

Case Report

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Primary squamous cell carcinoma of the breast: a rare entity, representation of two cases

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ABSTRACT

The aim of this study was to diagnose primary squamous cell carcinoma of the breast with clinical, radiological, pathological correlation. We report two cases of primary squamous cell carcinoma of the breast. Both the patients presented with a palpable lump, with no family history of breast carcinoma. Post-operative histopathological diagnosis was squamous cell carcinoma with immunohistochemistry positive for p63 and negative for hormone receptors. Primary squamous cell carcinoma (SqCC) of the breast is a very rare tumor accounting for less than 0.1% of all invasive breast carcinomas. It is known to be a very aggressive which is a hormone receptor negative and is treatment refractory tumor with poor prognosis. In both our cases, a final diagnosis of SqCC was made after an extensive work up for primary or metastatic disease.

Keywords: Hormone receptor negative, Primary breast cancer, P63 positive, Squamous cell carcinoma (SqCC)

INTRODUCTION

Primary squamous cell carcinoma (SqCC) of the breast is a very rare tumor accounting for less than 0.1% of all invasive breast carcinomas.¹ It is known to be a very aggressive which is a hormone receptor negative and is treatment refractory tumor with poor prognosis.³ We report two cases of this rare malignancy, after radiological, histopathological and immunochemistry evaluation and review the literature for current strategies for management.⁴

CASE REPORT

Case 1

A 47-year-old lady presented with a lump in the right breast for two weeks duration. The lump was gradually

progressive in size, not associated with pain or nipple discharge. There was no retraction or dimpling of the skin. Family history was negative for breast malignancy. Father had history of leukemia. Physical examination revealed a 3x3 cm lump at 12'o clock position in the upper outer quadrant with nodular surface. It was firm in consistency and moved with the breast tissue. There was no intrinsic mobility of the lump. Axillary lymph nodes were not enlarged.

X- ray Mammogram of the right breast demonstrated an oval, hyperdense lesion with partially obscured borders just superolateral to the nipple (Figure 1a and b). Speck of calcification was seen on the border of the lesion. The skin and the nipple-areola complex were not involved.

Ultrasound of the breast showed an irregular, not circumscribed, microlobulated hypoechoic lesion approximately measuring 3.6 x 1.9 cm in the subareolar

region (Figure 1c). The lesion showed posterior enhancement. Significant internal vascularity was noted (Figure 1e). On strain elastography, the strain ratio was 1.22 (Figure 1d). Right axilla showed lymph nodes with uniform cortical thickening, measuring upto 49 mm however the hilum was preserved.

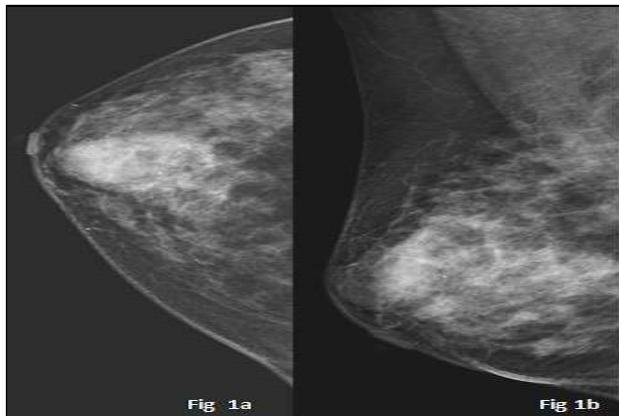


Figure 1a and 1b: X-ray mammogram showing oval hyperdense lesion with partially obscured borders superolateral to nipple in CC (Figure a) and RMLO (Figure b) views.

