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INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/23411
DOI URL: http://dx.doi.org/10.21474/IJAR01/23411

RESEARCH ARTICLE

PRIMARY SQUAMOUS CELL CARCINOMA OF THE BREAST: A DIAGNOSTIC ENIGMA

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Manuscript Info

Manuscript History
Received: 4 March 2026
Final Accepted: 8 April 2026
Published: May 2026

Key words:-
PSCC (Primary squamous cell carcinoma), BIRADS, HER-2

Abstract

Primary squamous cell carcinoma of the breast is an uncommon malignancy and accounts for a very small proportion of breast cancers. Because of its rarity and non-specific clinical presentation, diagnosis is challenging and often requires correlation of imaging, cytology, and histopathology. Pure squamous cell carcinoma of the breast can arise from the epidermis, the nipple, or the epithelium of a deep-seated epidermoid cyst, or from squamous metaplasia in a chronic inflammato ry background. We report the case of a 45-year-old female who presented with a painful lump in the left breast for three years. Imaging revealed a predominantly cystic lesion, and initial cytology suggested fibrocystic disease. However, histopathological and IHC examination of the lesion demonstrated features of primary squamous cell carcinom a. This case emphasizes the importance of histopathological confirmati on in breast lesions that clinically and radiologically resemble benign conditions.

Introduction:-

Squamous cell carcinoma (SCC) of the breast is an extremely rare malignant neoplasm, accounting for less than 0.1% (approximately 0.04–0.075%) of all invasive breast cancers [1,2]. The diagnosis of primary SCC of the breast is based on strict criteria, which include: (1) more than 90% of the malignant cells being of squamous cell origin, (2) the tumor being independent of the overlying skin and nipple, and (3) exclusion of a primary squamous cell carcinoma at any other site in the body [14]. Clinically and radiologically, these tumors have nonspecific findings and may mimic benign or inflammatory breast conditions. They are commonly hormone receptor- and HER2-negative [3], limiting treatment options and contributing to a poor prognosis. Due to its rarity, diagnostic challenges, and aggressive behavior, we present this case to contribute to the existing literature and improve understanding of this uncommon entity.

Case Presentation:-

A 45-year-old female presented with a history of a lump in the left breast for approximately three years, which gradually increased in size over time and was associated with pain. There was no history of nipple discharge, bleeding, ulceration of the skin, or trauma to the breast. The patient had no significant past medical illness or family history of breast malignancy. On clinical examination, a palpable mass was identified in the upper inner quadrant of the left breast. The swelling was localized to the breast tissue, and the overlying skin appeared normal without signs of ulceration or inflammatory changes. The nipple-areolar complex appeared normal. Radiological evaluation of the

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left breast revealed a large lobulated cystic lesion measuring approximately 5.1 × 4.8 × 3.5 cm, with a wider than tall orientation with no internal calcifications. The lesion was reported as a complex cystic lesion of the breast with a BI-RADS score of III (Fig 1).

