

**Case study**

Metastatic gastrinoma in the breast mimicking primary solid papillary carcinoma^{☆,☆☆}



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Summary We report a case of metastatic gastrinoma to the breast morphologically mimicking solid papillary carcinoma of the breast. A 59-year-old woman presented with a hypoechoic right breast mass that histologically revealed solid nests of small monotonous tumor cells, fibrovascular cores, and round to oval nuclei with fine chromatin and small nucleoli. Immunohistochemistry demonstrated chromogranin and synaptophysin positivity. Tumor prognostic markers showed weak positivity for estrogen receptor and negativity for progesterone receptor. Although an initial diagnosis of solid papillary carcinoma was rendered, subsequent identification of the patient's clinical history of pancreatic gastrinoma and an additional immunohistochemical stain for gastrin supported a diagnosis of metastatic gastrinoma. We report this rare case to increase awareness of metastatic neuroendocrine tumors in the breast. Multiple breast lesions and lack of expression of estrogen/progesterone hormone receptors should prompt careful review of the patient's clinical history to rule out metastatic neuroendocrine disease.

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1. Introduction

Solid papillary carcinoma (SPC) is an uncommon primary breast cancer representing less than two percent of breast carcinomas [1]. It is characterized histologically by a solid nodular growth pattern with closely opposed solid tumor nests, perivascular pseudorosettes, and thin fibrovascular cores. Tumor cells have round to oval nuclei and finely granular chromatin. Neuroendocrine differentiation is frequent, as demonstrated by positive immunohistochemical staining for neuroendocrine markers. It is also typically strongly positive for estrogen and progesterone receptors, and negative for HER2 expression. SPC is a clinically indolent entity and currently considered

carcinoma in situ by the World Health Organization if not accompanied by a conventional invasive component [2].

Gastrinoma is a well-studied neuroendocrine neoplasm that most commonly occurs in the duodenum and pancreas. It usually metastasizes to the liver or regional lymph nodes [3,4]. We herein report a case of metastatic gastrinoma to the breast. We summarize its clinical presentation, discuss the morphologic similarities between metastatic gastrinoma and primary SPC of the breast, and provide a few points to help proper pathologic differentiation of these two entities to ensure accurate diagnosis in the future.

2. Case report**2.1. Clinical history**

A 59-year-old woman presented with a 1.3 × 1.3 cm hypoechoic right breast mass on routine screening mammography. An

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excisional biopsy of this breast mass was performed. Then, bilateral magnetic resonance imaging (MRI) imaging was performed, revealing two additional right-sided small enhancing foci (Fig. 1). A sono-guided biopsy of one of the additional lesions was performed 2 weeks later.

2.2. Pathological findings

The excisional specimen contained a well-circumscribed ovoid lesion measuring $1.1 \times 1.1 \times 0.9$ cm. Microscopically, it was composed of solid nests of small monotonous tumor cells (Fig. 2A). Intermediate power demonstrated that the tumor cell nests contained fibrovascular cores (Fig. 2B). High power view revealed that tumor cells had round to oval nuclei, fine chromatin, and small inconspicuous nucleoli. The mitotic rate was very low. Immunohistochemical stains showed that tumor cells were positive for chromogranin (Fig. 2C) and synaptophysin. Tumor prognostic markers showed that tumor cells were weakly positive for estrogen receptor (Fig. 2D) and negative for progesterone receptor. The tumor had clear margins of excision. A diagnosis of SPC was rendered.

The subsequent core needle biopsy of the second lesion showed a tumor morphologically identical to the tumor in the previous excision. A diagnosis of SPC was made.

At this point, the patient's clinical history of stage IV pancreatic gastrinoma was brought to the attention of the pathologists. The patient was seen in an outside institution and was diagnosed and treated for pancreatic gastrinoma with small liver metastases three years ago. The outside pancreatic gastrinoma slides were not available for review. Based on the updated clinical history, an additional immunohistochemical stain for gastrin was ordered in both the breast excision and core needle biopsy specimens. The tumor cells were diffusely and strongly positive for gastrin in both cases (Fig. 3). The pathological diagnosis was then revised to metastatic gastrinoma. This patient was subsequently discussed in the

institution's multidisciplinary breast tumor board. Potential mastectomy was avoided.