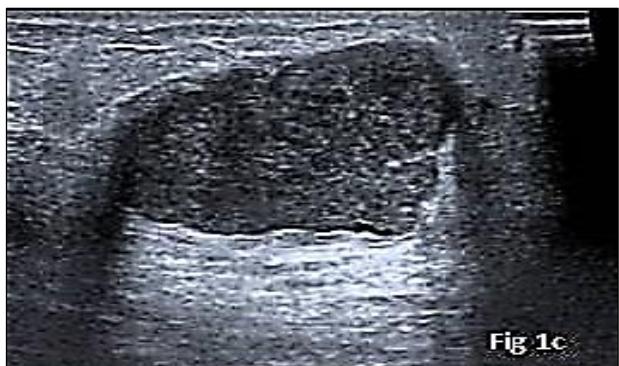


Figure 1c: Ultrasound showing irregular not circumscribed micro lobulated hypoechoic lesion with significant posterior enhancement.

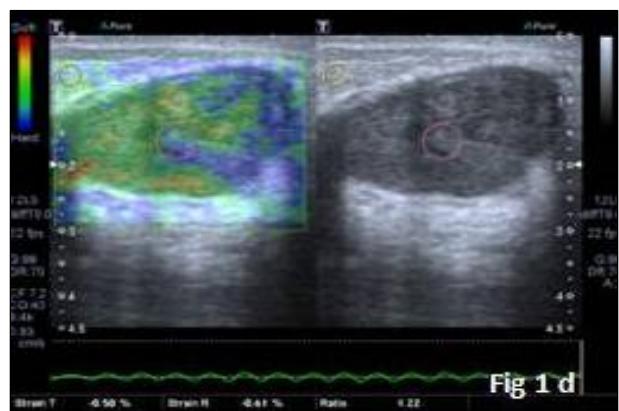


Figure 1d: On strain elastography lesion was indeterminate with the strain ratio of 1.22.

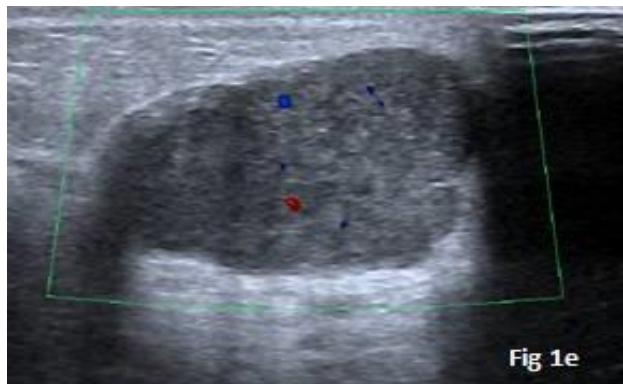


Figure 1e: Ultrasound showing intrinsic vascularity.

FNA of the lesion was positive for malignant cells. Trucut biopsy revealed invasive carcinoma of the breast. Right modified radical mastectomy was done. Grossly, the tumor was 3.0 x 2.5 x 2.0 cm in size. The cut section was gray white in appearance, firm in consistency with solid areas. The overlying skin and the areola was normal. Microscopically, the tumor was composed of sheets and clusters of round to polyhedral cells with pleomorphic hyperchromatic nuclei and a moderate amount of eosinophilic cytoplasm (Figure 1f). Individual cell keratinization and keratin pearls were also seen. Figure 1f shows sheets and clusters of round to polyhedral cells with pleomorphic hyperchromatic nuclei and moderate amount of eosinophilic cytoplasm.

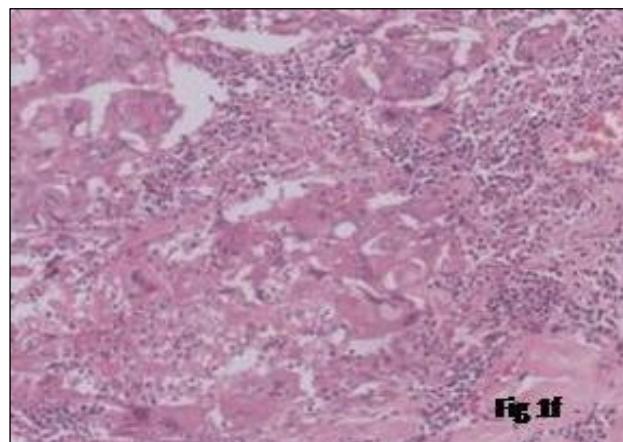


Figure 1f: H and E (X 200) squamous cell carcinoma breast.