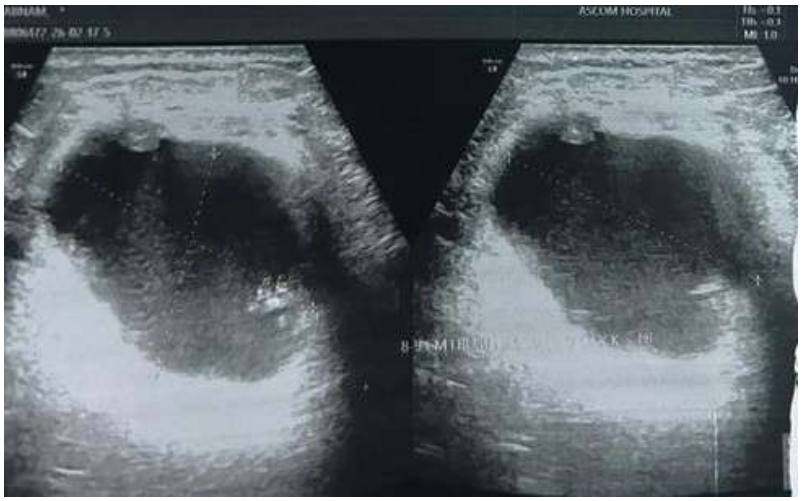

Fig. 1 Cystic lesion

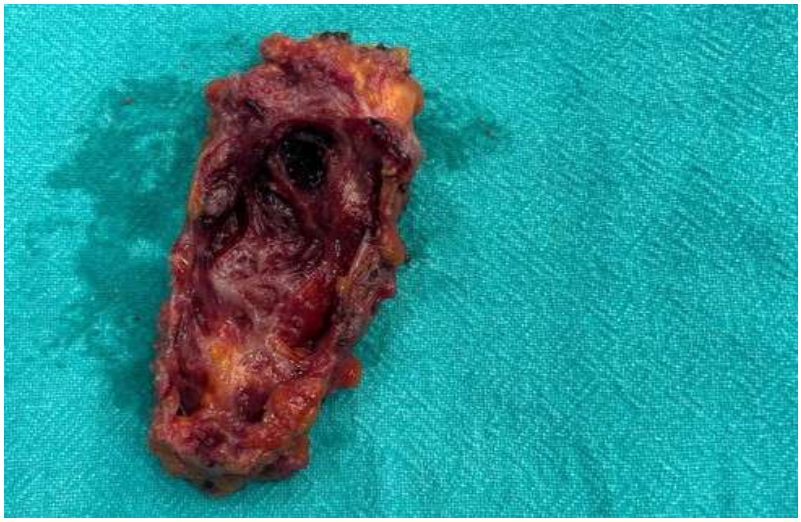

Fig.2 Cystic cavity with partial septations

On further evaluation by fine needle aspiration, approximately 20 mL of pale yellow fluid was aspirated. Microscopic examination showed numerous foamy macrophages, a few ductal epithelial cells, along with many neutrophils in a background of red blood cells. No atypical cells were seen. Cytological features suggested a benign cystic lesion consistent with fibrocystic change. In cystic breast lesions, FNAC may be limited by sampling error and dilutional effects, often yielding predominantly macrophages, necrotic debris, and degenerated epithelial cells. The malignant component particularly in rare entities such as primary squamous cell carcinoma, may be confined to the cyst wall and not adequately sampled, resulting in false-negative cytology. Hence, cytological findings should be interpreted with caution, and correlation with imaging and histopathology is recommended in suspicious or persistent lesions. Left breast lumpectomy was done, a globular mass measuring 5.6 × 4 × 3 cm was received. On cut section, a cystic cavity was identified with partial septations measuring 4.6 × 3 cm (Fig 2). No lymph nodes were retrieved. On microscopic examination, a cystic lesion was identified, which was partially lined by atypical squamous epithelium. In addition, several irregular nests and islands of tumor cells were seen infiltrating the surrounding breast stroma. The tumor cells exhibited moderate nuclear pleomorphism, hyperchromatic nuclei, abundant eosinophilic cytoplasm, prominent keratin pearl formation, and individual cell keratinization. Features

were consistent with squamous differentiation. The adjacent breast tissue revealed duct ectasia accompanied by dense chronic inflammatory cell infiltrate and preserved normal terminal ductal units. No atypical glandular elements were identified in the sections submitted (Fig 3). On immunohistochemistry, tumor cells showed diffuse cytoplasmic positivity for Pan-Cytokeratin (AE1/AE3), confirming epithelial origin. Strong CK5/6 and diffuse nuclear p40 positivity supported squamous differentiation. ER, PR, and HER2/neu were negative, with no glandular differentiation. Overall, findings were consistent with primary squamous cell carcinoma of the breast (PSCC).

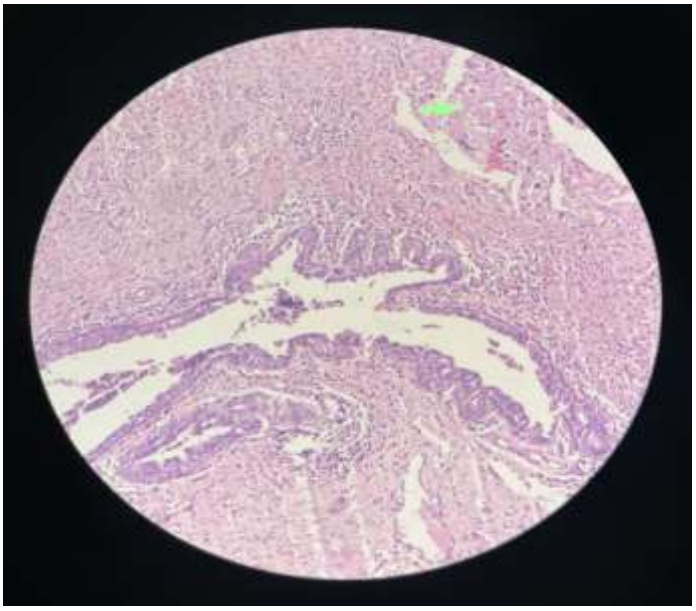

Fig. 3 Cavity lined by atypical squamous cells with island of malignant cell in surrounding area.

