

Squamous Cell Carcinoma of the Breast: A Case Report

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ABSTRACT

Primary squamous cell carcinoma of the breast is a very rare tumor accounting for less than 0.1% of all invasive breast carcinomas. It is a particularly interesting entity because it is a very aggressive tumor with negative hormone receptors and is refractory to usual treatment; it has a poor prognosis. We report here a case of primary breast cancer in a 48-year-old woman who presented with a purplish nodule in the left breast fold. Clinical trials including a large series of these rare tumors are needed to deepen our knowledge and improve the currently disappointing results. We report the case of a young 48-year-old patient treated for squamous cell carcinoma of the breast with squamous metaplasia. Through this case, we will review the literature to better define the management of these rare tumors.

Keywords: Breast, squamous cell carcinoma, Aggressive Subtype, Chemoresistance.

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INTRODUCTION

Primary squamous cell carcinoma of the breast, or squamous cell carcinoma, is a rare tumor representing 0.1–2% of breast cancers^[1,2,3,4]. It is of metaplastic origin; however, its histogenesis remains poorly defined^[1,2,5,6]. Few cases have been reported in the literature, and the indication and type of adjuvant treatment remain controversial^[6]. Unlike non-specific ductal carcinomas, it is not hormone-dependent and has low lymphotropism^[1]. However, it progresses rapidly, and its treatment is not well-established^[5,6].

CASE REPORT

We report the case of a 48-year-old woman, a mother of three, who presented in February 2018 with a purplish nodular mass in the left inframammary fold (Figure 1).

Histological examination of the percutaneous biopsy revealed a grade 3 invasive ductal carcinoma with squamous metaplasia, without intraductal or intralobular components. Immunohistochemistry identified a triple-negative subtype.

The disease was classified as cT4cN1M0. During a multidisciplinary team meeting, the medical case was reviewed, and surgeons deemed the disease inoperable. Neoadjuvant chemotherapy with 5-fluorouracil (5-FU) and cisplatin was initiated. However, tumor stability was observed after three cycles, followed by 40% clinical progression after another three cycles. A second-line chemotherapy regimen of docetaxel and epirubicin also resulted in clinical progression after three cycles. Two further lines of treatment with carboplatine plus gemcitabine, followed by vinorelbine also led to local progression and pulmonary metastases (Figure 1).

During treatment, a second biopsy was performed. Histological analysis confirmed epithelial proliferation arranged in trabeculae, cords, and lobules centered by hyaline keratin pearls. The tumor consisted of globular cells with hyperplastic, irregular, hyperchromatic nuclei, prominent nucleoli, and poorly defined eosinophilic cytoplasm with high mitotic activity. Immunohistochemistry confirmed a triple-negative tumor.

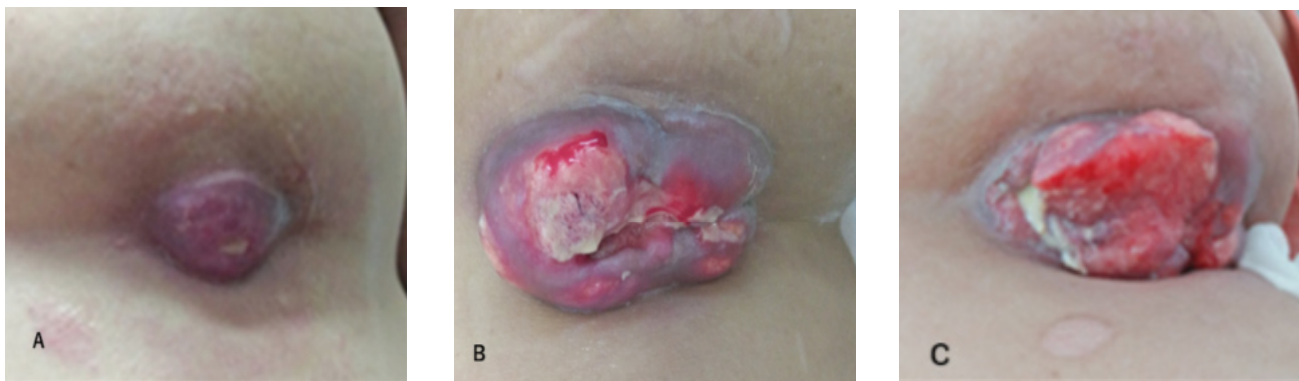


Figure 1. Tumor appearance evolution: A baseline, B post-Docetaxel-Epirubicin, C post-Vinorelbine. Credit Photo Dr. Amel ZEMMOUR

