대한영상의학회지

Primary Breast Carcinoma with Neuroendocrine Features: Imaging Features on Mammography and Ultrasonography

신경내분비 특징을 가지는 원발성 유방암: 유방촬영술과 초음파 소견

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Primary breast carcinoma with neuroendocrine features is an extremely rare and underrecog-nized subtype of the breast carcinoma. And up to present, its biologic behavior, the most effec-tive treatment, and prognosis are not well recognized. To diagnose this rare entity, special tu-mor stains of neuroendocrine markers are required, which are not routinely used. The imaging features of primary breast carcinoma with neuroendocrine features (BCNF) have not been ac-curately described due to the extreme rarity of this tumor type. We report the imaging features in a case of BCNF, with imaging findings different from the typical imaging findings of invasive breast carcinoma.

Index terms Breast; Breast Neoplasms; Carcinoma; Neuroendocrine Tumors; Carcinoma, Neuroendocrine

INTRODUCTION

Breast carcinoma is a heterogeneous disease, composed of many different subtypes with varying clinical characteristics. Neuroendocrine carcinoma is derived from neuro-endocrine cells that are present throughout the body and arises most commonly from the bronchopulmonary system and gastrointestinal tract. Primary neuroendocrine carci-noma of the breast is a distinct subtype, first recognized by the World Health Organiza-

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tion (WHO) in 2003 (1). In 2012, the WHO revised the category, renaming it as breast carcinoma with neuroendocrine features (BCNF) (2). Although there are some published reports regarding this rare pathological entity, only a few reports include its imaging characteristics (3-7). We report the imaging features in a case of primary BCNF (solid neuroendocrine carcinoma).

