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Case Report

Pure Squamous Cell Carcinoma of the Breast: Report Histological Features and Treatment Outcome of Two Cases

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Abbreviations SCC - Squamous Cell Carcinoma

Abstract

SCC is an uncommon and aggressive breast neoplasm. There are limited data in literature about its epidemiology and studies focusing on outcomes, so they are still unclear. It has significantly worse prognosis than other non squamous cell tumors of the breast. Strict histologic criteria should be used to determine diagnosis. Because of its rarity, it is still unclear which the most appropriate therapeutic regimen to use is. The role of different new chemotherapy regimens needs to be explored and biologic studies are needed to determine the tumour chemoresistance mechanisms and the potential use of other treatment targets that improve patients survival. Clinicians should be aware of the aggressive nature of the tumour when counseling patients.

Introduction

Squamous Cell Carcinoma (SCC) of the breast is an extremely rare disease. The reported incidences vary from 0.04% to 0.1% of all breast malignancies [1]. Pure primary SCC is defined when more than 90% of malignant cells are squamous type and no other neoplastic elements are detected in the tumour mass. It is important to discriminate this entity from malignancies of the breast skin or metastases from a squamous cell carcinoma elsewhere in the body. SCC of the breast is usually more common in elderly women and most of them present as a painless breast lump [2-4]. There are no typical mammogram findings for SCC. On ultrasound, they might appear as a suspicious complicated cyst or an inflammatory process [5,6].

The etiology and pathogenesis of squamous cell carcinoma of the breast is still unclear. It has been suggested that it may be a very extreme form of squamous cell metaplasia, developing from an adenocarcinoma. This hypothesis support the detection of the mixed forms [7,8]. Furthermore, some authors affirm that some cases of primary SCC develop after a previous benign disorder abscess, after a complicated cyst, after implantation of breast prosthesis or after radiation treatment [8-11].

The prognosis of primary pure SCC is still a subject of controversy, although some reports suggest that SCC is an aggressive tumour with an outcome comparable to poorly differentiated ductal carcinoma of the breast [5,12]. They are typically treated with a combination of surgery, radiation therapy and chemotherapy, even if sometimes they appear resistant to commonly used chemotherapy regimens [12,13].

Here we report two cases of pure primary SCC of the breast.

Case Report

Case 1

A 51-year-old Caucasian woman presented at our surgical department for a left breast lump. Her past medical history was not significant, and her family history for breast cancer was negative. She denied oral contraceptives use in the past. Physical examination revealed a palpable circumscribed elastic lump measuring about 40 mm in the left breast at the union of inferior quadrants, without fixation to the skin or pectorals muscle. There was no palpable axillary or supraclavicular lymph node. The right breast examination was normal.

Mammogram showed a round, high density mass with partially regular margin measuring approximately 40 mm. Ultrasound showed a round, high density cyst measuring 40 mm. Fine needle aspiration cytology revealed the presence of large sheets of malignant, poorly differentiated (G3) cells.

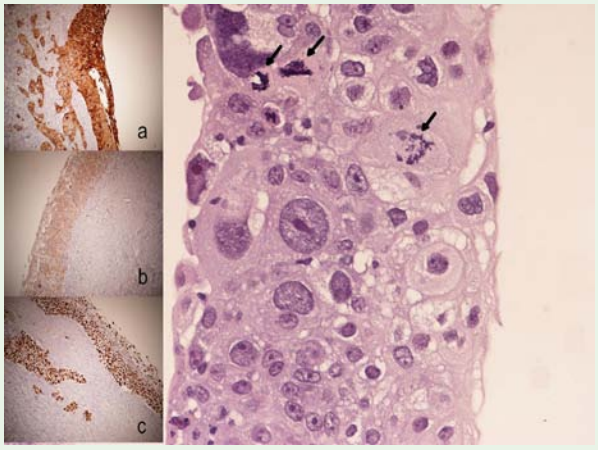

Figure 1: Case 1: the high magnification view of tumour cells shows large, poorly differentiated cells, without any hint of duct formation, with three atypical mitoses. The cancer cells showed a diffuse positivity for 34βE12 (inset a), only focal areas of 2+ HER2 score (inset b) and strong nuclear almost universal positivity for P53 (inset c) neoplasia shows a pure squamous differentiation with large cells. HE original magnification 40X; immunohistochemical stains, inset a, b, c, original magnification 20X.

The patient underwent a left quadrant ectomy. Macroscopically, the surgical resection, measuring 8x9x3 cm, showed a 3.8 cm cyst containing serous hemorrhagic fluid. The inner surface of the cyst was composed by neoplastic poorly differentiated cells showing stratification, with evident nucleoli and large glassy eosinophilic cytoplasms, with many atypical mithosis (Figure 1), infiltrating the surrounding adipose and connective for about 2.7 mm. The tumour cells showed an immunophenotype (CK5/6+ and CK34βE12+) consistent with squamous differentiation (Figure 1, inset a). There was no component of invasive ductal breast carcinoma or other features of metaplastic carcinoma. Therefore, pure primary squamous cell carcinoma of the breast was diagnosed. The squamous cells were negative for hormonal receptors, whereas HER2 was focally scored as 2+ (Figure 1, inset b). The Ki67 labeling index was really high (60 to 70%) and p53 positivity was almost 100% (Figure 1, inset c). Sentinel node examination was negative for metastatic cells. The tumour was classified as pT1N0(sn), according to TNM classification (6th edition). The patient received an adjuvant therapy based on CMF (cyclophos- phamide, methotrexate, fluorouracil) 6 cycles, and usual adjuvant radiotherapy was performed a total dose of 50 Gy. Patient had a regular clinical and imaging follow-up. There is no evidence of recurrence at 4 years from surgery.