A diagnosis of pT2N0cM0 Squamous cell carcinoma, Grade 3 was rendered, margins were free of tumour.

Immunohistochemistry showed the tumor cells were positive for p63, which confirmed the diagnosis of SqCC. They were negative for estrogen (Figure 1g) and progesterone (Figure 1h) receptors, HER2neu. All 15 axillary lymph nodes were free of tumor.

Pathological diagnosis was given as Squamous cell carcinoma. Margins free of tumour.

An extensive work-up ruled out other primary site or metastatic disease.

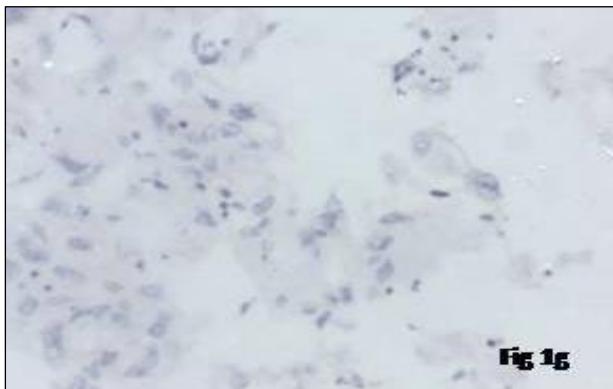


Figure 1g: Tumor negative for estrogen receptor by IHC

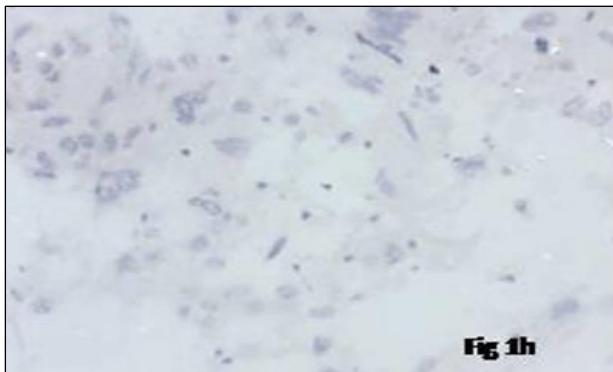


Figure 1h: Tumor negative progesterone receptor by IHC

Case 2

A 54-year-old lady presented with a lump in the right breast for past three months. The lump was static in size, not associated with pain, nipple discharge. There was retraction and dimpling of the skin. Patient had a history of fibroadenoma excision in her left breast 35 years back. History of hysterectomy eight years back was present. There was no family history of breast malignancy. Physical examination of the right breast revealed a 6.0 x 5.0 cm lump in the upper quadrant of the right breast, which was firm in consistency. It was fixed to the pectoralis major. Skin showed Peau'd orange appearance. Right central group of lymph nodes were enlarged and mobile.

X-ray mammogram was done which showed, an irregular high density, not circumscribed, microlobulated mass in the retroareolar region of the right breast (Figure 2a and 2b). Few equal density well circumscribed lesions were seen around this lesion. Pop corn calcification was seen in the lower inner quadrant.

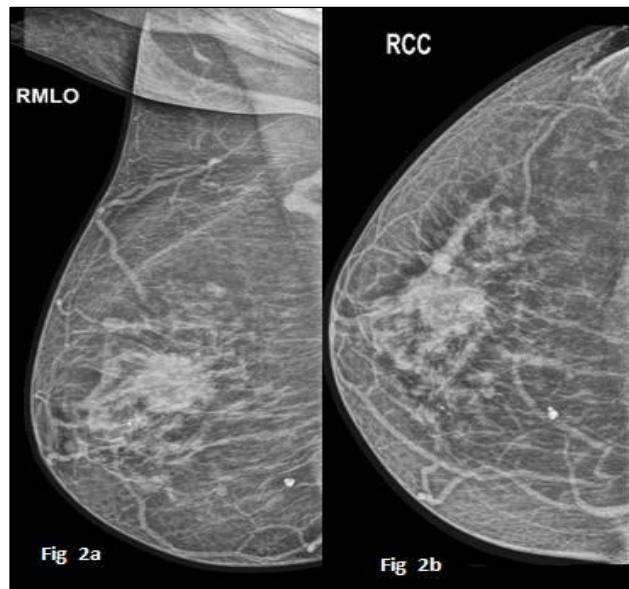


Figure 2a and 2b: X-ray mammogram showing irregular ill-defined not circumscribed microlobulated and speculated hyper dense mass in retroareolar region in CC (Figure 2a) and RMLO views (Figure 2b).

