Case Report

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Surgery Section

Primary Squamous Cell Carcinoma of the Breast: A Rare Clinical Entity with Diagnostic and Therapeutic Challenges

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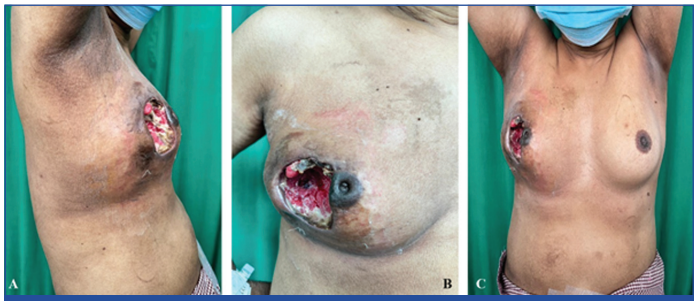
ABSTRACT

Primary Squamous Cell Carcinoma (PSCC) of the breast is an exceptionally rare and aggressive malignancy, often lacking well-defined clinical and radiological hallmarks. A 51-year-old postmenopausal woman arrived in septic shock with a necrotic, ulcerative mass in the upper outer quadrant of the right breast, initially misinterpreted as a chronic abscess. Imaging revealed a heterogeneous breast lesion with axillary lymphadenopathy and no distant metastasis. An emergency toilet mastectomy was performed due to progressive sepsis, followed by Vacuum-Assisted Closure (VAC) and split-thickness skin grafting. Histopathology confirmed high-grade squamous cell carcinoma with a minor ductal component (<10%). Immunohistochemistry demonstrated triple-negative receptor status, diffuse nuclear p63 positivity, positivity for CK6 and CK7, and a high Ki-67 index, fulfilling the diagnostic criteria for PSCC proposed by Macia et al. The patient remained disease-free at one-year follow-up after adjuvant radiotherapy. This case underscores the importance of recognising atypical infectious presentations of breast tumours and integrating clinical, radiologic and pathologic findings to distinguish PSCC from close differentials, including chronic abscesses, metastatic carcinomas and other inflammatory breast pathologies.

Keywords: Abscess, Case report, Metaplastic, Sepsis

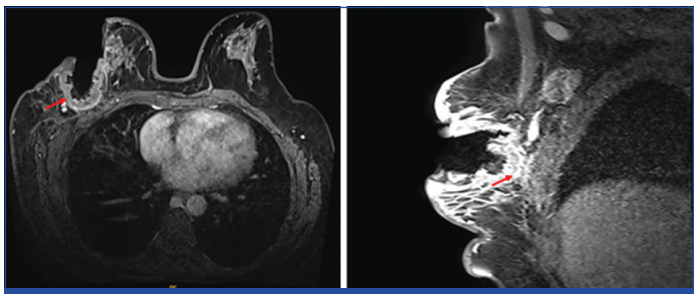
CASE REPORT

A 51-year-old postmenopausal woman presented to the emergency department in septic shock. Her complaints included a large ulcer on the right breast for two months and persistent fever with chills for one week [Table/Fig-1]. She was febrile, tachycardic and hypotensive, requiring inotropic support. History revealed the presence of a right upper outer quadrant breast lump for the past four months, gradually increasing in size from 1×1 cm to approximately 4×5 cm. The patient reported weight loss of 7-8 kg over two months. There was no family history of breast or ovarian malignancy. She had been evaluated at another facility with bilateral breast ultrasonography showing a liquefied abscess with peripheral solid components and right axillary lymphadenopathy {Breast Imaging Reporting and Data System (BI-RADS) 4A}. A tru-cut biopsy from the lesion showed a chronic abscess with no evidence of malignancy. Postbiopsy, the patient developed a non healing ulcer that enlarged to 6×7 cm, with foul-smelling discharge and bleeding from the nipple.

