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Primary Squamous Cell Carcinoma of Breast: A Case Report with Brief Review of Literature

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Abstract: Primary squamous cell carcinoma of breast is an unusual malignant neoplasm and has much lower incidence compared to other breast cancers. We report a case of primary squamous cell carcinoma in a 61 years old woman who presented with a palpable mass in the left breast of 2 months duration. FNAC smears revealed malignant squamous cells. Histopathological examination showed features of squamous cell carcinoma (large cell keratinizing) the tumor being composed entirely of neoplastic squamous cells. Skin or dermal adnexae of the breast and nipple were not involved by the tumor. There was no component of obvious invasive ductal carcinoma or other features of metaplastic carcinoma. All the axillary nodes dissected were free from tumor deposit. The tumor was negative for estrogen receptor (ER), progesterone receptor (PR) and Her2/neu oncoprotein expression. Through clinical examination and extensive investigations ruled out any other primary focus of tumor outside the breast. The patient received chemotherapy with 5-Flurouracil and Cisplatin following modified radical mastectomy and is asymptomatic in the 18 months follow up period. So, in a breast tumor showing malignant squamous cells on FNAC or histopathological examination, possibility of primary squamous cell carcinoma should be considered in the differential diagnosis. Diagnosis requires detailed clinical history, through examination and extensive investigations to exclude any extramamary primary along with careful histopathologic examination. This case is being reported for its extreme rarity.

Keywords: Primary Squamous cell carcinoma, breast cancer, metaplastic carcinoma

INTRODUCTION

Primary squamous cell carcinoma of breast is an extremely rare malignant neoplasm representing about 0.04% to 0.1% of all breast malignancies [1-3]. The clinical and radiographic characteristics are not specific. These tumors are usually hormone receptor negative and are aggressive, treatment refractory carcinomas with a poor prognosis. Here we report the clinical presentation, cytological and histopathological features of primary squamous cell carcinoma of breast with a brief review of literature considering its differential diagnosis, possible histiogenesis and current strategies for management.

CASE REPORT

A 61 years old woman presented with a firm, palpable lump in left breast of 2 months duration. Mammography revealed a round high density mass with partly irregular margins in the left inferior lateral quadrant, measuring approximately 2.0 cms in diameter. FNAC examination was done which showed cellular smears with malignant squamous cells in clusters and scattered singly. The cells had hyperchromatic enlarged nuclei, coarse chromatin and moderate amount of cytoplasm showing various degrees of keratinization. Background showed inflammatory cells and necrosis. Cytopathological features were suggestive of squamous cell carcinoma (Fig. 1C).

To exclude the possibility of metastatic squamous cell carcinoma to breast, through clinical evaluation and other relevant investigations were carried out. The patient was previously healthy with no history of any skin, oropharyngeal or anal lesions. Chest radiograph, CT scan of thorax and abdomen, endoscopy, laryngoscopy, colposcopy and cervical Pap smear did not reveal any extramamary cancer. All the biochemical parameters were within normal limits.

The patient underwent modified radical mastectomy with ipsilateral axillary node dissection. Gross examination revealed a tumor in the lower outer

quadrant measuring 2.0 cms in diameter with a greyish white cut section (Fig. 1A, 1B). The overlying skin was grossly free from tumor invasion. Microscopic examination showed a tumor composed of neoplastic squamous cells with hyperchromatic nuclei, occasional prominent nucleoli and abundant eosinophilic cytoplasm arranged in nests, sheets and trabaculae. Individual cell keratinization, keratin pearl formation and scattered mitotic figures were noted (Fig. 2A, 2B). Vascular or neural invasions were not identified. Skin or dermal adnexae of the breast and nipple were not involved by the tumor (Fig. 2C). There was no component of obvious invasive ductal carcinoma or other features of metaplastic carcinoma for example spindle cells, osseous or cartilaginous metaplasia. Eleven axillary nodes dissected were all free from tumor deposit.

Immunohistochemical examination was done and the tumor was negative for estrogen receptor (ER), progesterone receptor (PR) and Her2/neu oncoprotein expression.

Based on the FNAC and histological picture, correlating with clinical features and other relevant investigation findings, the diagnosis of primary sqamous cell carcinoma (large cell keratinizing type) was made.

The patient received chemotherapy with 5-Flurouracil and Cisplatin and is asymptomatic in the 18 months follow up period.



