

# Radiologic Findings of Metastatic Signet Ring Cell Carcinoma to the Breast from Stomach

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## Abstract

Two Korean women (41 and 23-years of age) presented with painful breast enlargement and redness. The involved breast was confirmed as metastatic signet ring cell carcinoma. Although metastatic signet ring cell carcinoma of the breast shows similar clinical symptoms to inflammatory breast cancer, the difference between the two is that this malignancy showed no microcalcifications or mass on radiographic findings (mammograms and US). Therefore, after the confirmation of signet ring cell carcinoma of the breast has been made, metastatic signet ring cell carcinoma should be considered if there are no microcalcifications or masses evident on radiographic findings.

**Key Words:** Breast cancer-breast metastasis-signet ring cell carcinoma, metastasis-mammography-ultrasonography

## INTRODUCTION

Signet ring cell carcinoma of the stomach is a subtype of all gastric malignancies. It occurs more frequently in women and the younger age groups.<sup>1</sup> The incidence of metastatic breast lesions from extra-mammary malignant tumors at autopsy ranges from 1.7 to 6.6%.<sup>2</sup> Melanoma and lymphomas are the most common sources of metastasis, followed by carcinomas of the lung, ovary, kidney, stomach, oropharynx and carcinoid.<sup>3</sup>

Metastatic signet ring cell carcinoma of the breast is rare tumor, arising from the gastrointestinal tract, and comparatively few cases have been reported.<sup>2</sup>

Recently we experienced two cases of metastatic signet ring cell carcinoma of the breast from stomach presenting with painful breast enlargement and redness. These patients showed no microcalcifications or masses, which differ from the known radiographic findings of inflammatory breast cancer.

## CASE REPORT

### Case 1

A 41-year-old woman presented with left breast enlargement, pain, and redness, of four months duration. She had no other symptoms apart from the breast lesion. Her past history was unremarkable. On mammography, diffuse increased density and skin thickening without calcifications were seen (Fig. 1A). Ultrasonography showed marked skin thickening, lymphatic dilatation, and axillary lymph node enlargement (Fig. 1B). The diagnosis of the breast was made by core-needle biopsy. The site of biopsy was selected by palpation, as the most thickened area, because of no discrete mass by mammography or ultrasonography. Biopsy specimens of breast were evaluated microscopically and immunohistochemically, and included estrogen receptor (ER) and gross cystic disease fluid protein-15 (GCDFP-15), for differentiating primary and metastatic breast cancer. Immunohistochemical study of ER and GCDFP-15 were negative, and she was accordingly confirmed with metastatic signet ring cell carcinoma of the breast. The stomach was evaluated by upper gastrointestinal series and an endoscope to evaluate the underlying malignancy. The stomach had a large ulcerative mass in the lesser curvature of the lower body (Fig. 1C). The mass from the stomach was revealed as a signet ring cell carcinoma. On abdomi-