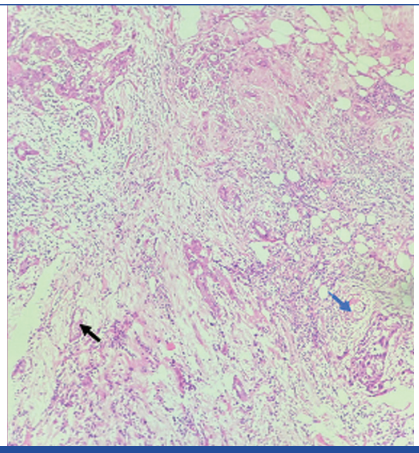


[Table/Fig-1]: Clinical pictures taken on presentation which showed an ulcer in the upper outer quadrant of the right breast with significant induration and purulent discharge.

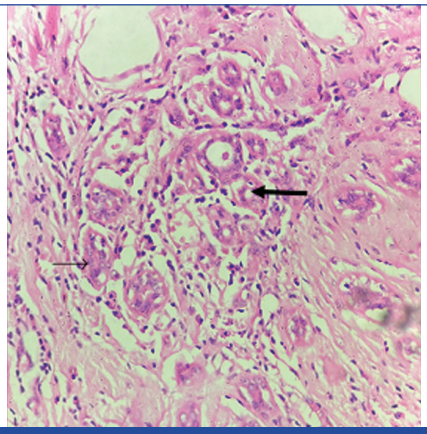
Following referral to our centre, an Magnetic Resonance Imaging (MRI) was ordered, which showed a large ulcerative, heterogeneous mass diffusely involving the right breast [Table/Fig-2]. Positron Emission Tomography Computed Tomography (PET-CT) revealed a hypermetabolic mass in the right breast with right axillary lymphadenopathy and a satellite lesion in the inferomedial quadrant. No evidence of distant metastasis or additional foci of squamous cell carcinoma was identified elsewhere in the body. A provisional diagnosis of carcinoma of the breast, cT4bN1M0, was made. Due to her deteriorating condition and persistent leukocytosis, the decision was made to perform a toilet mastectomy. A portion of the pectoralis major muscle was removed. Postoperatively, VAC therapy was employed to facilitate wound closure. After two weeks, the patient was scheduled for closure of the wound using a split-thickness skin graft. The patient had an uneventful recovery. Final histopathological evaluation revealed a high-grade carcinoma composed predominantly (>90%) of malignant squamous cells arranged in sheets, with a minor ductal component comprising less than 10% [Table/Fig-3,4]. Immunohistochemistry revealed a triple-negative status (ER-/PR-/HER2-) with diffuse nuclear positivity for p63, strong expression of CK6 and CK7 [Table/Fig-5-7] and a high Ki-67 proliferation index (>20%). Absence of TTF-1, p16, and CK20 expression effectively excluded pulmonary, cervical and gastrointestinal origins of squamous cell carcinoma. In accordance with the diagnostic criteria proposed by Macia M et al., in 1989, a definitive diagnosis of PSCC of the breast was established [Table/Fig-8] [1]. The final pathological staging was pT3N1M0. The patient was then advised adjuvant radiotherapy and was recurrence-free on the first annual follow-up visit.



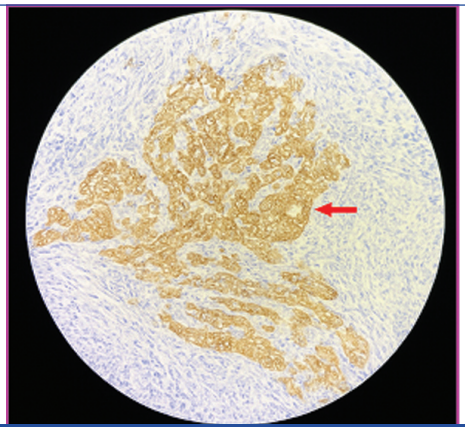
[Table/Fig-2]: The MRI breast images which revealed an ulcerative growth arising from the right breast with focal abutment with the underlying pectoralis major muscle without any discernible breast lump (Red arrow).



