Breast undifferentiated (pleomorphic) high-grade carcinoma - a case report

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ABSTRACT

Background: Pleomorphic carcinoma of the breast is a rare and aggressive histologic variant of invasive breast carcinoma characterized by the presence of highly atypical, bizarre, pleomorphic giant cells. It typically portends a poor prognosis and poses diagnostic challenges due to its undifferentiated morphology.

Case Presentation: We report the case of a 39-year-old woman who presented with a 5-month history of a progressively enlarging left breast mass. Imaging revealed a large, irregular lesion without overt metastatic disease. Histopathology demonstrated a high-grade pleomorphic undifferentiated epithelioid neoplasm, with triple-negative receptors expression. Immunohistochemistry suggested an undifferentiated epithelioid neoplasm requiring exclusion of metastasis. Modified radical mastectomy was performed, and PET <AQ1>-CT excluded other primary sources, confirming this as a primary breast malignancy.

Conclusion: Primary undifferentiated pleomorphic carcinoma of the breast is rare and diagnostically challenging. Multimodal imaging, expert histopathological analysis, and exclusion of metastasis are essential for diagnosis and management. This case underscores the need for clinical suspicion in atypical high-grade breast tumors.

Keywords: Breast, cancer, undifferentiated, pleomorphic, carcinoma.

Type of Article: CASE REPORT **Specialty:** General surgery/Breast surgery

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Background

Pleomorphic carcinoma of the breast represents a rare and diagnostically challenging subtype of invasive breast carcinoma of no special type (NST), characterized by the presence of pleomorphic, bizarre, often multinucleated tumor giant cells. Its undifferentiated morphology can lead to confusion with high-grade sarcomas, malignant phyllodes tumors, or metastatic malignancies. This diagnostic ambiguity highlights the critical role of comprehensive immunohistochemistry (IHC) and advanced imaging techniques in accurate diagnosis and staging.

A comparison of the main clinicopathological features of pleomorphic carcinoma of the breast reported in English literature is presented in Table 1 [1].

The rarity of pleomorphic carcinoma has resulted in a lack of standardized treatment algorithms, often necessitating the extrapolation of treatment strategies from triple-negative breast cancer (TNBC) or poorly differentiated NST carcinomas. While surgical excision remains the cornerstone of therapy, adjuvant chemotherapy and radiation therapy play crucial roles in managing this aggressive disease. The prognosis is generally unfavorable, influenced by factors such as large tumor size, high histological grade, and lympho-vascular invasion.

This case report presents a unique instance of pleomorphic carcinoma of the breast, emphasizing the importance of multidisciplinary management and the need for further research to improve our understanding and treatment of this rare and aggressive tumor. The following discussion will delve into the diagnostic challenges, the role of IHC, treatment considerations, and prognostic implications, contributing to the limited body of literature on this entity.

Case Report

A 39-year-old lady reported to our breast disease clinic with a 5-month history of a left breast lump. She did not seek medical care within this period due to the COVID-19 pandemic. The lump was increasing in size gradually within that period. There were no nipple discharges; she had no other complaints. The patient is a mother of four children, has regular and normal periods, has no comorbidities, has no family history of breast cancers or other malignancies, and she is not using any form of contraceptives.

Table 1. *A comparison of the main clinicopathological features of pleomorphic carcinoma of breast.*

AUTHOR	YEAR	CASES	AGE (YEAR)	TUMOR SIZE (CM)	LYMPH NODES STATUS
Silver and Tavassoli [1]	2000	26	28-96 (median, 51)	0.5-15 (average, 3.9)	12/23 positive*
Lenicek et al [2]	2007	1	83	5.8	Negative
Nguyen et al. [16]	2010	37	23-78 (median, 49)	1.2-11.6 (average, 3.5)	17/33 positive*
Zhao et al. [4]	2010	10	23-78 (median, 50)	1.0-15.0 (average, 4.4)	4/10 positive*
Yamaguchi et al [2]	2010	1	17	5.5	Positive
Caruso et al [2]	2011	1	65	2.5	Positive
Tacchini et al [2]	2011	1	44	1.2 & 0.6#	Negative
Cordoba et al [2]	2012	2	76 & 46	5.0 & <1.0	NM

*Positive cases/total detected cases.
This case has two independent masses.
NM not mentioned.