On correlation with ultrasound right breast showed irregular, ill-defined, microlobulated, predominantly hypoechoic lesion of size 2.6 x 2.0 cm in the subareolar region (Figure 2c). This lesion showed minimal posterior enhancement. No obvious vascularity was seen within this lesion. On strain elastography, the strain ratio was 4.4 (Figure 2d). Multiple tiny subcentimeters, round, well defined, hypoechoic satellite nodules were noted around this lesion.



Figure 2c: Ultrasound showing irregular not circumscribed microlobulated hypoechoic mass with posterior enhancement.

Multiple lymph nodes with irregular thickened cortex measuring upto 5.2 mm with distorted hilum were noted in the right axilla.

The lesion was assigned BIRADS-5 category. Trucut biopsy was suggested for HPE correlation.

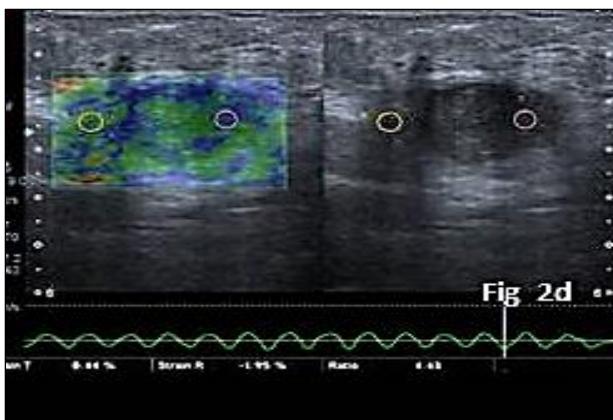


Figure 2d: On elastography lesion showed mosaic pattern with strain ratio of 4.4.

FNA and Core biopsy of the lesion showed features of invasive carcinoma of the breast. Right modified radical mastectomy was done.

Grossly, the tumour was 6.5 x 6.1 x 5.2 cm in size. The cut section showed gray white appearance, firm in consistency with solid areas. On histopathology, diagnosis of SqCC without involvement of surgical margins was given. Microscopically, Nottingham histologic score was grade -3 squamous cell carcinomas (metaplastic carcinoma). The tumor was composed of sheets and clusters of round to polyhedral cells with pleomorphic hyperchromatic nuclei and a moderate amount of eosinophilic cytoplasm (Figure 2e). Individual cell keratinization and keratin pearls were also seen. Total number of nodes examined were 27, out of which metastasis was found in 9 axillary lymphnodes.

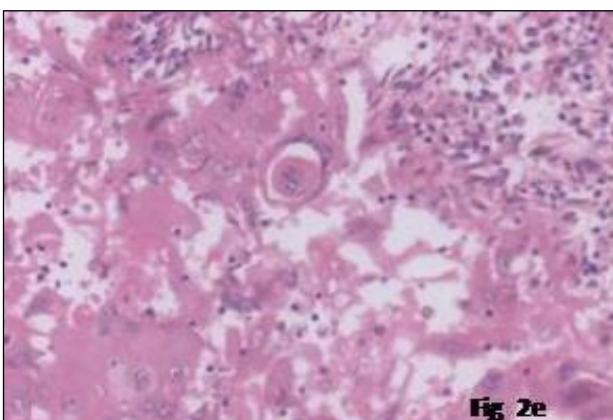


Figure 2e: H and E (x200) showing sheets and clusters of round to polyhedral cells with pleomorphic hyperchromatic nuclei and moderate amount of eosinophilic cytoplasm suggesting of squamous cell carcinoma a.