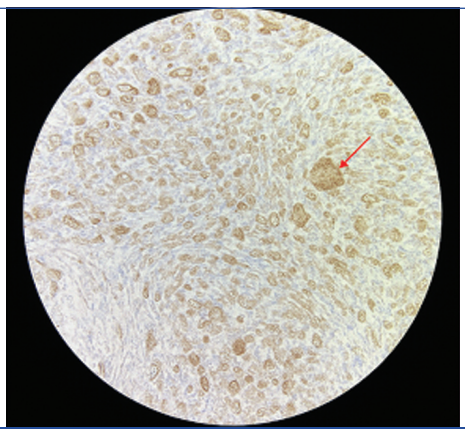
[Table/Fig-3]: Low-power view (H&E stain, 10×) showing sheets and nests of malignant squamous cells with areas of keratin pearl formation (black arrow) and central necrosis (blue arrow) within a desmoplastic stroma.



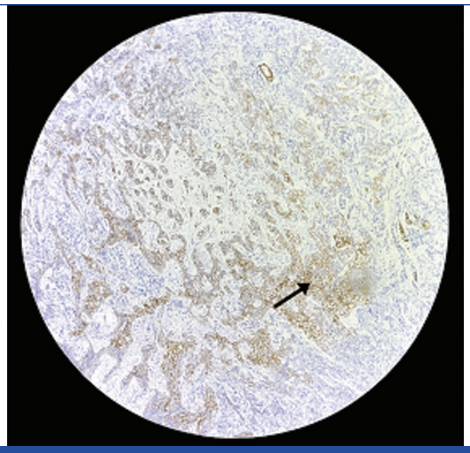
[Table/Fig-4]: High-power view (H&E stain, 40×) revealing atypical squamous cells with intercellular bridges and keratin pearls (black arrows), consistent with well-differentiated squamous cell carcinoma.



[Table/Fig-5]: Immunohistochemistry (IHC) staining showing CK6 positivity (red arrow) in malignant cells supporting squamous differentiation (20x magnification).



[Table/Fig-6]: Immunohistochemistry (IHC) staining showing diffuse nuclear p63 positivity (red arrow) in malignant squamous cells (20x magnification).



[Table/Fig-7]: Immunohistochemistry (IHC) staining showing CK7 positivity in malignant squamous cells indicative of squamous differentiation in Primary Squamous Cell Carcinoma (PSCC) of the breast (20x magnification).

Diagnostic criterion [1]	Present case findings
>90% of tumour is composed of malignant squamous cells	High-grade squamous carcinoma comprises>90% of tumour histology
Absence of non mammary Primary Squamous Cell Carcinoma (PSCC) elsewhere	PET-CT showed no other foci of Primary Squamous Cell Carcinoma (PSCC) elsewhere in the body
Tumour not originating from overlying skin or dermal structures	No evidence of cutaneous origin; tumour located in deeper breast parenchyma
Minimal/no glandular (ductal) component	Focal ductal component comprising <10% of tumour

[Table/Fig-8]: Diagnostic criteria for Primary Squamous Cell Carcinoma (PSCC) of the breast and correlation with present case findings [1].

DISCUSSION

Breast cancer remains the most common cancer affecting women worldwide and represents a significant public health challenge. According to GLOBOCAN 2020 estimates, breast cancer accounted for approximately 2.3 million new cases and 685,000 deaths globally [2]. In India, it has emerged as the most commonly diagnosed malignancy among women, surpassing cervical cancer, with more than 162,468 new cases and nearly 87,090 deaths per year [3]. Histologically, breast cancer encompasses a wide spectrum of epithelial tumours. Invasive Ductal Carcinoma (IDC) is by far the most common subtype, accounting for approximately 70-80% of all breast cancers. Less common histological variants include invasive lobular carcinoma, mucinous carcinoma, tubular carcinoma and medullary carcinoma [4].

PSCC of the breast represents a distinct and exceedingly rare variant of breast cancer that diverges markedly from the conventional adenocarcinomas encountered in clinical practice. PSCC, now classified within the spectrum of metaplastic breast carcinomas, constitutes less than 0.1-0.2% of all breast malignancies and accounts for under 1% of invasive breast carcinomas [5]. In the Indian context, literature on PSCC of the breast remains exceedingly limited, largely restricted to isolated case reports and single-centre experiences [Table/Fig-9] [6-11]. On a genetic level, IDC, the most