Fig. 1A: Gross appearance of mastectomy specimen; B: Cut section of specimen showing a grayish white tumor with slightly irregular margins (marked by arrow); C: FNAC smear- highly cellular, malignant squamous cells with hyperchromatic enlarged nuclei, coarse chromatin and moderate amount of cytoplasm showing various degrees of keratinization.(Low power, MGG stain)



Fig. 2A: Low power view- neoplastic squamous cells arranged in nests, sheets and trabaculae (Haematoxylin & Eosin stain); B: High power view- tumor cells show hyperchromatic nuclei, occasional prominent nucleoli and abundant eosinophilic cytoplasm with individual cell keratinization and keratin pearl formation (H& E stain); C: Overlying skin free from tumor (H& E stain)

DISCUSSION

Primary squamous cell carcinoma of breast is a rare tumor constituting 0.04% to 0.1% of all breast carcinomas [1-3]. This tumor have been reported in women of ages 29 to 90 years [4] with a median age of 52 [5]. It is more common in postmenopausal women [6]. Our patient was a 61 years old postmenopausal woman.

Macia and colleagues defined pure squamous cell carcinoma of breast as a tumor which fulfills the following criteria:

- No other neoplastic components such as ductal or mesenchymal elements are present in the tumor.
- The tumor origin must be independent from the overlying skin and nipple.
- Absence of an associated primary squamous cell carcinoma in a second site (oral cavity, bronchus, esophagus, renal pelvis, bladder, ovary and cervix)

In our case all the diagnostic criteria laid down by Macia *et al.* [7] were fulfilled. No other neoplastic component was found on histological examination. Overlying skin and nipple were free and primary carcinoma was not found at a second site on clinical examination and extensive investigations.

The theories explaining the histiogenesis of this rare malignancy include:

- Malignant growth from intrinsic epidermal elements (epidermal or dermoid cyst)
- Metaplasia from breast parenchyma (Benign disease like cystosarcoma plylloides, fibroadenomas or breast malignancies like intraductal carcinoma)
- From chronic abscess [8]

Clinically the patient presents with a rapidly growing mass with a median size of 2-5 cm. Mammographic features are not characteristic with some tumors having irregular, indistinct border while some showing well circumscribed borders [9]. Microcalcification is consistently absent [10]. In our patient the tumor had slightly irregular border with lack of microcalcification on mammography.

FNAC of breast may show squamous cells in various benign lesions like epidermoid cyst, subareolar abscess, fibroadenoma, infracted papillomas, spindle cell metaplasia, phyllodes tumor which may sometimes mimic malignant squamous lesion. The malignant squamous cells are more pleomorphic, mitotically active and dyskeratotic as was seen in the FNAC smears in our case. The differential diagnosis of malignant squamous cells in FNAC of the breast includes primary SCC and metastatic SCC of the breast [11].

Histologically pure primary squamous cell carcinoma is entirely composed of squamous cells that may be keratinizing, nonkeratinizing and less frequently spindle cell and acantholytic types, some showing combination of these pattens [6]. In our case a similar microscopic picture was observed. Most of the primaries SCC are ER, PR and Her2/neu (triple) negative. Our case supports this observation [12-14].

These tumors are associated with significantly lower rate of lymph node metastasis compared to ductal adenocarcinomas of breast. About 70% of the patients do not present with axillary node involvement but due to unpredictable lymph node dissemination, axillary lymph node dissection must always be performed for staging purposes [2]. All the 11 lymph nodes dissected in our case were free from tumor deposit.

Prognosis of this tumor appears to depend on several factors most importantly tumor size and stage. The SEER database from 1988 to 2001 included 137 cases of squamous cell carcinomas of breast with a mean 5 year survival rate of 64% [1].

The management of primary squamous cell carcinoma of breast include modified radical mastectomv with adjuvant radiotherapy or chemotherapy. As this tumor is usually hormone receptor negative [12-14]. Hormone based therapy may not be effective. Hennessy et al proposed early adjuvant radiotherapy as these tumors are often radiosensitive. Rostoch et al. review suggests that squamous cell carcinoma is not sensitive to chemotherapeutic agents commonly used in ductal carcinoma [15]. Adjuvant and neoadjuvant CT regimes used at M.D. Anderson Cancer Centre include 5-flurouracil alone. 5flurouracil/cisplatin, 5-flurouracil/taxane, 5flurouracil/cisplatin followed by pacitaxel and cyclophosphamide plus methotrexate plus luorouracil [16, 17]. Hennessy et al. report no benefit to neoadjuvant chemotherapy [17]. Our patient received chemotherapy with 5-flurouracil and Cisplatin following modified radical mastectomy and responded well to treatment.

CONCLUSION

Primary squamous cell carcinoma of breast is a rare, generally aggressive tumor. In presence of malignant squamous cells in breast FNAC or histopathological examination, possibility of primary squamous cell carcinoma should be considered in the differential diagnosis. Diagnosis requires detailed clinical history, through investigations to exclude any extramamary primary and careful histopathologic examination. The current surgical management is similar to conventional adenocarcinoma. However, effective adjuvant and neoadjuvant therapy is not available for this tumor. Future research should focus on molecular biology like epidermal growth factor receptors to develop tumor specific therapy.

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