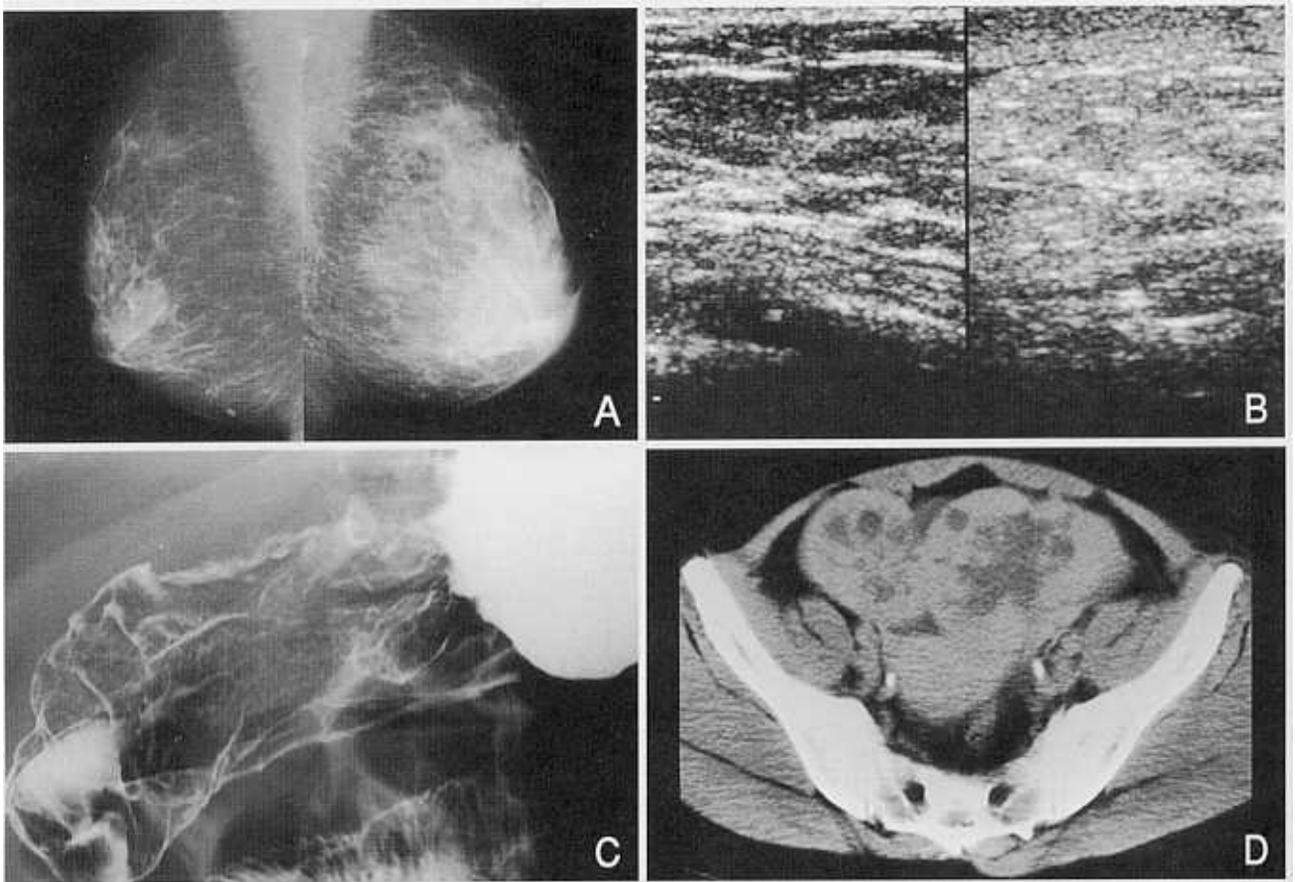
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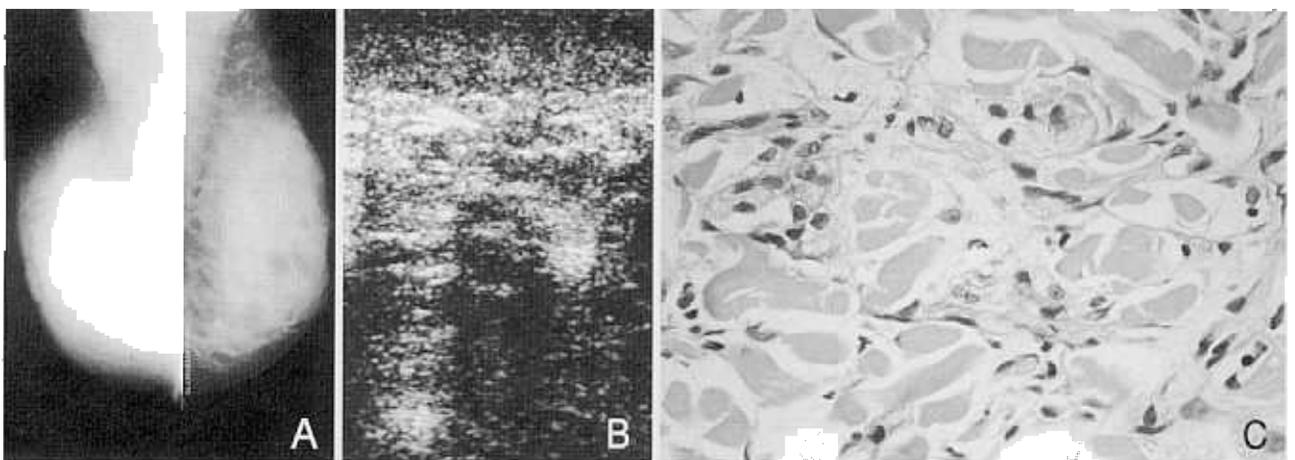
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*Fig. 1.* 41-year-old woman with a history of left breast enlargement for 4 months. (A) Left breast showed skin thickening, nipple retraction, and ill defined increased density on the mediolateral oblique mammogram. (B) On ultrasonography, left breast showed diffuse skin thickening (right side) with increased echogenicity of the subcutaneous fat layer. In contrast to this, the right breast appears normal (left side). (C) Large diffuse infiltrative mass was seen in the upper gastrointestinal series. (D) Pelvic CT showing bilateral heterogeneously enhancing ovarian mass.



*Fig. 2.* 23-year-old woman with right breast enlargement and redness for 4 months. Endoscopic finding was ulcerative mucosal lesion in antrum (not shown). (A) Right breast showed increased density and diffuse skin thickening on mediolateral oblique mammogram. (B) On ultrasonography, the right breast showed diffuse skin thickening without definite evidence of mass. (C) Photomicrograph showing scattered signet ring cells in the dermal layer of the breast (H & E,  $\times 200$ ).

nal and pelvic CT, a bilateral solid ovarian mass was seen, which might have been metastasis (Fig. 1D).

