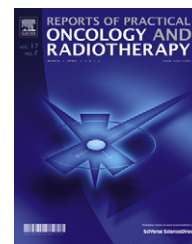


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## Case report

# Primary squamous cell carcinoma of the breast: A rare case report

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## ARTICLE INFO

## Article history:

Received 4 April 2012

Received in revised form 4 June 2012

Accepted 13 July 2012

## Keywords:

Squamous cell carcinoma

Breast cancer

Outcome

## ABSTRACT

**Background:** Squamous cells are normally not found inside the breast. Therefore, a primary squamous cell carcinoma of the breast is an exceptional phenomenon and the management of this type of disease is still debated.

**Aim:** Clinical outcome assessment of a patient with squamous cell carcinoma of the breast.  
**Materials and methods:** We report a case of primary squamous cell carcinoma of the breast (T1cN0M0) in a 51-years-old woman who underwent breast conserving surgery plus adjuvant chemotherapy and radiation therapy (RT).

**Results:** With a follow up of 43 months, the patient is alive with no evidence of local or distant recurrence. The patient had Grade 2 acute skin toxicity. No late skin or respiratory toxicity was observed.

**Conclusions:** Pure primary squamous cell carcinoma of the breast is a rare and aggressive disease, often treatment-refractory. Our case shows that the addition of RT after breast conserving surgery, allows to achieve a high local control without adding severe toxicity. A multidisciplinary approach seems to be the optimal management for early stages in this rare disease.

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## 1. Background

Squamous cell carcinoma (SqCC) is a well-known malignancy of the skin and other organs composed of squamous

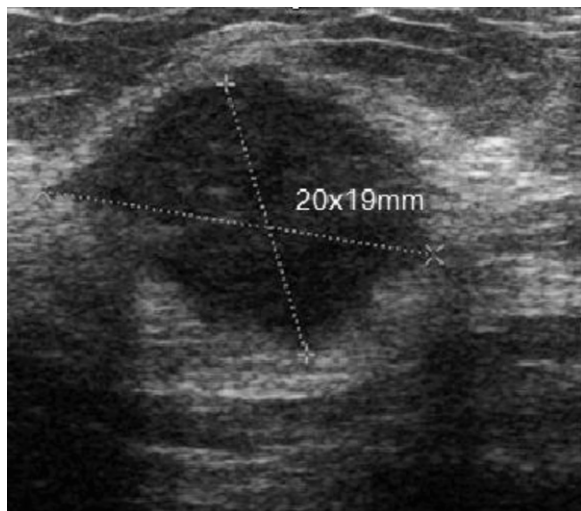
cells. SqCC of the breast is a very rare disease. The incidence of primary SqCC of the breast is 0.04–0.1% of all breast carcinomas.<sup>1–3</sup> It is important to discriminate this entity from malignancies of the skin of the breast or metastasis of a SqCC somewhere else in the body. In the literature, only a few

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<http://dx.doi.org/10.1016/j.rpor.2012.07.004>



**Fig. 1 – Breast ultrasound showing an irregular shaped lesion containing liquid material.**

small series are reported.<sup>1-3</sup> Clinical and radiographic characteristics are not specific, and tumors are usually hormone receptor negative. In general, this tumor is very aggressive and treatment-refractory with a poor prognosis. We report a case of this rare breast malignancy treated with breast conserving surgery, adjuvant chemotherapy and radiation therapy (RT).

## 2. Aim

To assess the clinical outcome of a patient with squamous cell carcinoma of the breast who underwent postoperative RT.

## 3. Methods and results

A 51-years-old, non-smoker woman with prior history of mastitis when she was 20 presented with a lump in the left breast. A mammogram demonstrated an irregular abnormality in the left breast, which was classified as BI-RADS 4. Then, the breast ultrasound revealed a hypoechoic lump measuring 25 mm × 18 mm with a thick ring (Fig. 1). Fine needle aspiration was performed with no evidence of malignancy in the cytology. However, due to the high radiologic suspicion of malignity, the patient underwent tumorectomy and the pathology revealed a 20 mm × 19 mm well-differentiated SqCC, originated from a focus of squamous metaplasia, close to a papillary lesion and a fibrocystic mastopathy area (Fig. 2). Optimal surgical margins were obtained. Although a sentinel lymph node biopsy<sup>4</sup> is a standard for assessment of the status of the axillary lymph nodes in patients with clinical stage I-II breast cancer, the surgeon underwent a lymphadenectomy due to the diagnosis uncertainty prior to the surgical procedure. Seventeen axillary lymph nodes were dissected with no evidence of disease. Hence, the tumor was classified as stage IA (pT1pN0M0) according to the clinical TNM staging system (American Joint Committee on Cancer Staging Manual, 7th edition, 2002). Immunohistochemical evaluation was negative for estrogen and progesteron receptors as well as for