Study/ case	Age (years)	Tumour size (cm)	Receptor and IHC profile	Primary treatment	Outcome / follow-up
Wu Y et al., [6]	56	1.7×2.5	ER-, PR-, HER2-; CK5/6+, CK14+, Ki-67 80%	MRM + chemo + RT	CR at 24 months
Yao J et al., [7]	32	4.8×4.3	ER+, PR-, HER2-; Ki-67 50%	NACT (nab-paclitaxel/ EC) → MRM → RT + tamoxifen + capecitabine	No disease at 6 months

Flikweert ER et al., [8]	72	4.0	ER+, PR-, HER2-	MRM + hormonal therapy (tamoxifen → AI)	Metastatic relapse at 2 years, deceased
Yoneto T et al., [9]	44	1.1	ER-, PR-, HER2-	Partial mastectomy + axillary clearance + chemo	Relapse at 5 years → death
	58	3.1	ER-, PR-, HER2-	MRM	Disease-free at 4 yrs
Bhatt A et al., [10]	49	5.2×5.0	Triple-negative; CK5/6+, p63+, Ki-67 > 30%	MRM + adjuvant chemotherapy	No recurrence at 18 months
Vaidya T et al., [11]	54	6.5×4.2	Triple-negative; p63+, CK14+, Ki-67 60%	Toilet mastectomy + VAC + RT	Disease-free at 6 months
Present study	51	~6×7	Triple-negative; p63+, CK6+, CK7+, Ki-67 high (>20%)	Toilet mastectomy + VAC + split-skin grafting + adjuvant RT	Disease-free at 12 months

[Table/Fig-9]: Clinicopathological features of Primary Squamous Cell Carcinoma (PSCC) of the breast as reported in global and Indian literature [6-11].
ER: Oestrogen receptor; PR: Progesterone receptor; HER2: Human epidermal growth receptor; CK: Cytokeratin; MRM: Modified radical mastectomy; RT: Radiation therapy; CR: Complete response; NACT: NeoAdjuvant chemotherapy; VAC: Vacuum-assisted closure

prevalent subtype of breast carcinoma, arises from luminal epithelial cells of the terminal duct-lobular unit and is driven by a complex interplay of somatic mutations and epigenetic deregulation. Common alterations include mutations in TP53 and PIK3CA, loss of heterozygosity in BRCA1 and BRCA2 (particularly in hereditary cases) and epigenetic silencing of tumour suppressor genes such as CDH1 and RASSF1A through promoter hypermethylation [12]. In contrast, PSCC of the breast, a rare metaplastic malignancy, likely originates from basal/myoepithelial ductal progenitors undergoing squamous trans-differentiation [13].

Clinically, PSCC of the breast often presents as a rapidly enlarging, occasionally painful mass, frequently measuring more than 4-5 cm at diagnosis. Ulceration, necrosis and secondary infection are not uncommon, adding to the complexity of the presentation and often resulting in delayed or incorrect diagnosis [14]. In present case, the patient presented in septic shock, a rare yet life-threatening manifestation of PSCC of the breast necessitating emergent surgical intervention.

Similar presentations have been reported by Damin DC et al., who described a 39-year-old woman presenting with a large breast abscess, high-grade fever and signs of sepsis [15]. Intraoperative histopathology unexpectedly revealed PSCC of the breast, and the patient underwent modified radical mastectomy with resolution of the infectious symptoms. Similarly, Wrightson WR et al., described a case initially managed as a breast abscess, in which surgical drainage revealed underlying PSCC, highlighting the risk of overlooking malignancy in the context of infection [16]. Further, Tan PH et al., reported necrotic, non resolving breast lesions treated initially with antibiotics that later progressed to systemic inflammatory states and were ultimately confirmed as PSCC on histopathology [17].

Accurate diagnosis of PSCC of the breast requires a comprehensive radiologic assessment integrated with clinical suspicion. Initial evaluation begins with mammography, which in PSCC may reveal a dense, irregular mass with indistinct margins, often lacking the characteristic microcalcifications commonly seen in IDC [18]. Ultrasonography in PSCC typically demonstrates a complex lesion with both cystic and solid components, central necrosis and posterior acoustic enhancement, features that may mimic abscesses or cystic neoplasms. This contrasts with IDC, which more frequently appears as a hypoechoic, irregular and spiculated solid mass without cystic degeneration [19]. MRI provides superior soft-tissue contrast and is invaluable in characterising ambiguous or aggressive lesions. PSCC lesions often exhibit heterogeneous signal intensity on T2-weighted images, with rim enhancement and central necrosis on contrast sequences, reflecting rapid tumour growth and necrotic core formation [20]. Dynamic contrast-enhanced MRI commonly shows a Type III (washout) kinetic curve, reflective of necrosis and aggressive growth. While IDC may also demonstrate washout kinetics, it more often displays uniform enhancement with periductal distribution, particularly in hormone receptor-positive subtypes [21].