Immunohistochemistry, showed the tumor cells were negative for estrogen (Figure 2g) and progesterone (Figure 2h) receptors, HER2neu (Figure 2f).

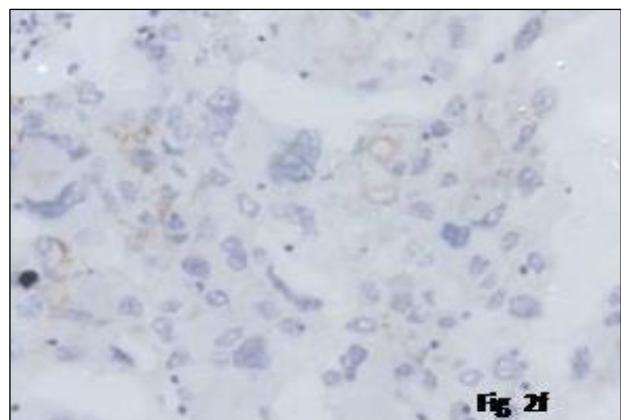


Figure 2f: Immunohistochemistry staining, negative HER 2 NEU receptor

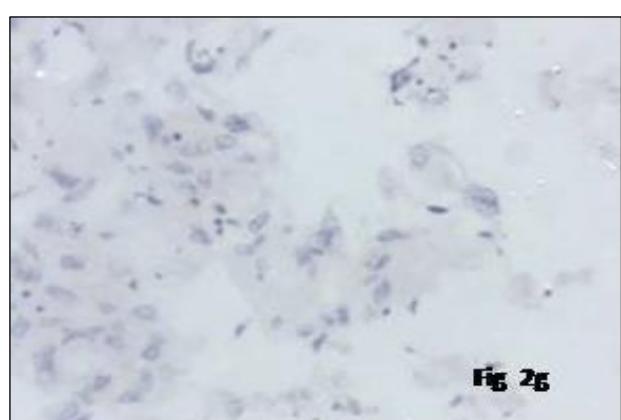


Figure 2g: Immunohistochemistry staining, negative estrogen receptor

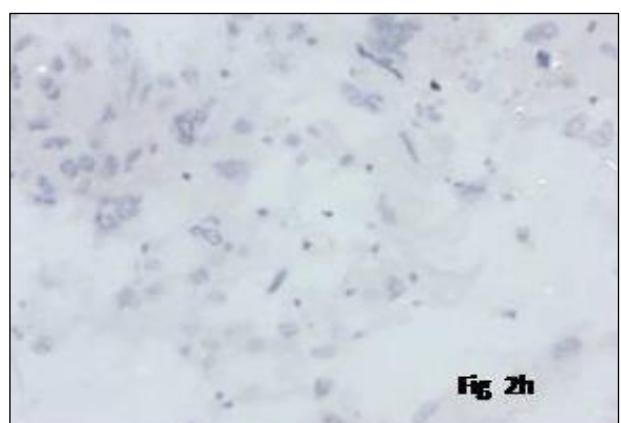


Figure 2h: Immunohistochemistry staining, negative progesterone receptor

Pathological diagnosis was given as, squamous cell carcinoma breast. Skin and margins free of tumor

In both our cases, extensive work-up ruled out other primary site or metastatic disease.

RESULTS

Two middle aged women presented with palpable masses in the breasts, with no family history of breast cancer. On, X-ray mammogram and ultrasound, scoring of BI-RADS-V was given with involvement of ipsilateral lymphnodes in both. This was followed by a Trucut biopsy which revealed invasive carcinoma of the breast in both patients.

Extensive work up was done to look for other primary focus/metastasis.

Both cases underwent modified radical mastectomy. The final histopathology proved both the cases as primary squamous cell carcinoma of the breast with no skin involvement and free surgical margins. Immunohistochemistry, showed the tumor cells were negative for estrogen and progesterone receptors and HER2neu.