Fig. 1. A 47-year-old woman with palpable lump in the left breast.
A. Left craniocaudal mammogram shows a 2.7 cm sized, oval isodense mass with circumscribed margin in the sub-areolar region of upper outer quadrant.
B. Ultrasonography reveals circumscribed oval hypoechoic mass with posterior enhancement and cystic foci (arrow).
C. Color Doppler exam shows increased vascularity of the lesion.
D. Microscopic sections of left breast nodule show the tumor consisting of cellular nests and trabeculae of tumor cells, with spindle to ovoid cells in rosette formation (hematoxylin-eosin stain; left panel × 200, right panel × 400).
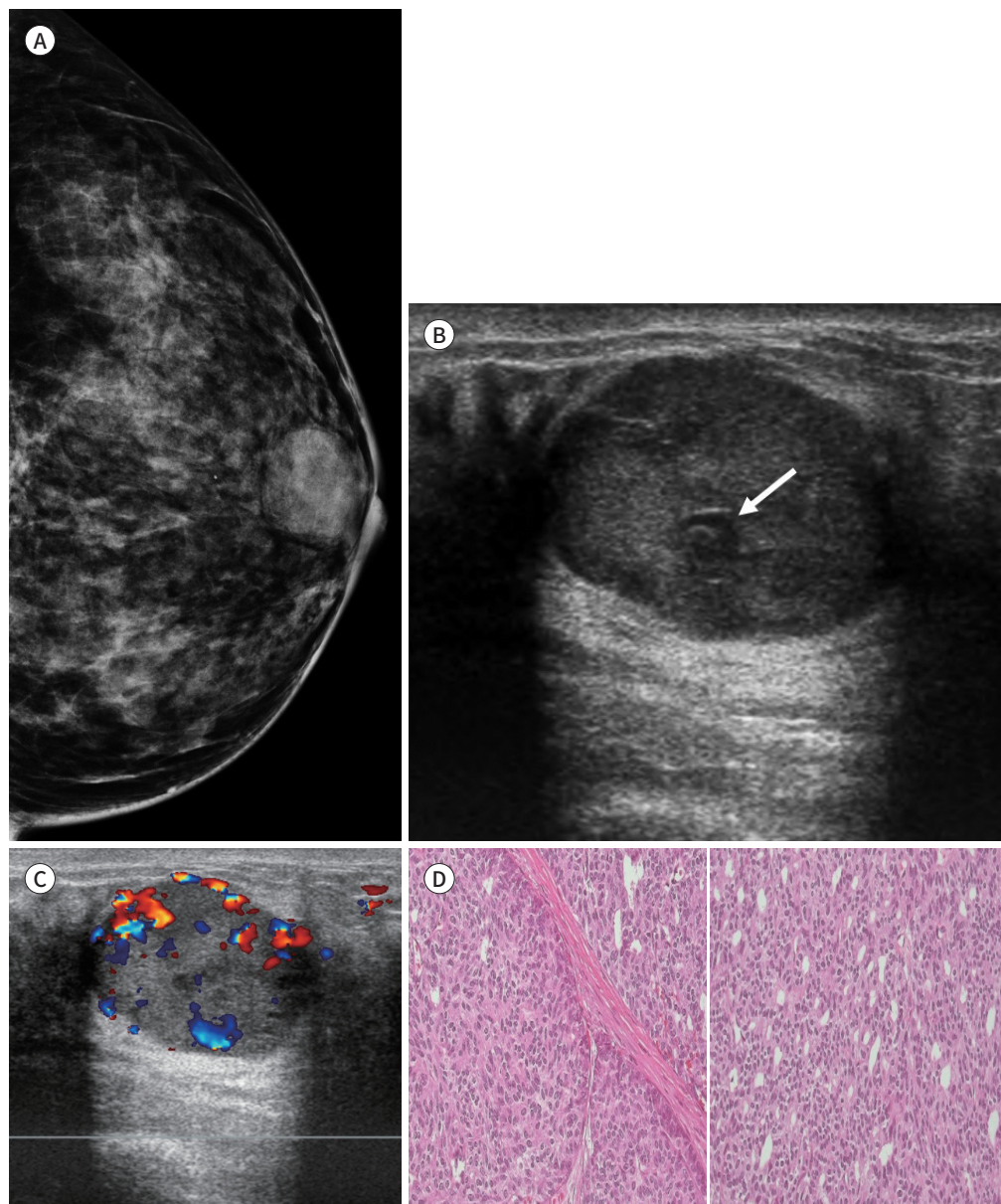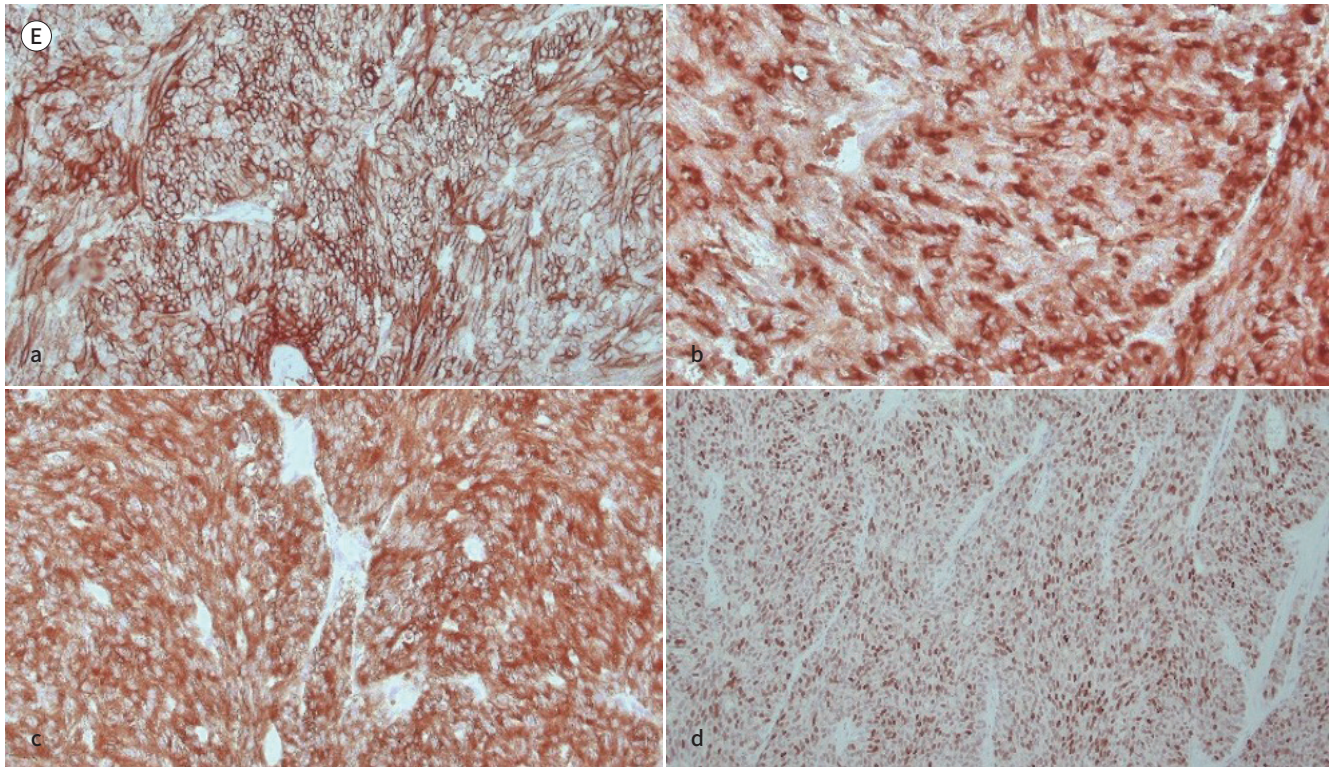
Fig. 1. A 47-year-old woman with palpable lump in the left breast.
E. Immunohistochemistry shows carcinoma cells diffusely positive for CD56 (a, × 200), chromogranin (b, × 200), synaptophysin (c, × 200), estrogen receptor, and progesterone receptor (d, × 100).