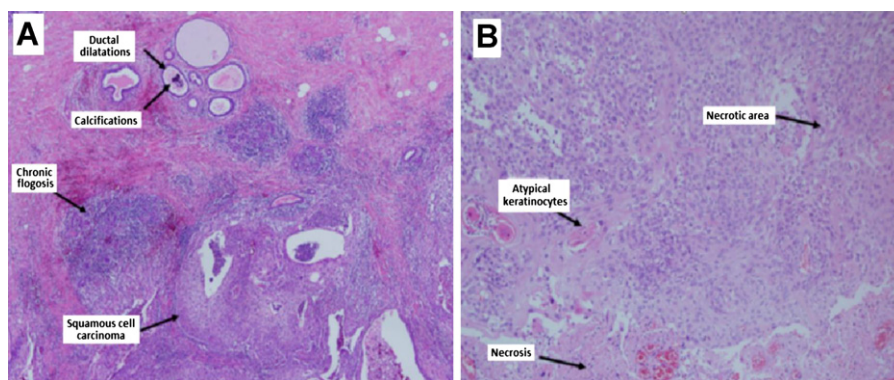
Her2/neu and Bcl2. It was positive for the epidermal growth factor receptor (++) , P54 (+++), and Mib1 (+++). In addition, the Ki-67 proliferation index was found to be high. A magnetic resonance imaging of the left breast was performed after surgery without any pathological enhancement. The diagnostic work up to rule out other primary sites of SqCC included: whole body scanning using computed tomography (CT), gynaecological evaluation, and nose and throat examination.

The patient received adjuvant chemotherapy with four cycles of 5-fluorouracil, doxorubicin, and cyclophosphamide plus another four cycles of Taxol. Then, the patient underwent adjuvant RT with a three-dimensional conformal treatment planning system. A CT simulation scan covering the entire thoracic region from the apex of the lung to the diaphragm was performed. Target and non-target volumes were outlined according to the criteria of the International Commission of Radiation Units and Measurements 62.<sup>5,6</sup> The clinical target volume (CTV) was defined as the entire palpable breast tissue starting 5 mm below the skin. The planning target volume (PTV) was obtained by adding a 10 mm margin to the CTV, except in the skin. Radiation fields were appropriately customized by a multileaf collimator when needed in order to spare the surrounding healthy tissues. The angle of the beams was adjusted to minimize the irradiation of the lung parenchyma and left ventricle. Appropriate physical wedge compensation was used to ensure a uniform dose distribution throughout the target volume. The total dose prescribed to PTV was 50 Gy, delivered with 2 Gy daily for 5 days a week. A boost dose of 10 Gy in 5 fractions was given using 6 MV photon beams, depending on the depth of the original tumor site. The tumor bed was boosted mainly for two reasons: (1) the unfavorable histology (squamous cell carcinoma) and (2) the young age of the patient (51 y/o). The treatment technique consisted primarily of four tangential fields using 6 MV photon beams and then, for the boost, two fields at 0° and 90°. The dose volume histogram (DVH) for the lung and heart was calculated. No more than 9% of the lung received more than 20 Gy, and no more than 1% of the heart received more than 10 Gy. During the course of radiotherapy, the patient was seen weekly for clinical evaluation and disease management. The patient experienced acute Grade 2 skin toxicity, according the Radiation Therapy Oncology Group (RTOG) scoring system. No late skin or respiratory toxicity was observed.

The patient was evaluated at approximately 3 months after completion of therapy and then 3-6 months afterwards. Follow-up evaluations consisted of an interval history and physical examination. Follow-up imaging typically involved a mammography. Additionally, tumor markers including carcinoembryonic antigen, carbohydrate 15-3 and SqCC antigen were assessed during the follow-up, always staying in the normal range. With a follow-up of 43 months, the patient is alive with no evidence of local or distant recurrence.