DISCUSSION

The histogenesis of Squamous cell carcinoma of breast is unclear. Theories include malignant growth of intrinsic epidermal elements (epidermal or dermoid cysts), metaplasia from the breast parenchyma (benign disease, e.g., cystosarcoma phylloides, fibroadenomas, or breast malignancies, e.g., intraductal carcinoma,) and from chronic abscess. Perhaps these tumors have varying degrees of homogeneity. A tumor is considered “pure SqCC (Squamous cell carcinoma)” if it meets Macia et al. criteria, including: (1) no other neoplastic components such as ductal or mesenchymal elements are present in the tumor, (2) if the tumor is independent of adjacent cutaneous structures, (3) no other primary epidermoid tumors present in the other sites (oral cavity bronchus, esophagus, renal pelvis, bladder, ovary, and cervix).¹ It has been suggested that it may be a very extreme form of squamous cell metaplasia developing into an adenocarcinoma. This could also explain the mixed forms. Moreover, squamous cell metaplasia is also seen in cysts, chronic inflammations, abscesses and adenofibromas. In our case, however, there was no such preexistent abnormality. SqCC of the breast is the tumor of elderly age group. Tumors frequently reach large volumes and can be as large as 5 cm

Characteristic features of pure SqCC include keratinization, malignant cells, squamous cell differentiation, and lack of ductal carcinoma in situ; each of these factors was seen at histologic examination in these two cases. Grenier et al have described common immunohistochemical findings of pure SqCC as p63 positivity; CK 5/6 positivity; and ER, PR, and HER2 negativity. Conversely, common immunohistochemical findings of infiltrating ductal carcinoma with focal squamous metaplasia include ER and PR positivity, CK 5/6 negativity, and p63 negativity. The immunohistochemistry findings in this case matched the

common features of pure SqCC described by Grenier et al except for ER positivity. However, according to Tse et al, a small percentage of pure SqCCs have ER positivity. Given the characteristic histologic and immunohistochemical findings of SqCC, this mass was consistent with pure SqCC of the breast, a rare lesion.³

Estrogen and progesterone receptors are negative in more than 90% of the cases of pure SqCCB which was same in our case. The only case of HER-2/neu over expression in SqCCB was reported by Karamouzis et al to the best knowledge. There is only one reported case of a BRCA 1 gene mutation in a patient with SqCCB.

SqCCB does not have characteristic mammographic features. Some tumors have been reported to have irregular, indistinct borders, whereas others have been reported to have well circumscribed borders. Both our cases had non-circumscribed, microlobulated margins. Both cases had few discrete specks of calcification at the periphery of the mass. The most consistent feature of SqCCB on mammogram is the lack of microcalcifications. Only one reported case of SqCCB has shown microcalcifications on mammogram.¹

Prognosis appears to be dependent upon several factors, most importantly tumor size and tumor stage. The SEER database from 1988 to 2001 included 137 cases of SqCCB with a 5-year survival rate of 64%.¹

The initial management of SqCCB is modified radical mastectomy with adjuvant radiotherapy and/or chemotherapy/hormonal therapy. Breast conservation therapy is not usually possible because most patients present with locally advanced disease.²

The breast SqCC is usually a high-grade and hormone receptor-negative tumor. This means that hormone based therapy may not be effective in these tumors. Human epidermal growth factor receptor 2/neu is also usually not over-expressed or amplified in this disease. The high frequency of epidermal growth factor receptor (EGFR) positivity is interesting and may be exploited in the development of future treatments. The prognosis of this type of breast cancer is still regarded as somewhat controversial, though many studies suggest that it is an aggressive disease that may behave like poorly differentiated breast carcinoma. The 5-year survival is 67% in a small retrospective series of eleven patients.⁴

CONCLUSION

Primary SqCC of the breast is a very rare and aggressive tumor having poor prognosis. Poor response of the tumor to chemotherapeutic regimens commonly used in treating breast cancer, suggests that EGFR inhibitors and platin based regimens could be a promising option for the treatment of these tumors. Clinical trials including large series of these rare tumors are needed to increase our overview in order to improve patient's outcome.

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