CASE REPORT

A 47-year-old woman presented with a palpable lump in her left breast, which she had detected 3 months back. On physical examination, a 5-cm sized, firm, movable lump was observed upon palpation in the upper outer sub-areolar region of her left breast. A mammography revealed an oval isodense mass with circumscribed margin in the sub-areolar region of the upper outer quadrant, with no microcalcification (Fig. 1A). Breast ultrasonography (US) revealed a circumscribed, oval, hypoechoic mass with posterior enhancement and cystic foci (Fig. 1B). A color Doppler examination showed increased vascularity in the lesion (Fig. 1C). Neither of the imaging modalities showed any evidence of lymphadenopathy in the axillae. The mass was categorized as Breast Imaging Reporting and Data System category '4A', with a low suspicion for malignancy. Since the patient was referred to our hospital from an external local clinic with the suspicion of breast cancer, she underwent surgery without preoperative US-guided core needle biopsy. During the operation, the frozen section diagnosis was of a malignant tumor, type deferred; hence, she underwent breast conservation surgery. Grossly, the tumor appeared as a well-demarcated, partly encapsulated, pinkish tan, soft and solid mass, measuring 2.5 × 2.2 cm. On the cut surface of the resected tumor, multifocal small cystic spaces were noted, whereas pathologically, there was no evidence of metastatic lymphadenopathy. Histopathologically, the tumor consisted of cellular nests and trabeculae of tumor cells, revealing spindle to ovoid cells in rosette formation (Fig. 1D). Immunohistochemi-

cal staining revealed positive results for CD56, chromogranin, synaptophysin, estrogen receptor, and progesterone receptor (Fig. 1E). Based on these pathologic findings, we considered this tumor to be a solid neuroendocrine carcinoma. PET-CT showed the absence of an abnormal uptake, suggesting that the breast was the only primary site. Annual follow-up breast US and mammography were performed for 7 years and PET-CT was performed annually or bi-annually for 4 years, showing no evidence of local recurrence or distant metastasis.

DISCUSSION

Primary BCNF is an underrecognized and extremely rare subtype of breast carcinomas, accounting for 0.27% to 0.5% of histopathologically proven breast cancers (8). Currently, its biologic behavior, most effective treatment, and prognosis are not well recognized. Although no consensus has been reached on the prognosis, large-scale population studies have shown poor outcomes as compared to invasive breast carcinomas (8, 9).

