How to differentiate between invasive lobular carcinoma metastasis and type 4 advanced gastric cancer: The importance of immunohistochemistry

Ryuhei Jinushi[1], Tomonori Kawasaki[1], and Shomei Ryozawa[1]

[1]Saitama Medical University International Medical Center

February 10, 2023

Abstract

Gastric metastases originating from breast carcinomas and type 4 advanced gastric cancers are often difficult to distinguish because of their similar endoscopic and pathologic characteristics. This often delays early intervention and accordingly affects prognosis. Immunohistochemical analyses are important for both diagnosis and treatment of breast carcinomas.

Title

How to differentiate between invasive lobular carcinoma metastasis and type 4 advanced gastric cancer: The importance of immunohistochemistry

Ryuhei Jinushi, MD[1]; Tomonori Kawasaki, MD, PhD[2]; Shomei Ryozawa, MD, PhD[1]

ORCID:

RJ 0000-0002-0422-6723, TK 0000-0003-1629-2549, SR 0000-0003-4128-9990

Author affiliations:

[1] Department of Gastroenterology, Saitama Medical University International Medical Center, Saitama 350-1298, Japan

[2] Department of Pathology, Saitama Medical University International Medical Center, Saitama 350-1298, Japan

Correspondence:

Tomonori Kawasaki, MD, PhD

Department of Pathology,

Saitama Medical University International Medical Center

1397-1 Yamane, Hidaka, Saitama 350-1298, Japan

Tel: +81-42-984-0609

Fax: +81-42-984-0609

E-mail: tomo.kawasaki.14@gmail.com

Data availability statement

The data that support the findings of this study are available from the corresponding author (TK) upon request.

Funding statement

This work was supported by JSPS KAKENHI Grant Number JP21K06910.

Conflict of interest disclosure

The authors have no conflicts of interest to declare.

Patient consent statement

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

Key clinical message

Gastric metastases derived from breast carcinomas and type 4 advanced gastric cancers are often difficult to distinguish because of their similar endoscopic and pathologic findings. Therefore, immunohistochemical analyses are key to diagnosis.

Abstract

Gastric metastases originating from breast carcinomas and type 4 advanced gastric cancers are often difficult to distinguish because of their similar endoscopic and pathologic characteristics. This often delays early intervention and accordingly affects prognosis. Immunohistochemical analyses are important for both diagnosis and treatment of breast carcinomas.

Keywords: breast neoplasms; carcinoma; immunohistochemistry; neoplasm metastasis; stomach neoplasms

Main text

A 74-year-old woman was diagnosed with stage IV breast carcinoma at our hospital in 2016 and is currently undergoing chemotherapy. Chest and abdominal computed tomography (CT) showed axillary lymph node metastases and osteolytic bone metastases in the skull and the spine. There were no obvious metastasis in the gastrointestinal tract. In December 2022, she visited her previous doctor for treatment of anorexia. An esophagogastroduodenoscopy (EGD) conducted by her previous doctor revealed sclerosis and poor extension of the gastric wall, which indicated that it was a type 4 advanced gastric cancer (AGC; Figure 1). EGD was performed again at our facility and 8 biopsies were taken. All these biopsies showed poorly differentiated adenocarcinoma, indicating that the metastasis originated from the breast carcinoma. Furthermore, to confirm this diagnosis, the expression levels of hormone receptors in cancer tissues were examined by immunohistochemical (IHC) analyses. The proportions of estrogen- and progesterone-receptor-positive cells were 60 and 5 % (Allred's total scores: 6 and 4), respectively. Human epidermal growth factor receptor 2 (HER2) score was estimated at 2+ (equivocal), and FISH analysis revealed no HER2 gene amplification. Ki-67 (MIB-1) labeling index was 25 % in the hot spot (so-called luminal B-like subtype). E-cadherin was mostly negative, or weakly positive, GATA binding protein 3 were diffusely positive, gross cystic disease fluid protein 15 were variously positive, and mammaglobin was focally positive. In addition, cytokeratin 7 was positive, whereas cytokeratin 20 was negative (Figures 2 and 3). Based on these pathological findings, the diagnosis of gastric metastasis derived from invasive lobular carcinoma was confirmed.

Currently, endocrine therapy for breast carcinoma contributes significantly to mortality reduction and recurrence control.[1] However, the endoscopic and pathologic findings of gastric metastases derived from breast carcinomas are often mistaken to be the findings of type 4 AGC, thereby delaying correct diagnosis and therapeutic intervention. Gastric metastases derived from breast carcinomas should be especially kept in mind in cases of women with a history of breast carcinoma. Accurate endoscopic diagnosis, EGD-biopsies, and pathological examinations, including IHC, are important for differentiating between gastric metastases derived from breast carcinomas and type 4 AGCs. In addition to highlighting the importance of IHC, we

have focused on another interesting point in the present study: owing to EGD-biopsies, cases of gastric metastases derived from breast carcinomas are easier to diagnose than cases of type 4 AGCs. In our current case, cancer tissue was abundant in all eight biopsy specimens. In the case of type 4 AGC, the diagnosis of adenocarcinoma using EGD-biopsy specimens is not so common, as clinical reports have shown that the proportion of definitive diagnoses made on the basis of EGD-biopsy results is approximately 50 %.[2, 3] In the future, examining the proportion of diagnosis by EGD-biopsies in both may contribute to the rapid diagnosis of gastric metastases derived from breast carcinomas.

Acknowledgments

We thank our patient for her invaluable contribution to this project. The support for compiling the manuscript based on the authors' detailed instructions was provided by Editage (*www.editage.com*), a division of Cactus Communications.

Author contributions

R Jinushi: Writing – Original draft preparation, review and editing.

R Jinushi, and T Kawasaki: Writing – Review and editing.

R Jinushi, T Kawasaki, and S Ryozawa: Approved the manuscript.

All authors read and approved the final manuscript.

References

1. Rasha, F., Sharma, M., and K. Pruitt. 2021. Mechanisms of endocrine therapy resistance in breast cancer. Mol Cell Endocrinol 532:111322.

2. Voutilainen, M. E., and M. T. Juhola. 2005. Evaluation of the diagnostic accuracy of gastroscopy to detect gastric tumours: clinicopathological features and prognosis of patients with gastric cancer missed on endoscopy. Eur J Gastroenterol Hepatol 17:1345-1349.

3. Kim, J. I., Kim, Y. H., Lee, K. H., et al. 2013. Type-specific diagnosis and evaluation of longitudinal tumor extent of Borrmann type IV gastric cancer: CT versus gastroscopy. Korean J Radiol 14: 597-606.

Figure legends

Figure 1. Endoscopic images.

Type 4 advanced gastric cancer-like sclerosis and poor extension of gastric wall are observed.

Figure 2 and 3. Pathologic findings of invasive lobular carcinoma metastasis.

Hematoxylin and eosin (H&E)-stained images show poorly differentiated adenocarcinoma infiltrating into the gastric lamina propria in a trabecular or an isolated pattern. Estrogen receptor (ER) shows varying degrees of positive expression in carcinoma cells, whereas progesterone receptor (PgR) expression is restricted to a few carcinoma cells. E-cadherin is mostly negative, but weak and incomplete expression can be seen in some carcinoma cell membranes. GATA binding protein 3 (GATA3) is diffusely positive. Gross cystic disease fluid protein 15 (GCDFP15) is reactive. Cytokeratin 7 is positive, and cytokeratin 20 is negative.