## Case 2

A 23-year-old female was admitted because of a painful right breast enlargement and redness for four months. Her symptoms started at third the trimester of pregnancy. The breast lesion was evaluated 2 months after delivery. Mammography showed diffuse increased density and skin thickening without mass or calcifications (Fig. 2A). On ultrasonography, diffuse skin thickening was seen without evidence of mass (Fig. 2B). Ipsilateral lymph node enlargement was seen. The lesion of the breast was confirmed using the same method as case 1. Endoscope and upper gastrointestinal series were performed, and the antrum of the stomach was diagnosed as signet ring cell carcinoma by endoscopic biopsy. The photomicrograph shows scattered signet ring cells in the dermal layer of the breast (Fig. 2C).

## DISCUSSION

Infrequently the only manifestation of breast metastases is diffuse skin thickening, clinically mimicking inflammatory breast carcinoma.<sup>4</sup> In one report, 4 patients presented clinical features similar to inflammatory carcinoma of the breast; the diagnoses were metastases from squamous cell carcinoma of the tonsil and lung and from pancreatic and anaplastic adenocarcinomas. Three out of 4 were the first manifestation of an unknown extramammary primary.<sup>4</sup> Pathologically tumor cells permeated the lymphatics and blood vessels resulting in diffuse involvement, particularly dermal, which meant unusual blood-borne metastases.<sup>4</sup> Cavazzini et al reported the clinical and radiologic features of breast metastasis from gastric signet ring cell cancer.<sup>2</sup> The clinical manifestation was highly suggestive of inflammatory carcinomas (red and edematous skin) and the radiologic pattern of the mass (irregular poorly defined mass without calcifications) was suspicious for malignancy.<sup>2</sup> Park et al. reported the sonographic findings of metastatic breast lesion from adenocarcinoma.<sup>5</sup> They showed a very ill-defined, irregular, and mixed-echogenic solid mass lesion on US. In our patients, the breast was the first manifestation, and they had no gastrointestinal sym-

ptoms. Clinical findings were similar to inflammatory breast cancer, but mammography and US showed no microcalcifications or mass.

Predisposing factors were not identified for the development of breast metastasis. However, hormonal factors are suggested in males with metastatic breast lesions<sup>6</sup> and in young females with lesions from rhabdomyosarcoma.<sup>7</sup> The relatively younger age of women with metastases in the breast suggests that the physiological status of the breast may provide a fertile soil for metastases.<sup>8</sup> The overall prognosis of patients with metastatic cancer to the breast is extremely poor with more than 80% dying within 1 year.<sup>9</sup> Metastases to the breast suggests advanced systemic disease.<sup>6</sup>

Differentiation of primary and metastatic breast carcinoma is important because the recognition of such metastasis can eliminate unnecessary procedures such as radical surgery and prolong survival with anti-estrogen therapy. Careful attention is necessary when the breast lesion is the first manifestation in an unknown primary malignancy, especially in younger patients. Nearly one quarter of metastatic breast carcinomas are the presenting manifestation of an otherwise occult malignant disease elsewhere in the body.<sup>9</sup> In our country, stomach cancer has a high incidence, so we strongly suspect the stomach as a primary focus of breast metastasis.

The evaluation of primary malignancy is often difficult in the case of breast carcinoma showing signet ring cell features, radiologically and pathologically. Radiologically, gastric metastasis of breast carcinoma usually manifests as an extrinsic mass without involving mucosa or presenting as multiple masses.<sup>10</sup> But, primary signet ring carcinomas of the breast show a propensity to involve unusual metastatic sites-serosa of the gastrointestinal tract, urinary tract and spleen.<sup>11</sup> Therefore, the linitis plastica pattern can occur.<sup>10</sup> In immunohistochemical stain, ER is known to be found in hormone-dependent tumors, such as breast cancer, endometrial cancer, and prostatic cancer,<sup>10</sup> but a recent report showed 23% of primary gastric carcinoma was ER positive.<sup>12</sup> Yim et al reported that immunochemical stain with GCDFP-15 has higher positivity (90%) in invasive lobular carcinoma with signet cell differentiation.<sup>10</sup> Therefore, immunohistochemical expression of GCDFP-15 may be an useful marker for the confirmatory diagnosis of metastatic signet ring cell carcinoma of

the breast from the stomach.<sup>10</sup>

We believe firmly that our cases are metastatic signet ring cell carcinoma from the stomach for several reasons. Firstly, the stomach lesions showed definite mucosal abnormality by endoscopic findings, which were different from metastatic stomach cancer from primary breast signet ring cell carcinoma, which often involve serosa. Secondly, our patients were relatively young, for primary breast signet ring cell carcinoma. Lastly, immunohistochemical stains with ER and GCDFP-15 were negative, which indicated a non-mammary origin.

In conclusion, for those with clinical features suggesting inflammatory breast carcinoma, after the confirmation of signet ring cell carcinoma of the breast has been made, metastatic signet ring cell carcinoma should be considered if there are no microcalcifications or masses on radiographic findings.

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