There are 2 main theories on the histogenesis of primary BCNF (10). The first, which is more controversial, is that these tumors evolve from neoplastic transformation of native endocrine cells. However, the more accepted theory is that neuroendocrine differentiation arises from the divergent differentiation of neoplastic stem cells into epithelial and endocrine cell lines during early carcinogenesis. This theory is supported by the lack of benign neuroendocrine tumors of the breast and evidence that the neuroendocrine cells are clonally related to malignant epithelial cells.

The diagnosis of primary BCNF requires detection of the expression of neuroendocrine markers by means of tumor-specific stains, which are not routinely used. Therefore, we can assume that neuroendocrine differentiation in breast carcinomas may have gone unrecognized in routine practice. Tang et al. (3) reported that neuroendocrine differentiation was missed in up to 69% (51 of 74) of breast carcinomas. In the same vein, the actual incidence and clinical features of primary BCNF are still difficult to define. Hence, knowledge of the imaging features of this entity will be helpful to ensure the correct diagnosis and to define its nature.

There are a few reports that described the imaging features of primary BCNF (4-7). The results of those studies suggest that the mammographic findings of primary BCNF differ from typical findings of invasive breast carcinomas, which tend to be irregular in shape with speculated margins and associated microcalcifications. Chang et al. (4) and Yoon et al. (7) described cases of primary BCNF showing high density masses with indistinct margins on mammography imaging; hypoechoic masses with posterior acoustic enhancement on US imaging; and increased vascularity on color doppler exam. Lee at al. (6) described a case of primary BCNF demonstrating an irregularly shaped, hypoechoic mass on US imaging. Park et al. (5) reported that primary BCNF generally presents as high-density, round or oval masses with circumscribed margins on mammography, and solid, irregular, hypoechoic, hypervascular masses with indistinct margins and posterior enhancement or no posterior acoustic features on US. Our case also showed similar features, revealing an oval shaped mass with circumscribed margins on mammography, and a hypoechoic lesion with posterior enhancement and increased vascularity on US. These are distinguishing features of circumscribed malignancies, such as papillary, medullary, and mucinous carcinomas, which mimic be-

nign lesions.

Although not seen in our case, the MRI findings of BCNF frequently suggest characteristics associated with malignancy, in contrast to the findings of mammography and US. The most frequent MRI finding is an irregular mass with irregular margins and washout time-intensity kinetics, which are highly suspicious features of malignancy (4-7).

Park et al. (5) also reported a high incidence of positive results for estrogen and progesterone receptors, and negative results for human epidermal growth factor receptor-2 (HER-2)/ neu, histologically. Similar features were noted in our case, which revealed pathologically positive results for estrogen and progesterone receptors, and equivocal results for HER-2/ neu. However, including the cases stated above, the number of cases with radiological findings has been far too small to generalize the results.

Meanwhile, large-scale population studies about primary BCNF suggest that it has a poor prognosis with a higher rate of local and distant recurrence, compared to invasive breast carcinomas (8, 9). In contrast, our patient had a relatively good prognosis for up to 7 years after breast conservation surgery, with follow-up studies (mammography, breast US, and PET-CT) revealing no evidence of local recurrence or distant metastasis, even without postoperative chemotherapy and radiotherapy.

In this report, we present a case of primary BCNF (solid neuroendocrine carcinoma) of the breast, together with its mammographic and sonographic features. More reports of new cases will be necessary in order to describe the imaging features of primary BCNF. Furthermore, more reports regarding the treatment and prognosis of this entity will help develop the most effective treatment plan.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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신경내분비 특징을 가지는 원발성 유방암은 매우 드물며 간과되고 있는 원발성 유방암의 아형이다. 또한 지금까지 이의 생물학적인 양상, 효과적인 치료와 예후는 정확히 알려지지 않았다. 이를 진단하기 위해서는 통상적으로 사용되지 않는 특정 신경내분비표지자에 대한 면역화학염색이 필요하다. 신경내분비 특징을 가지는 원발성 유방암은 매우 드물기 때문에 이에 대한 영상의학적 소견은 명확히 정립된 바가 없다. 저자들은 침윤성 유방암의 전형적인 영상의학적 소견과 차이를 보이는 신경내분비 특징을 가지는 원발성 유방암의 사례를 경험하였기에 이의 영상의학적 소견을 보고하고자 한다.

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