DISCUSSION

According to the WHO, this carcinoma belongs to metaplastic carcinoma category and includes areas of squamous-type metaplastic remodeling. Metaplastic carcinomas exhibit a diverse range of morphological features, for which numerous classification systems have been proposed. In 1989, Wargotz et al. described five types of metaplastic carcinomas: spindle cell carcinoma, carcinosarcoma, carcinoma with matrix production (bone or cartilage), metaplastic carcinoma with osteoclast-like giant cells, and ductal squamous cell carcinoma^[7-11] (Figure2). This metaplasia can be partial or total; in the latter case, it is referred to as pure squamous cell carcinoma of ductal origin^[5]. This definition is based on the potential metaplasia of a cell (with debated origin

epithelial, myoepithelial, or reserve totipotent) into another epithelial or mesenchymal cell type. Some authors require the absence of ductal or mesenchymal components and the absence of distant squamous cell carcinoma to classify a tumor as primary squamous cell carcinoma.

The age of onset is similar to that of non-specific carcinomas, and no predisposing factors have been identified. However, local trauma has been observed. The histogenesis remains unclear^[6,12], with two hypotheses:

1. An undetected squamous cell carcinoma of adenocarcinomatous origin.
2. Degeneration of predominant squamous metaplasia (over 90%)^[6], observed in adenofibromas, papillomas, or even myoepithelial cells^[12-14].

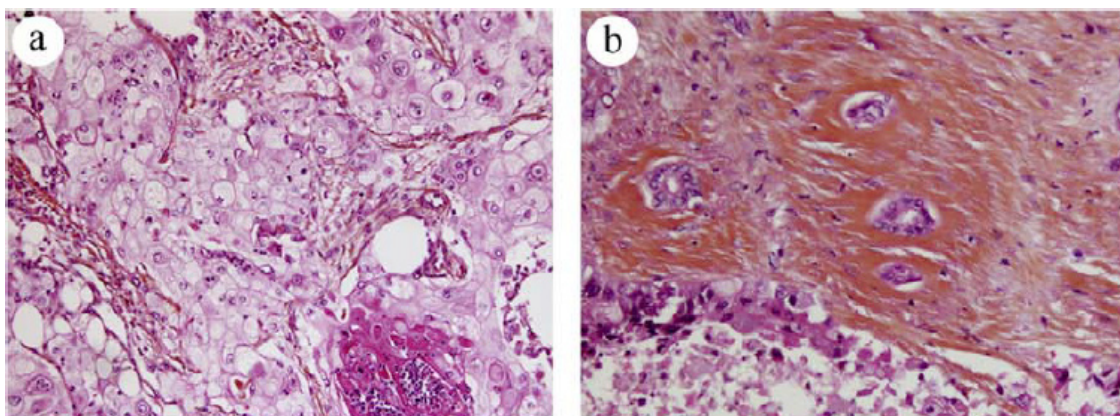


Figure 2 . (a) squamous cells metaplasia (HES, $\times 100$); (b) focal glanduliform carcinomatous structures (HES, $\times 200$).

Some authors also suggest a tumor origin from a mammary dermoid cyst, chronic breast abscess, abscess-like tumors^[15], complete squamous metaplasia of mammary glandular tissue, or from a phyllodes tumor.

Clinically, there are no specific presentations. Squamous cell carcinoma is rarely bilateral^[16]. The locoregional recurrence rate ranges from 9% to 18%^[17]. However, large tumors may undergo central cystic degeneration, ulcerating and invading the overlying skin, and exhibit rapid growth^[12].

Radiologically, mammographic findings are non-specific^[12]. Typically, they appear as rounded masses

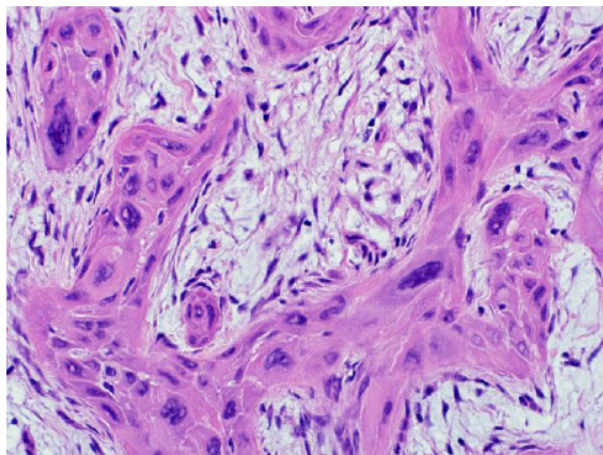
without spiculations, partially irregular, with a cystic center, explaining their pseudo-cystic or abscess-like appearance^[9]. Ultrasound may reveal cystic lesions and necrosis.