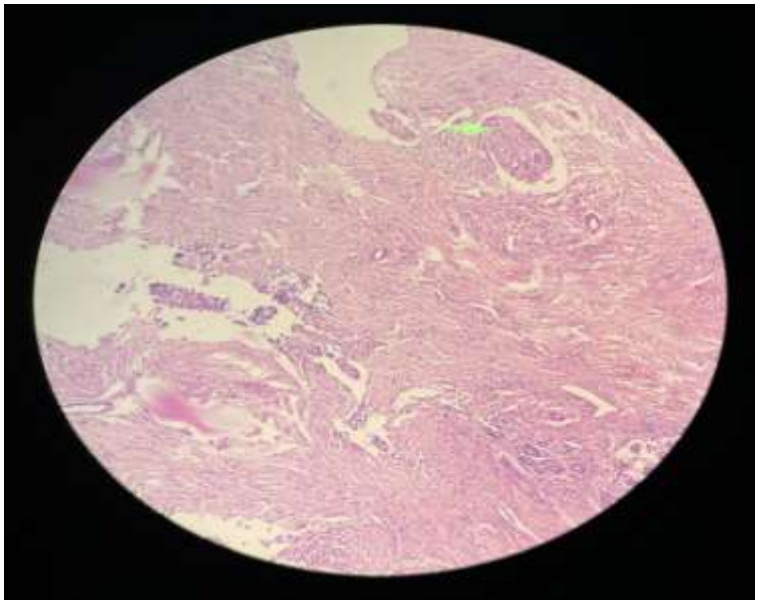

Fig 4 Squamous cell carcinoma with normal ductal lobular unit (H&E 100x)

Discussion:-

Primary squamous cell carcinoma of the breast is a rare entity. It is termed “pure” when the tumor is composed entirely of malignant squamous cells, with no connection to the overlying skin or nipple, and when a primary tumor at another site has been excluded [8,9]. It is important to differentiate it from mixed tumors with squamous differentiation and from metastatic squamous cell carcinoma arising elsewhere. The exact etiology and pathogenesis

remain unclear. Malignant transformation following squamous metaplasia in benign conditions such as cysts, chronic inflammation, abscesses, and fibroadenomas has been proposed. This is supported by reports of SCC developing in association with long-standing benign lesions, breast implants, or prior radiation therapy [9,1,11]. In the present case, the patient had a multiloculated cystic lesion for three years, which may support this proposed mechanism. The patient was 45 years old, which is comparable to the reported median age of 52 years. It has been observed that SCC of the breast may occur in slightly younger females compared to infiltrating duct carcinoma [12]. Radiologically, these tumors lack specific features and may mimic benign conditions. In this case, ultrasound demonstrated a complicated cystic lesion. Such cystic changes may be attributed to central necrosis or degeneration.

According to the literature, these tumors are frequently mistaken for benign lesions on imaging [13]. Approximately 70% of cases show no axillary lymph node involvement [1]. Menes et al. [3] reported a lower rate of nodal metastasis (22%) but a significant incidence of distant metastasis even in the absence of nodal disease. In our case, axillary lymph nodes were not involved. Cytological diagnosis may be challenging in cystic lesions. While some studies have reported malignant cells on FNAC, our case showed features consistent with a benign cystic lesion, highlighting the risk of false-negative results due to sampling limitations. Immunohistochemistry further aids in confirmation, and in our case, positivity for pan-cytokeratin, CK5/6, and p40 with ER/PR/HER2 negativity supported squamous differentiation and a triple-negative profile. Squamous cell carcinomas are typically hormone receptor-negative, as also observed in our case [8–10]. Surgical management remains the mainstay of treatment. In our case, the patient underwent lumpectomy with axillary clearance. However, mastectomy with axillary clearance is generally considered the treatment of choice [15,16]. The role of adjuvant therapy remains uncertain, particularly due to variable radiosensitivity. The reported 5-year survival rate is approximately 67% [1].

Conclusion:-

Primary squamous cell carcinoma of the breast is a rare malignant tumor that may clinically, radiologically, and on cytology resemble benign breast lesions. This case illustrates the importance of thorough clinical workup and histopathological evaluation in patients presenting with long-standing breast lumps, abscesses, and cysts, particularly when imaging and cytology suggest benign conditions. This case highlights that cystic breast lesions with benign FNAC findings should be interpreted with caution, as malignancy, particularly rare entities like primary squamous cell carcinoma may be missed due to sampling limitations, underscoring the need for clinicoradiological correlation and histopathological confirmation in persistent or suspicious cases. Accurate diagnosis is essential to guide appropriate management. 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 [7].

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