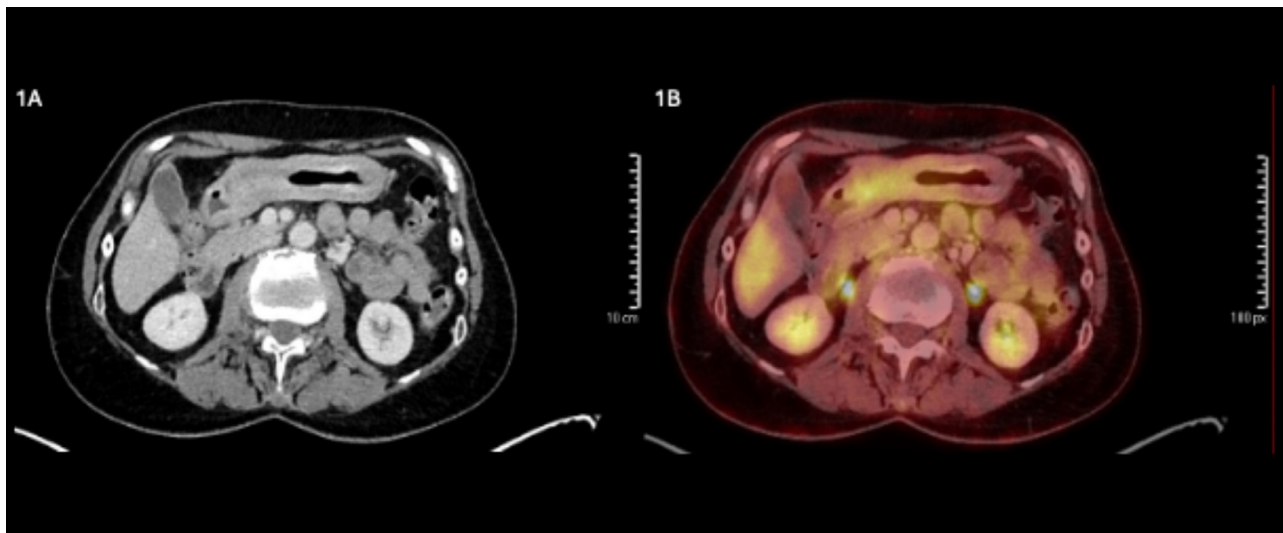
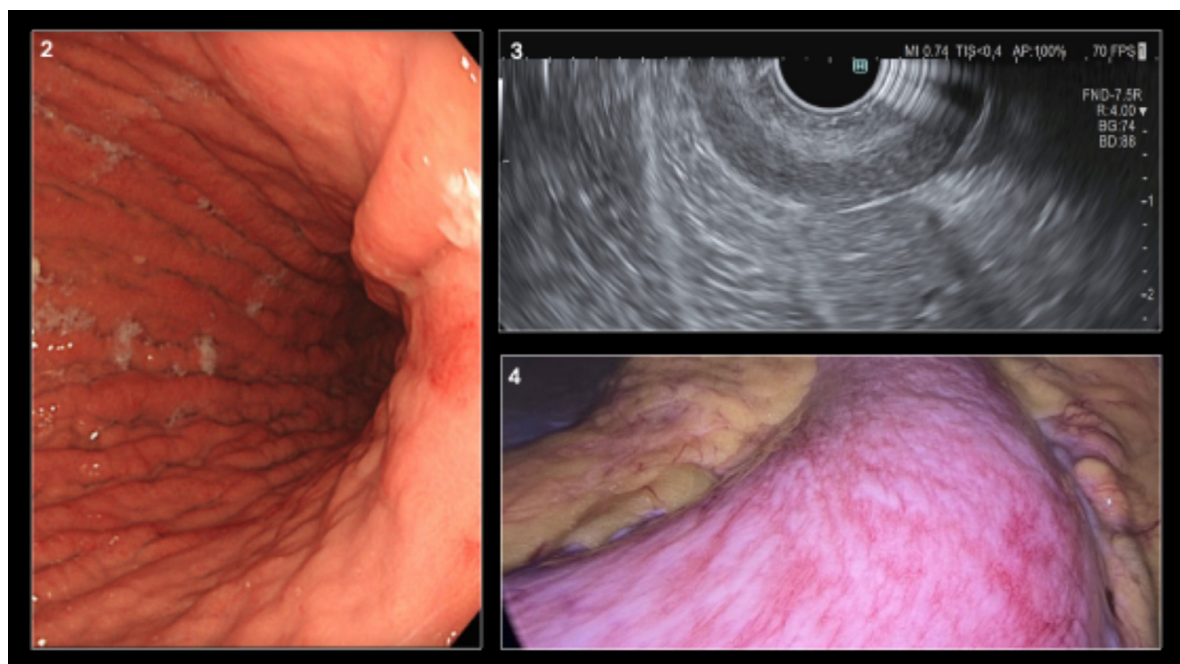


Figure 1A - 1B. — FDG-PET-CT-scan. The CT-scan (Fig. 1A) revealed the diffuse wall thickening, not present on a CT scan two years earlier. The FDG-PET scan (Fig. 1B) revealed the moderate uptake of FDG in the thickened stomach wall.



Figures 2, 3 and 4. — Figure 2 shows the thickened stomach ridges. Figure 3 illustrates the inability to distinguish between different parts of the stomach wall, characterized by a thickened, hypo-intense band in the outer half of the wall. The stomach wall was measured (9.6 mm). Figure 4 shows the intraoperative image of the serosal surface of the stomach demonstrating diffuse thickening and induration, with the characteristic 'leather bottle' appearance consistent with linitis plastica.

