Case Report

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Squamous Cell Carcinoma Arising from Epidermal Inclusion Cyst of Breast: Imaging Findings and Literature Review

유방의 표피낭종에서 발생한 편평세포암종: 영상 소견 및 문헌고찰

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Commonly, epidermal inclusion cysts (EICs) are benign cutaneous lesions that are lined with stratified squamous epithelium and may occur in all body parts, including the breasts. EICs in the breast (EICB) are commonly encountered clinically; it may be under-reported because of their mild and non-specific clinical presentation. Malignant transformation of EICs is extremely rare, occurring 0.011%–0.045%. Presently, we report a rare case of squamous cell carcinoma arising from an EICB of a woman with invasive ductal carcinoma.

Index terms Epidermal Inclusion Cyst; Squamous Cell Carcinoma; Breast; Mammography; Ultrasonography

INTRODUCTION

Epidermal inclusion cysts (EICs) result from the proliferation and implantation of epidermal elements within a circumscribed space in the dermis. Cutaneous epidermal cysts are common lesions, but malignant transformation in their epithelium is extremely rare (1). EICs may occur anywhere in the body, though they are commonly found in the head, neck, trunk, and extremities. EICs of the breast are also common, but if it is small and painless they often do not prompt individuals to seek medical attention, unless the lump size increas-

es or becomes painful. Breast EICs can cause complication such as spontaneous rupture leading to inflammation and abscess formation while they rarely undergo malignant transformation into squamous cell carcinoma (SCC). Herein, we report the mammographic and ultrasonographic findings of a patient with SCC arising from an EIC that was detected through the follow-up. The relevant literature was also reviewed in accordance to the report for future reference.

CASE REPORT

A 41-year-old woman underwent screening mammography which detected a mass of 2.3 cm in diameter in the upper outer quadrant of the left breast. Subsequently, a biopsy revealed a histologic diagnosis of an invasive ductal carcinoma, grade 2, with estrogen receptor (ER) negative, progesterone receptor (PR) negative, and human epidermal growth factor receptor 2 (HER2) negative. She had undergone neoadjuvant chemotherapy, including four cycles of doxorubicin plus cyclophosphamide and an additional four cycles of docetaxel. After receiving the neoadjuvant chemotherapy, the patient then underwent a left breast lumpectomy with sentinel lymph nodes biopsy, which yielded a complete response. This was followed by a postoperative radiation and an imaging surveillance of the both breasts. Initial mediolateral oblique view showed a radiolucent round mass of fat density with a thin wall in the upper portion of right breast that overlapped with pectoralis muscle (Fig. 1A). This lesion was not shown on the craniocaudal view because it was found at too peripheral location and it was initially identified as a benign cystic mass such as an oil cyst. Breast surveillance mammography was performed 5 years after the lumpectomy revealed a round mass with a wall that had gradually thickened over the past 5 years in the right upper breast (Fig. 1B). US discovered a round, isoechoic solid mass with a peripheral halo at the 12 o'clock direction of the right breast subcutaneous fat tissue locating 10 cm from the nipple (Fig. 1C). There was no evidence of cancer recurrence at the left breast. One year later, a follow up mammography and US revealed that the right upper breast mass had grown, with an even thicker wall and newly detected internal calcifications (Fig. 1D). US demonstrated a round complex solid and cystic mass which showed more heterogeneous echogenicity in the internal solid portion and the size increased to 16 mm × 13 mm. The patient had no symptoms of palpable lump or pain and the lesion was classified as category 4A according to the Breast Imaging Reporting and Data System (BI-RADS), which is low suspicious for malignancy. We recommended to undergo a biopsy of the lesion, but the patient refused to perform the biopsy. The screening mammography a year later showed the continued growth of the preexisting round mass, in association with increased number of coarse calcifications. US also revealed that the diameter of the complex mass had increased to 20 mm, with more heterogeneous echogenicity on the internal solid portion (Fig. 1E).

Based on the serial mammographic and US features, we assessed the mass as a moderate suspicion for malignancy (category 4B) according to the BI-RADS criteria. A fine needle aspiration was performed at the cystic portion of the complex mass followed by an ultrasound–guided core needle biopsy at the solid portion of the complex mass. An aspiration cytology showed no evidence of malignant cells and a histopathologic examination revealed atypical

