

Letter to the editor

**Synchronous squamous cell carcinoma of the breast
and invasive lobular carcinoma**

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Running title: Squamous cell carcinoma of the breast

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Squamous cell carcinoma (SCC) is an uncommon breast carcinoma with a variable proportion of ductal carcinoma cells mixed with tumor cells of squamous differentiation forming a mature keratinizing tissue. SCC tends to grow rapidly, and lymph node metastasis is reported to occur in approximately 54% of cases (1). Invasive lobular carcinoma (ILC) is the second most common type of breast cancer after invasive ductal carcinoma (IDC). The classic form of ILC is characterized by the “Indian file” growth pattern; that is, small, relatively uniform, neoplastic cells invade the stroma, resulting in linear strands of cells. We encountered an SCC with a synchronous ILC, which, to our knowledge, has not been described previously.

A 57-year-old woman visited us complaining of recent onset of pain, swelling and tenderness in her right breast. Physical examination revealed right breast erythema, hyperemia, and sensitivity to touch, mainly in the upper outer quadrant. Right partial mastectomy and lymph node dissection were performed. The right breast and supraclavicular region were treated postoperatively by radiation therapy.

Gross examination of the surgical specimen revealed a solid and cystic tumor, located in the center to upper outer quadrant of the breast. The tumor was 5cm in diameter, firm, gray-white and solid; the cavity was filled with necrotic debris (Figure 1). Histologically, the tumor was composed of two main components (Figure 2A) that were hard to distinguish each component. One was SCC around the cystic lesions, with cells containing modest to abundant eosinophilic cytoplasm and enlarged, hyperchromatic nuclei with irregular nuclear membranes (Figure 2B). Intercellular

bridges and keratin material were focally identified. Some areas of typical IDC were also identified slightly. Non-neoplastic ductules were entrapped within islands of SCC. The other component was ILC, with massive infiltration of small, relatively round tumor cells (Figure 2C). The neoplastic ILC cells each had a round-to-ovoid nucleus and thin rim of cytoplasm with an occasional intracytoplasmic lumen. Loosely cohesive tumor cells diffusely infiltrated the mammary stroma. The uninvolved mammary parenchyma showed fibrocystic change.

Staining for ER and PgR was positive only in the ILC by immunohistochemistry. Staining for Her2/neu was negative in all three components. The typical ductal carcinoma was 34 β E12 negative and E-cadherin positive; expression was quite the opposite in the ILC. In the SCC, staining for 34 β E12, E-cadherin (Figure 2D), CK5/6, p63 and p53 (Figure 2E) was positive.

The present case involved colocalization of SCC and ILC and appeared unique. A simple nomenclature for mixed-type carcinoma has been incorporated into the WHO classification of tumors of the breast (2) and refers to a neoplasm of which 10 to 49% is composed of cells arranged in a ductal pattern not otherwise specified (NOS), and the remainder is a recognized special type. Thus, the neoplasm would be a mixed ductal and special type or a mixed ductal and lobular carcinoma. This nomenclature, however, is not suitable for the tumor we describe herein because of the SCC, not ductal NOS.

There are several theories about the origin of breast SCC. Degenerated cystic areas are often encountered, especially in tumors with squamous metaplasia such as the tumor in our case (3-4). Breast SCC has been reported to originate from an epidermal or dermoid cyst of the breast (5-6), chronic abscess (6), skin (7) and complete metaplasia

of glandular breast tissue (8-9). It is likely that breast SCC arises through multiple histogenic pathways, but we speculate that the SCC in our case was due to the metaplastic change associated with the IDC, because accumulation of p53 was found in both IDC and SCC, but not in ILC.

In our case, each component was clearly identified on the basis of the different histological and immunohistochemical patterns by using E-cadherin for IDC, 34 β E12 for ILC, and p63, CK5/6, E-cadherin and 34 β E12 for SCC. Negativity for Her2/neu is reported in 93% of breast SCCs (10). Breast SCC never expresses ER or PgR (10). In our case, staining for Her2/neu was negative in all components, and staining for ER and PgR was positive only in the ILC. The final diagnosis was synchronous SCC and ILC, after an extensive work-up including CT scanning ruled out metastasis from another primary SCC. To our knowledge, SCC with synchronous ILC has not been described previously.

In summary, we report a distinct type of composite SCC and ILC arising in the right breast. The morphology of this tumor differs from previously reported mixed ductal and lobular carcinomas.

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Figure 1.

(A) Gross features of the resected specimen. The tumor was solid and cystic, and 5.0 cm in maximum diameter. (B) Distribution of the two main components. SCC is outlined in black, ILC is outlined in red.

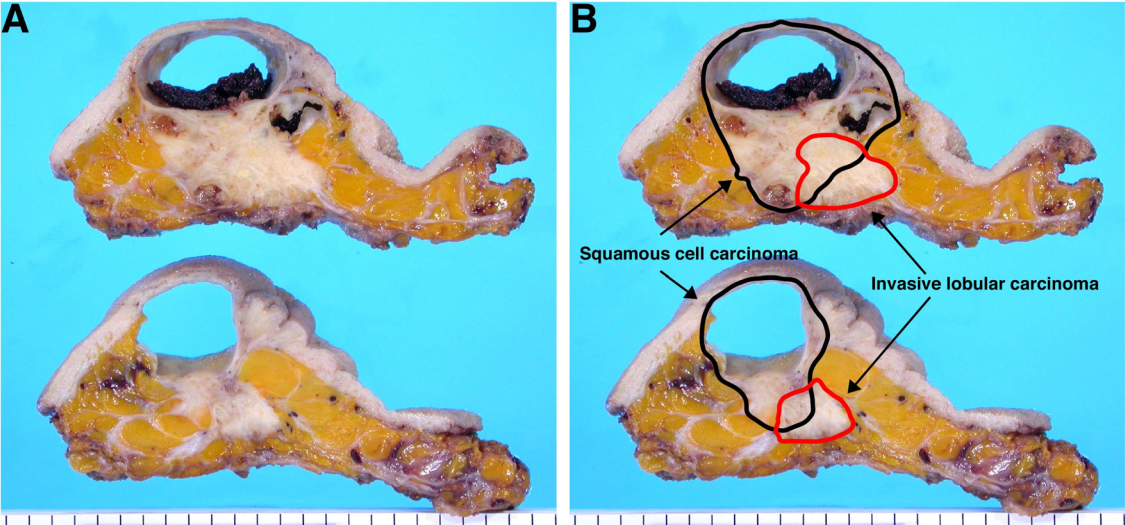


Figure 2.

SCC and contiguous ILC. (A) Two distinct morphologic patterns are seen, SCC on the left and ILC on the right. (B) SCC. Sheets of malignant squamous cells contain enlarged nuclei with prominent nucleoli and some intercellular bridges. (C) ILC. Each neoplastic cell has a round-to-ovoid nucleus and thin rim of cytoplasm. Loosely cohesive tumor cells diffusely infiltrate the mammary stroma. Immunostaining is positive for E-cadherin (D) and p53 (E) in SCC. E-cadherin is expressed in the cell membranes, and p53 is expressed in the cell nuclei.