Preoperative diagnosis is made via biopsy, with histopathological examination crucial for detecting any possible adenomatous component. The diagnosis is established when more than 90% of cells are squamous^[14].

Histologically, the tumor shares the same architecture and cytological features as squamous cell carcinoma at

other sites. Pathological examination shows squamous proliferation with large cells containing prominent nuclei, eosinophilic cytoplasm, and desmosomes [4].

These tumors can be purely epithelial, with a mix of adenocarcinomatous and squamous cell carcinoma



components, or they can be mixed, combining epithelial and connective tissue elements (Figure 3). The connective tissue component may include cartilaginous or bony metaplasia, and in some cases, a true sarcomatous component [4-5].

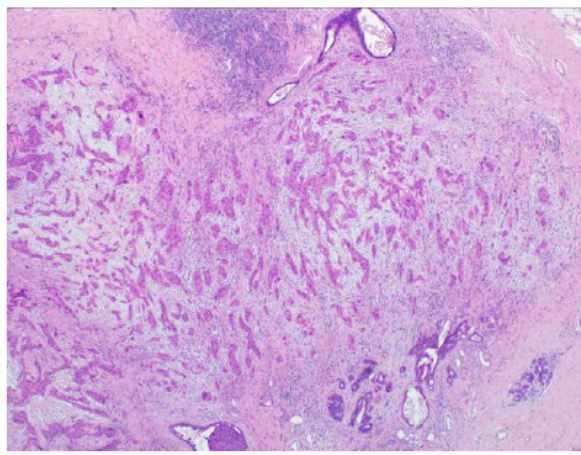


Figure 3. Histopathological aspect of a squamous cell carcinoma of the breast: left-high magnification, right-low magnification [24]

Squamous cell carcinoma produces keratin and is associated with keratohyalin granules [5], as in this case. Hormonal receptor negativity is typical [1,5,13], and Her2 is also usually negative [14]. Immunohistochemistry shows expression of high molecular weight cytokeratins CK14, CK5/6, CK17, and EGFR in tumor epithelial cells, while MUC1 and β -catenin are often absent [6,19,20].

Treatment is primarily surgical [12,23], involving total or partial mastectomy with lymph node dissection, followed by radiotherapy. Unfortunately, surgery was not feasible in this case due to the tumor's fixed nature, and radiotherapy was not indicated.

Chemotherapy is similar to that for other carcinomas, with 5-fluorouracil and cisplatin being effective options [6,12]. However, neoadjuvant chemotherapy aimed at conservation is not recommended due to this carcinoma's chemoresistance. EGFR (Her1) overexpression may indicate responsiveness to EGFR-targeting treatments, and PARP inhibitors have shown promising results.

Our patient had triple-negative breast cancer (TNBC), characterized by the absence of hormone receptors and HER2 overexpression. TNBC is an aggressive subtype constituting 10-15% of breast cancers and is primarily treated with chemotherapy [24-25]. Neoadjuvant chemotherapy is standard for early-stage TNBC, with dose-dense regimens and carboplatine associated with improved response. Immunotherapy, such as pembrolizumab, has shown promise [26-28]. However, our patient was unable to tolerate carboplatine and immunotherapy was not accessible.

Prognostic factors include tumor size and axillary lymph node involvement [12,29]. In this case, Henessy reported

50% lymph node involvement in a series of 33 patients [21]. Other factors include spindle cell components [12] and acantholysis [18].

The prognosis for squamous cell carcinoma is poor [3,12] with 5-year survival between 38% and 86% [12,18,29].

CONCLUSION

Overall, squamous cell carcinoma of the breast is a rare tumor with a poor prognosis, peaking in mortality at two years. Its clinical presentation is distinctive, but its management resembles that of non-specific carcinoma due to the limited number of published cases, making therapeutic protocols and standardization difficult to evaluate.

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