PET-CT serves a dual role in the evaluation of PSCC of the breast, facilitating accurate locoregional staging while also excluding distant PSCCs, particularly in the lung, cervix and head and neck regions [22]. In present case, PET-CT revealed no extramammary foci, thereby reinforcing the diagnosis of a primary breast origin. PSCC often exhibits intense Fluorodeoxyglucose (FDG) uptake on PET-CT, similar to high-grade triple-negative IDC, but distinguishing features such as central necrosis, cavitation, or satellite nodules may suggest PSCC in the appropriate clinical context.

Histopathologically, IDC is characterised by infiltrating malignant epithelial cells arranged in duct-like structures, nests, or cords within a desmoplastic stroma. Tumour cells typically exhibit nuclear pleomorphism, hyperchromasia and variable mitotic activity, with high-grade lesions often showing central necrosis and solid architecture. In contrast, PSCC of the breast is composed entirely of malignant squamous cells demonstrating keratinisation, intercellular bridges and well-formed keratin pearls, without any evidence of glandular differentiation. A dense inflammatory infiltrate and fibrotic stroma are frequently observed [23].

On immunohistochemistry, IDC exhibits subtype-dependent profiles, with luminal tumours showing ER/PR positivity, HER2-enriched subtypes overexpressing HER2, and basal-like variants typically triple-negative. PSCC, by contrast, consistently shows a triple-negative profile (ER-/PR-/HER2-) and expresses squamous markers such as p63, CK5/6, and CK14, with a high Ki-67 proliferative index often exceeding 30-40%. Diffuse nuclear p63 positivity serves as a key discriminator from other metaplastic subtypes [24]. Unlike mucosal SCCs, breast PSCCs are not associated with Human Papillomavirus (HPV), reinforcing their distinct pathogenesis [25].

Management of PSCC is complex due to its resistance to standard breast cancer protocols. Surgery remains the cornerstone of treatment, with modified radical mastectomy often favoured given the size and necrotic nature of most tumours. The role of adjuvant chemotherapy is uncertain, with some reports suggesting limited efficacy of anthracycline- or taxane-based regimens [26]. Platinum-based therapies, such as cisplatin or carboplatin, have demonstrated relative activity in some cases. Radiotherapy is utilised for local control but may offer limited benefit due to relative radio-resistance. Hormonal therapy is generally ineffective in triple-negative cases. Emerging data on immunotherapy, particularly PD-L1 inhibitors like atezolizumab, suggest potential avenues for refractory cases, though clinical trials specific to PSCC are lacking [27].

Prognostically, PSCC carries a worse outlook compared with its adenocarcinomatous counterparts. Five-year survival rates are significantly lower, often ranging between 40-60%, with high local recurrence and early metastasis being common [13].

In the Indian healthcare context, PSCC poses particular challenges. Limited access to high-resolution imaging, constrained pathology services and inadequate awareness contribute to delays and mismanagement. Moreover, in rural or resource-limited areas, the ulcerated or infected presentation of PSCC is frequently mistaken for abscesses or fungal infections, leading to inappropriate antibiotic use or incision and drainage procedures.

To overcome these barriers, clinicians must maintain vigilance when evaluating atypical breast lesions, especially in older, postmenopausal women with rapid progression, non resolving infections, or ulcerated masses.

CONCLUSION(S)

The PSCC of the breast is a rare and aggressive neoplasm requiring prompt diagnosis and individualised management. Its resemblance to benign inflammatory lesions can lead to diagnostic delays, adversely affecting prognosis. A high index of suspicion, comprehensive imaging and timely histopathological confirmation are essential.

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