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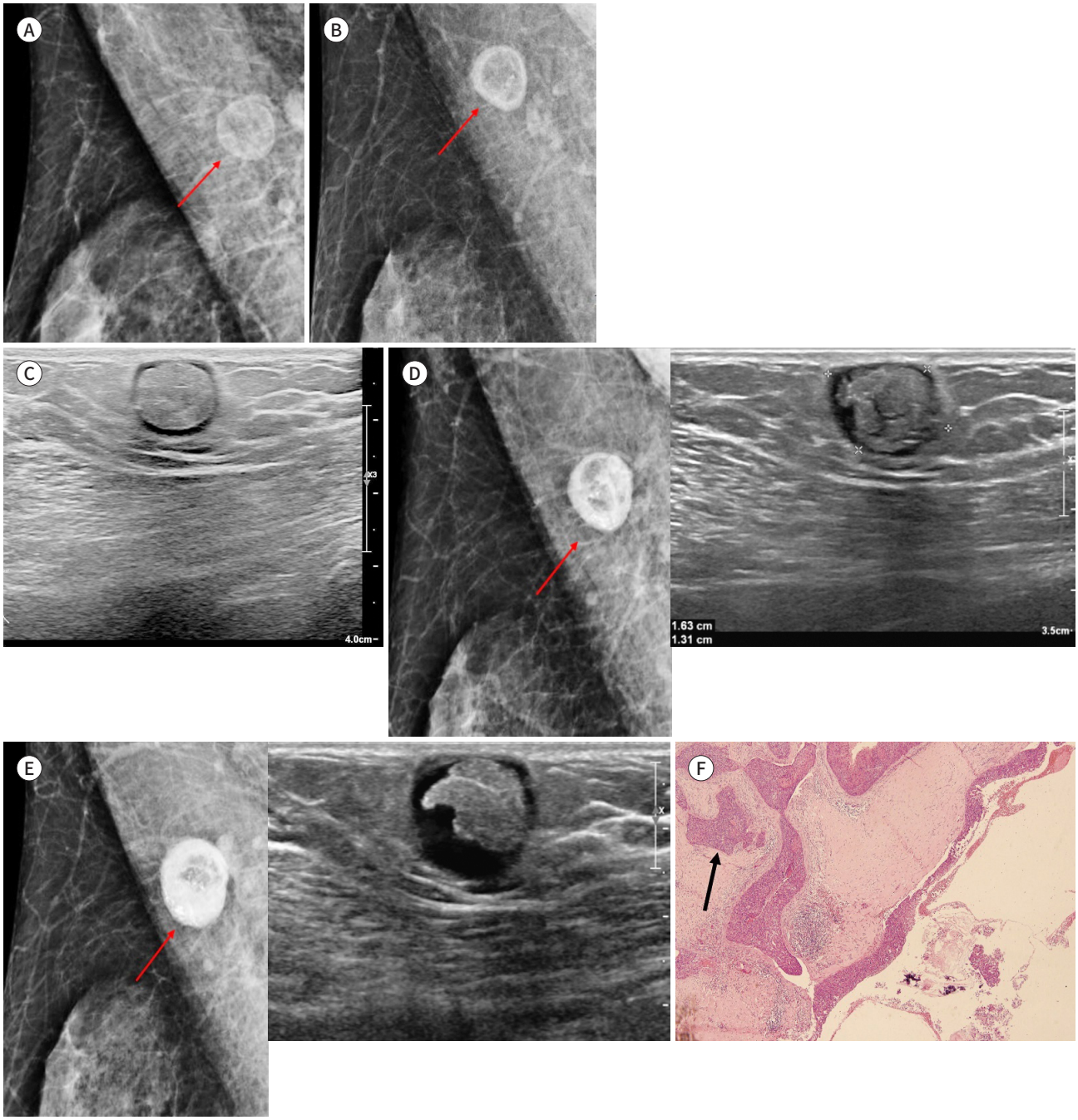
Fig. 1. A 48-year-old woman with squamous cell carcinoma arising from an epidermal inclusion cyst of the breast.
A. Initial mediolateral oblique mammogram shows a radiolucent round mass with central lucency and a thin wall in the right breast's upper portion that overlaps with the pectoralis muscle (arrow).
B. Follow-up mammogram after five years shows a round mass with a gradually thickened wall (arrow).
C. US performed simultaneously with (B) shows a round, isoechoic solid mass with a peripheral halo in the subcutaneous fat tissue's 12 o'clock direction, 10 cm from the nipple.
D. Follow-up mammogram and US performed after 6 years show a round high density mass with an increased size of 16 mm × 13 mm, more thickened wall, newly detected internal calcifications (arrow), and more heterogeneous echogenicity of the internal solid portion.
E. Follow-up mammogram and US after 7 years show that the preexisting round mass has increased in size, with denser wall thickened, increased number of coarse internal calcifications (arrow), and more heterogeneous echogenicity of the internal solid portion.
F. Atypical squamous epithelial cells (arrow) invade the surrounding dermal stroma (hematoxylin and eosin stain, × 100).



epithelial cells with the inflamed fibrotic tissue. The patient underwent an excisional biopsy, which yielded a histopathologic diagnosis of SCC of the dermis of the right breast (Fig. 1F).

Microscopic findings were consistent with the presence of an EIC lined by stratified squamous epithelium showing dysplastic changes and a focus of malignant transformation from where the SCC nest, cords and strands were infiltrating the breast parenchyma. All margins and lymph nodes were free of tumor.