## 4. Discussion

Pure primary squamous cell carcinoma of the breast is a rare condition and is considered to arise through metaplastic change of ductal carcinoma cells.<sup>7</sup> The concept of a disease continuum with varying degrees of squamous metaplasia



**Fig. 2 – Histology appearance of squamous cell carcinoma well-differentiated on hematoxylin and eosin stain showing (A) atypical keratinocytes and necrotic areas and (B) ductal dilatations, calcifications, and chronic flogosis.**

was supported by Stevenson et al. who concluded that SqCC mostly represents an extreme form of squamous metaplasia within adenocarcinoma.<sup>7</sup> An alternative theory is that it arises directly from the epithelium of the mammary ducts. The SqCC of the breast is generally large (>4 cm) at diagnosis and cystic in 50% of cases.<sup>1</sup> The prognosis of this type of breast cancer is still regarded as somewhat controversial, although many studies suggest that it is an aggressive disease that may behave like a poorly differentiated breast carcinoma.<sup>8–10</sup>

The breast SqCC is usually a high grade and hormone receptor-negative tumor.<sup>11</sup> This means that hormone based therapy may not be effective in these tumors. Her2/neu is also usually not over-expressed or amplified in this disease.<sup>12</sup> The immunohistology of our case is consistent with those findings. The high frequency of EGFR positivity is interesting and may be exploited in the development of future treatments.

In contrast with other studies,<sup>13</sup> which showed that no findings on mammography are specific for this diagnosis, which may explain the advanced disease stage at the diagnosis, our case had a mammogram demonstrating an irregular abnormality in the left breast. This finding allowed to detect an early stage. Breast ultrasound has been reported to be more helpful with these tumors appearing as solid hypoechoic masses with complex cystic components.<sup>14</sup>

Because of its rarity, the most appropriate therapeutic regimen for SqCC of the breast is still unclear. A recent literature review reveals that an average of 70% of patients with SqCC of the breast do not present axillary lymph nodes involvement but due the unpredictable lymph nodes dissemination, axillary lymph nodes dissection could always be performed for staging purpose.<sup>7</sup> As a result of the lack of data, the issue of whether to prescribe adjuvant treatment for SqCC of the breast, remains unsolved.<sup>2</sup> Some contribution can be derived from the review by M.D. Anderson group<sup>15</sup> of clinical pathologic features, management and outcome of SqCC of the breast in a series of 33 patients. Nineteen of the 31 patients with localized disease received adjuvant chemotherapy and 5 patients received neoadjuvant chemotherapy. The tumor did not respond to neoadjuvant chemotherapy in any patients. No significant difference was seen in relapse free survival or overall survival rates between the patients treated with adjuvant or neoadjuvant chemotherapy and those not treated.<sup>16</sup> These

findings are consistent with Rostock et al. who suggested that SqCC is not sensitive to chemotherapeutic agents commonly used for ductal carcinoma such as methotrexate, cyclophosphamide, 5-fluorouracil (5-FU) and anthracycline.<sup>12</sup> In our case report the patient received adjuvant chemotherapy with 5-FU and cisplatin based on other experiences derived from some reports.<sup>2,8,17,18</sup> The role of radiation therapy has been reported as unclear in many studies. Although SqCC are generally radiosensitive, loco regional relapse occurred frequently also in irradiated fields. It seems that SqCC of the breast is often relatively radioresistant.<sup>2,7,17,18</sup> However, considering the conservative surgery performed, our case underwent RT with no evidence of disease after 43 months of follow up.

## 5. Conclusions

Pure primary squamous cell carcinoma of the breast is a rare and aggressive disease often reported as treatment-refractory. Rates of local failure after surgery for such patients have been reported to be as high as 30%.<sup>15</sup> Our case shows that the addition of RT after breast conservation surgery, allows to achieve a high local control without adding severe toxicity. The dose of radiation therapy used was similar to that typically employed in the treatment of more common infiltrating carcinomas. The good control achieved argues against the idea that these tumors are inherently radio resistant. Therefore, a multidisciplinary approach seems to be the optimal management for early stages of this rare disease. Future studies using novel radiation approaches,<sup>19,20</sup> such as partial breast irradiation, are needed for this particular type of disease.

## Conflict of interest

The content has not been published or submitted for publication elsewhere and all persons listed as authors have given their approval for the submission of the paper. Authors declare that we do not have any financial support or relationships that may constitute a conflict of interest.

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## Financial disclosure

None declared.

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