Intraoperatively, the stomach appeared diffusely thickened and indurated, displaying the characteristic 'leather bottle' appearance consistent with LP, but without evidence of peritoneal metastases (Fig. 4). A full-thickness gastric specimen measuring 2×1 cm was excised from the anterior gastric wall using electrocautery. The defect was closed with a 3-0 V-Loc™ suture. Due to the moderate quality and rigidity of the gastric tissue, an omentoplasty was performed to reinforce the closure.

Immunohistochemistry showed ER(+), PgR(-), HER2(-); pANCA, CAM5.2, GATA3, CK7(+); CD45 only in leukocytes; loss of E-cadherin; mammaglobin

and CK20(-). The biopsy showed that the patient had LP-like ILC metastasis with mutations in PIK3CA, PTEN, and CDH1, which suggests that the lobular phenotype is aggressive. The patient could not tolerate CDK4/6 inhibitors, thus paclitaxel was started.

Discussion

In case of gastrointestinal metastasis from ILC, the stomach is the most common site involved (2,3). The characteristic molecular profile of ILC has primarily explained this metastatic behavior, and the currently

accepted view is that it is related to the loss of E-cadherin expression, which facilitates the tumor's single-cell infiltration pattern and underlies its propensity to form LP-type metastases (3).

In our case, initial diagnostic uncertainty resulted from vague gastrointestinal symptoms. Early elevation of tumor markers raised suspicion for metastatic recurrence, but nonspecific clinical findings like nausea, early satiety, and weight loss may delay diagnosis. A full-thickness stomach biopsy revealed mutations in PIK3CA, PTEN, and CDH1, associated with endocrine resistance and aggressive ILC (4).

These results highlight the importance of utilizing molecular analysis in cases where endoscopic and radiologic evaluations are inconclusive. Although results may improve with hormone responsiveness, survival in metastatic ILC manifesting as gastric LP ranges from 10 to 28 months.

Role of imaging

Imaging methods have significant limitations, making the diagnosis challenging.

Radiologically, fluoroscopy is less sensitive than endoscopy or CT for early diagnosis, but can show classic GLP indications when typical symptoms are present. During a barium meal study, the wall of the stomach does not expand properly and exhibits diffusely thickened mucosal folds, resulting in a characteristic "leather bottle-like" appearance. The absence of significant peristalsis is also important (2).

CT findings may be nonspecific and may only show mild gastric wall thickening without definite malignant features. Due to the characteristically low metabolic activity of ILC, FDG-PET often yields false-negative results in gastric metastases of ILC, such as GLP (typically SUV <4.0), which may overlap with physiological gastric uptake resulting from smooth muscle activity or inflammation. In our case, mild-moderate metabolic activity and diffuse antral wall thickening of the stomach on FDG-PET-CT-scan were alarming when the patient's malignant tumor history and complaints were considered. Although in the English literature, FES PET offers superior specificity in detecting hormonally active metastases by identifying ectopic estrogen receptor expression, clinical experience in this area is unfortunately limited (5). In case of LP or LP-like conditions, EUS shows a homogeneous, hypointense, thickened band (>6 mm) instead of the normal alternating hyper- and hypointense five layers of the stomach wall (max 4 mm), due to the infiltrating process in the lamina propria, compressing all the other layers as shown in our case (6). The thickest point is best for the biopsy. Imaging with the MR Whole-body technique is promising and even recommended in the guidelines in the United Kingdom in patients with ILC to clarify equivocal findings of other imaging modalities or to detect metastatic disease (7). The LP-like appearance

of the stomach wall is characterized by a thickened, diffusion-restrictive wall resulting from the restricted mobility of water molecules caused by the malignancy. Additionally, MR whole-body examination is ideally suited for detecting possible accompanying peritoneal metastases, as ILC tends to spread along peritoneal and serosal surfaces.

Sampling Limitations

The diagnostic process is further complicated by limitations in sampling. Conventional endoscopic biopsies have a false-negative rate of up to 30% because of the predominant submucosal infiltration pattern of the tumor (5). Although various advanced biopsy techniques are available during endoscopic procedures, such as Jumbo biopsies, mucosal incision-assisted biopsy (MIAB), and EUS-guided fine needle biopsy (EUS-FNB), each has different efficacy. Recent studies have shown that a Franseen-type EUS-FNB provides superior diagnostic yield by obtaining large tissue samples for histological analysis. At the same time, MIAB is more effective for smaller (<20 mm) subepithelial lesions (8).

Differentiating Metastatic ILC from Primary Gastric Adenocarcinoma

In cases where GLP is detected, it is essential to determine whether it is associated with primary gastric adenocarcinoma or LP metastasis from ILC. In both cases, the presence of signet-ring cells further complicated the histological differentiation (3, 9). Immunohistochemical analysis is essential for distinguishing metastatic ILC from gastric adenocarcinoma. However, ER/PR positivity typically indicates breast origin, whereas receptor mismatch between primary and metastatic sites has been detected in 15-40% of cases. Interestingly, 32% of primary gastric cancers seem to be ER-positive, which may necessitate a comprehensive immunohistochemical analysis. In ILC metastasis to the stomach, immunohistochemical positivity for GATA3, ER, PR, and CK7 is expected, but negativity for CK20 and CDX2 is observed. In contrast, for the diagnosis of gastric adenocarcinoma, CK20, CDX2, and sometimes HER2 are expected to be positive, while GATA3 and ER/PR positivity are generally expected to be negative (9).

Conclusion

This case highlights the diagnostic challenges and the critical role of radiologic evaluation in detecting LP-like gastric metastasis of ILC. Radiologic identification of metastatic features in the stomach, with diffuse wall thickening and subtle FDG uptake, was crucial in the tumor board, which led to guidance on further diagnostic interventions, and ultimately resulted in the definitive diagnosis and the appropriate therapy.

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