Case 2

A 81-years-old Caucasian woman presented at our department for a local swelling in her left breast located behind the nipple. There was neither nipple retraction, nor nipple discharge. The woman had given birth to 3 children. Her family history was negative for breast cancer. Personal history mentioned appendectomy, tonsillectomy, cholecystectomy and hypertension. Physical examination revealed an elastic swelling measuring about 3 cm, located in the upper inner quadrant of left breast near to the nipple, without fixation to the skin or to pectoralis muscle fascia. No abnormalities were observed both in the right breast, and in axillary or supraclavicular lymph nodes. A mammogram showed a mass of about 35mm with regular margins positioned behind the nipple. Ultrasound examination revealed a defined 30mm mass with a thick rind and reduced central echogenicity, consistent with a cystic space. A fine needle aspiration was obtained. The pathologist described atypical epithelial cells with polymorphism and atypia suspicious for cancer (C4). Tumors markers were within normal range. She underwent a wide local excision of the upper internal quadrant of the left breast. Gross examination revealed a 3.5cm tumour with central cystic space. Microscopically, the central cystic space contained keratin and necrotic debris. The neoplasm was composed by large poorly differentiated squamous cells with eosinophilic glassy cytoplasms. No component of obvious invasive ductal carcinoma or other features of metaplastic carcinoma were detected. There was no vascular or neural invasion. The keratin expression (CK5/6+ and CK34βE12+) was in keeping with a squamous differentiation (Figure 2). Immunohistochemical evaluation for estrogens and progesterone receptor was negative, HER2 was scored as 3+, P53 expression was almost universal (100%) and Ki 67 labeling index was 17.7%. Afterwards patient refused radiation and chemotherapy. Seven months after surgery she presented to follow up with an ulcerated lesion occurred at surgical incision scar. She was treated with ambulatory medications and she underwent a biopsy with diagnosis of recurrent tumour. For this reason, the patient underwent to radical left mastectomy. Histopathological analysis revealed an undifferentiated metaplastic carcinoma pT4pN2 (5/14) with extensive areas of necrosis. Additionally immunohistochemical analysis demonstrated high expression of cytocheratin 34bE12 and cytocheratin5/6 within the tissues, suggestive for squamous carcinoma. The breast tumor profile was negative for progesterone and estrogen receptors and HER2/neu over expression. Nevertheless patient refused any further medical treatment. At six months follow up she underwent bone scintigraphy and following pelvic and sternal computer tomography scan with finding of metastasis to the right sacroiliac joint and inferior portion of the sternum. She was treated with pain management therapy. She died three months later.

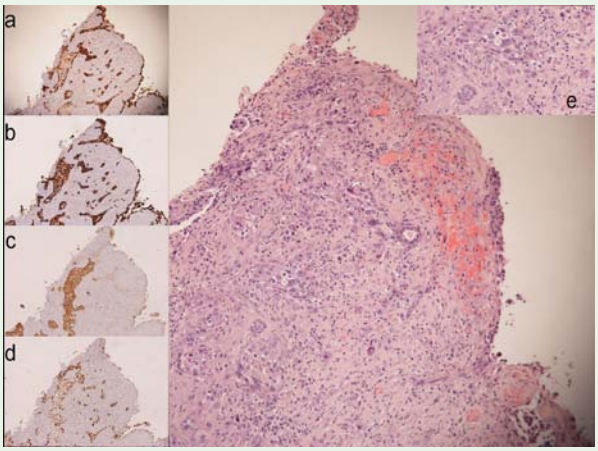

Figure 2: Case2: the neoplasia shows a pure squamous differentiation with large cells with glassy eosinophilic cytoplasm (inset e), without any component, either *in situ* or invasive, of ductal differentiation. Immunohistochemical phenotyping showed diffuse CK5/6 positivity (inset a), 34βE12 (inset b), complete strong membrane positivity for HER2 (score3+) (inset c) and almost universal nuclear positivity for P53 (inset d). HE original magnification 10X, immunohistochemical stains, inset a, b, c, d, original magnification 10X, inset e enlarged from original HE.

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Conclusion

Pure primary squamous cell carcinoma of the breast generally presents large at diagnosis and cystic in 50% of the cases. No mammographic or ultrasonographic features were detected suggestive of SCC, while MRI generally detects a circumscribed mass with a necrotic core [14]. Although SCC is a rare disease, many studies suggest it is usually a high-grade cancer with a negative hormone receptor status [13]. For this reason, hormone based therapy may not be an effective treatment for some patients. Even HER2 is not usually over expressed in SCC [5,13]. Some investigators believe that SCC is a metaplastic variant of the basal type or triple negative invasive ductal carcinomas [13]. For this reason, most of the patients were treated similar to infiltrating ductal carcinoma. Similar to chemotherapy, the role of radiation has been also reported as unclear in many series. Indeed, locoregional relapse occurred frequently also in irradiated field although SCC are generally radiosensitive [5,9]. Nowadays, the most appropriate therapeutic regimen for SCC of the breast is still unclear and the prognosis is poor [5].

In both our cases, a high nuclear positivity for P53 was detected whereas hormone receptors were negative. HER2 over expression was shown just in the second case. Patient 1 received adjuvant chemotherapy and radiotherapy, considering the conservative surgery performed. In the second case, adjuvant treatments were not administered according to patient's will. This lead to an early tumour recurrence.

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