3. Discussion

Gastrinoma is a functional well-differentiated neuroendocrine tumor that occurs most frequently in the duodenum, followed by the pancreas with a minority of tumors occurring at other sites. These tumors may result in Zollinger-Ellison Syndrome, which is characterized by hypergastrinemia, gastric acid hypersecretion, peptic ulcer disease, abdominal pain, nausea, heartburn and often diarrhea [4]. Gastrinomas may occur sporadically or in the setting of multiple endocrine neoplasia 1/MEN1 (roughly 20% of individuals with gastrinomas have MEN1) [4,5]. Between 60% and 90% of gastrinomas are clinically malignant with metastases to the lymph nodes, liver, or other distant sites at diagnosis [5-7]. Pancreatic gastrinomas tend to show liver metastases (incidence of approximately 50%) more frequently than duodenal tumors [5,7]. To the best of our knowledge, this represents the first reported case of metastatic gastrinoma to the breast. There are two reports in the literature of metastatic pancreatic neuroendocrine tumor to the breast [8,9].

This case is interesting to report in that metastatic gastrinoma mimics primary SPC of the breast in morphology and immunohistochemistry. It is well established that SPC of the breast has architectural and cytologic neuroendocrine features. It contains solid nests of tumor cells with fibrovascular cores. Tumor cells are round to oval with finely granular chromatin and inconspicuous nucleoli. It also demonstrates immunoreactivity for neuroendocrine markers including synaptophysin and chromogranin [10]. This pattern is nearly identical to that seen in metastatic neuroendocrine tumors, such as the metastatic gastrinoma in our case. Indeed, APC is considered part of the spectrum of the neuroendocrine tumor of the breast. It is

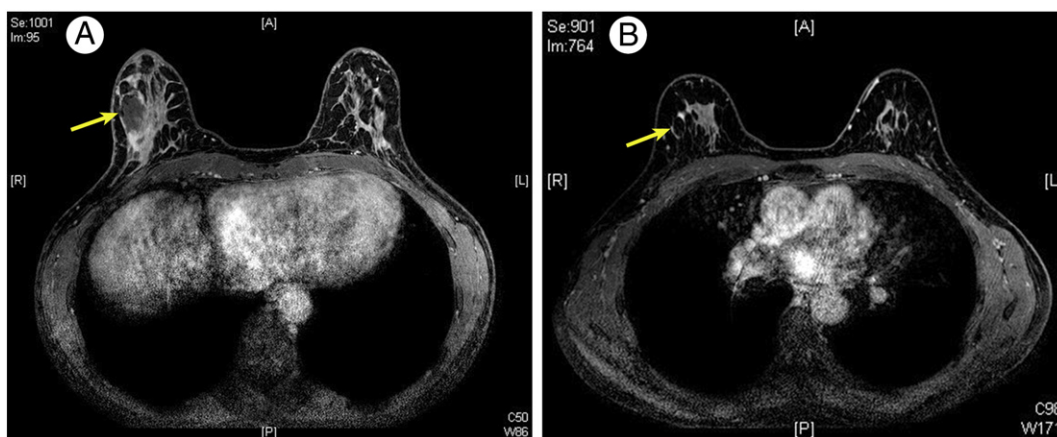


Fig. 1 Magnetic resonance imaging of the right breast, enhanced T1 high-resolution isotropic volume excitation (eTHRIVE). A, Imaging demonstrates a 4.0×2.2 cm ovoid fluid collection in the lateral right (9:00) breast following excisional biopsy of the first lesion. B, An additional 0.5 cm ring-enhancing mass within the upper outer (11:00) right breast.

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