Additionally, immunohistochemical staining revealed ER, PR and HER2 negativity, along with a Ki-67 proliferation index of 80%. For the precise evaluation for the presence of remnant tumor, the patient underwent a right lumpectomy, which revealed no residual tumor.

This case report was approved by our Institution Review Board, and the requirement for informed consent was waived (IRB No. 2022-11-011).

DISCUSSION

EICs and SCC are both cutaneous tumors that are commonly encountered in clinical practice. However, the development of SCC from an EIC is extremely rare. The incidence of SCC arising from EICs have ranged from 0.011% to 0.045% of EIC cases (1, 2). Frank et al. (2), found that the mean age at which SCC arose from an EIC was 61.8 years (range from 28–96 years) among 41 patients, with the SCC transition occurring more frequently in men (69.0%). The most common site was the head and neck (54.8%), and only one patient had a breast lesion. The mean cyst diameter was 5.0 cm (range from 0.7–20 cm). The mean duration of cyst presence was 92.6 months (range, 0.5–480 months), and the most common symptoms were rapid cyst enlargement (48.6%); overlying skin changes, such as erythema, ulceration or drainage (38.2%); and pain (24.2%).

It is important to distinguish a cyst with malignant changes from cystic SCC. Malignant lesions arising from an epidermal cysts are confined only to the cyst wall; such tumors have no connection with the epidermis, whereas cystic SCCs directly originate from the epidermis (2-4). In our case, the epidermis was not involved by the tumor.

The mechanism underlying the malignant transformation of EICs to SCC has not been clearly delineated. Some reports have proposed that chronic cyst irritation, such as that caused by inflammation or infection, can trigger malignant change. Sze et al. (5) reported other etiologic factors of malignant transformation of cysts including direct trauma, human papilloma virus, immune suppression and actinic damage.

EICs of the breast are not rare, but they may remain underreported because of their insignificant clinical presentation. Malignant transformation to SCC is very rare, although there are variable reports on its frequency. Suhani et al. (6) reported a case of SCC arising from EIC of the breast, which is indistinguishable from the breast cancer on mammography. Menville (7) found that 19% of the patients with EIC in their series had histopathologically confirmed malignant squamous cell lining. However, Cameron and Hilsinger (8) found that malignant transformation of the cyst wall epithelium occurred very rarely (0.045%).

Malignant changes occur more frequently in association with breast EICs than with EICs of other sites. Such malignant transformation in the breast may be found due to squamous metaplasia of the mammary duct epithelium (9).

On mammography and ultrasonography, EICs have been characterized by benign features; they are typically solid, circumscribed and homogeneous mass. An "onion-ring appearance" with alternating concentric hyperechoic and hypoechoic rings has also been described, corresponding to the laminated keratin (10).

Warning symptoms of malignant transformation arising in an existing EIC include pain, rapid growth, and overlying skin changes; however, the absence of such symptoms does not preclude the diagnosis, as multiple cases have been reported to be associated with gradual growth. In our case, the patient had no symptoms, but serial imaging revealed that the mass was gradually growing, and the internal echogenicity began to change heterogeneously on ultrasound.

The primary treatment method for cutaneous SCC is wide excision with an adequate margins of 4 mm to 6 mm (2). In our case, to facilitate tumor clearance, the patient underwent a lumpectomy after local excision.

In this report, we presented a case of SCC arising from an EIC of the breast, including details of serial mammographic and sonographic findings. Breast EICs appears as non-calcified, well circumscribed lesions on mammography and as solid, circumscribed and complex masses on ultrasonography. The possibility of malignant changes in a breast EIC should be considered when the size of the lesion begins to increase or when its internal echogenicity begins to change heterogeneously. Awareness of these characteristics can aid diagnosis and confirmation of suspected cases can be achieved via biopsy and histopathologic examination.

Author Contributions

Conceptualization, K.Y.M.; software, H.Y.J.; supervision, K.Y.M.; writing—original draft, all authors; and writing—review & editing, all authors.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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유방의 표피낭종에서 발생한 편평세포암종: 영상 소견 및 문헌고찰

한영주 · 김유미*

표피낭종은 중층 편평상피로 구성되어 있는 진피층에서 흔하게 발생하는 양성질환으로, 유방을 포함한 신체 모든 부위에서 발생할 수 있다. 유방에서의 표피낭종은 임상에서 흔하게 볼 수 있으나, 임상적인 중요성이 떨어져 보고된 바가 적고, 표피낭종의 악성변형은 발생 빈도가 0.011%–0.045% 정도로 매우 드물다. 저자들은 침윤성 유관암의 과거력이 있는 환자에게서 발생한 유방의 표피낭종에서 기원한 편평세포암종에 대한 증례를 보고하고자 한다.

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