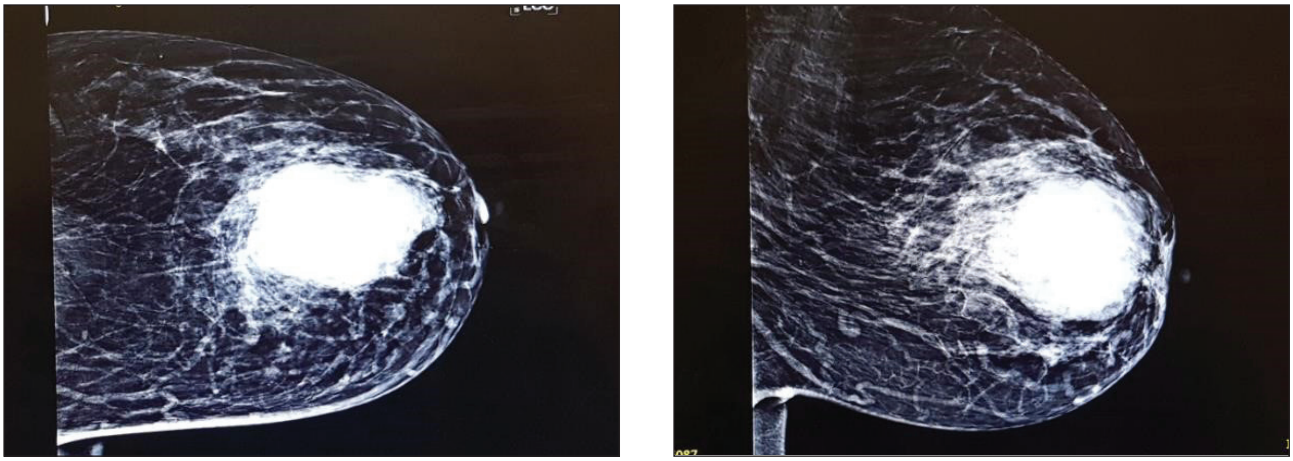

Figure 1. *LMLO and LCC view of the mammogram of the left breast.*

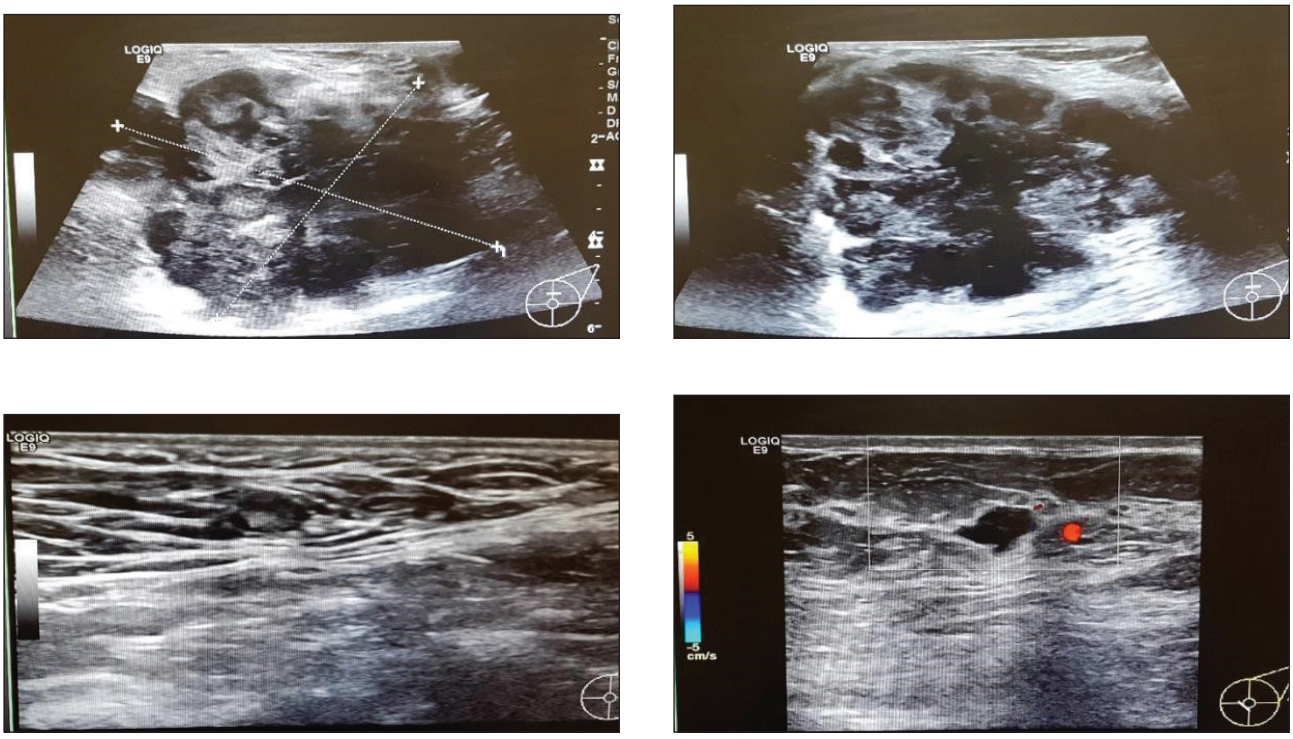

Figure 2. *USS of the left breast.*

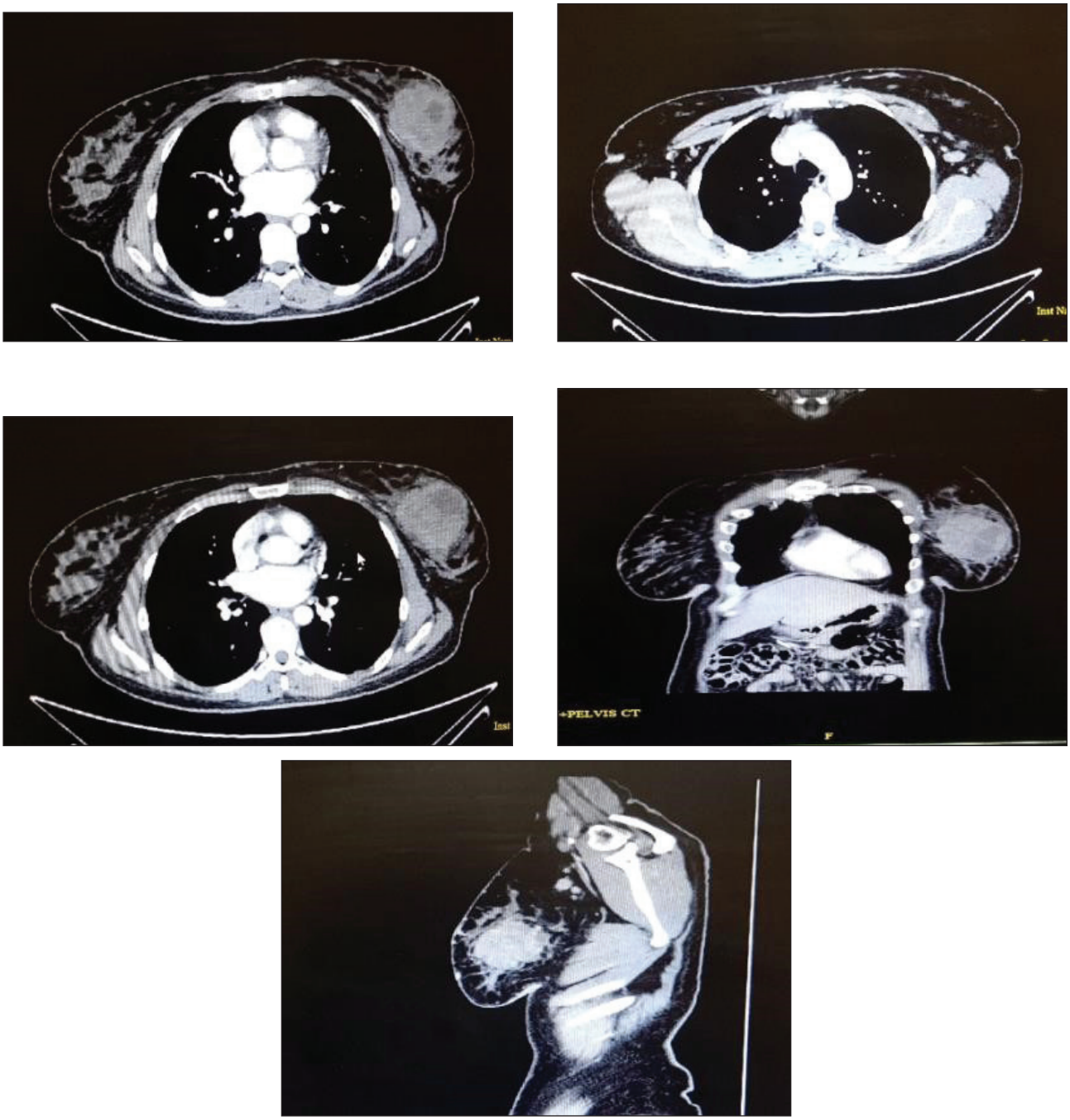

Figure 3. *CT scan of breast as part of the staging CT: (a., b., c.: transverse planes.) (d: Coronal plane.) (e: Sagittal plane).*

In examination, there was a hard lump felt in the retro-areolar area and extending cephalad, measuring around 6 × 7 cm, hard in palpation, not fixed to tissues beneath. The lymph nodes were not palpable.

The patient underwent a mammogram (Figure 1) and reported the presence of micro-lobulated density related to the upper outer quadrant Upper Outer Quadrant, measuring 7.1 × 7.3 cm, with partially obscured margins.

The patient underwent an ultrasound (Figure 2), which showed a large hypoechoic mass with irregular margins seen in the upper outer quadrant and the center of the left breast corresponds to the mammographic abnormality. The mass measures 7 × 5.9 × 7 cm. No enlarged lymph nodes.

The right breast is normal apart from a small hypoechoic lesion, 9 × 4 mm may represent a complicated cyst. Bilateral lymph nodes with benign features.

A tru-cut biopsy is taken and sent to the histopathology laboratory. It shows: High-grade, malignant epithelioid neoplasm. In our hospital, we send the specimen to an expert opinion when there is a rare lesion needing more consensus. The expert reports stated the presence of a pleomorphic undifferentiated epithelioid malignant neoplasm, high grade. The appearances do not fit neatly into any well-defined type of primary breast tumor, and

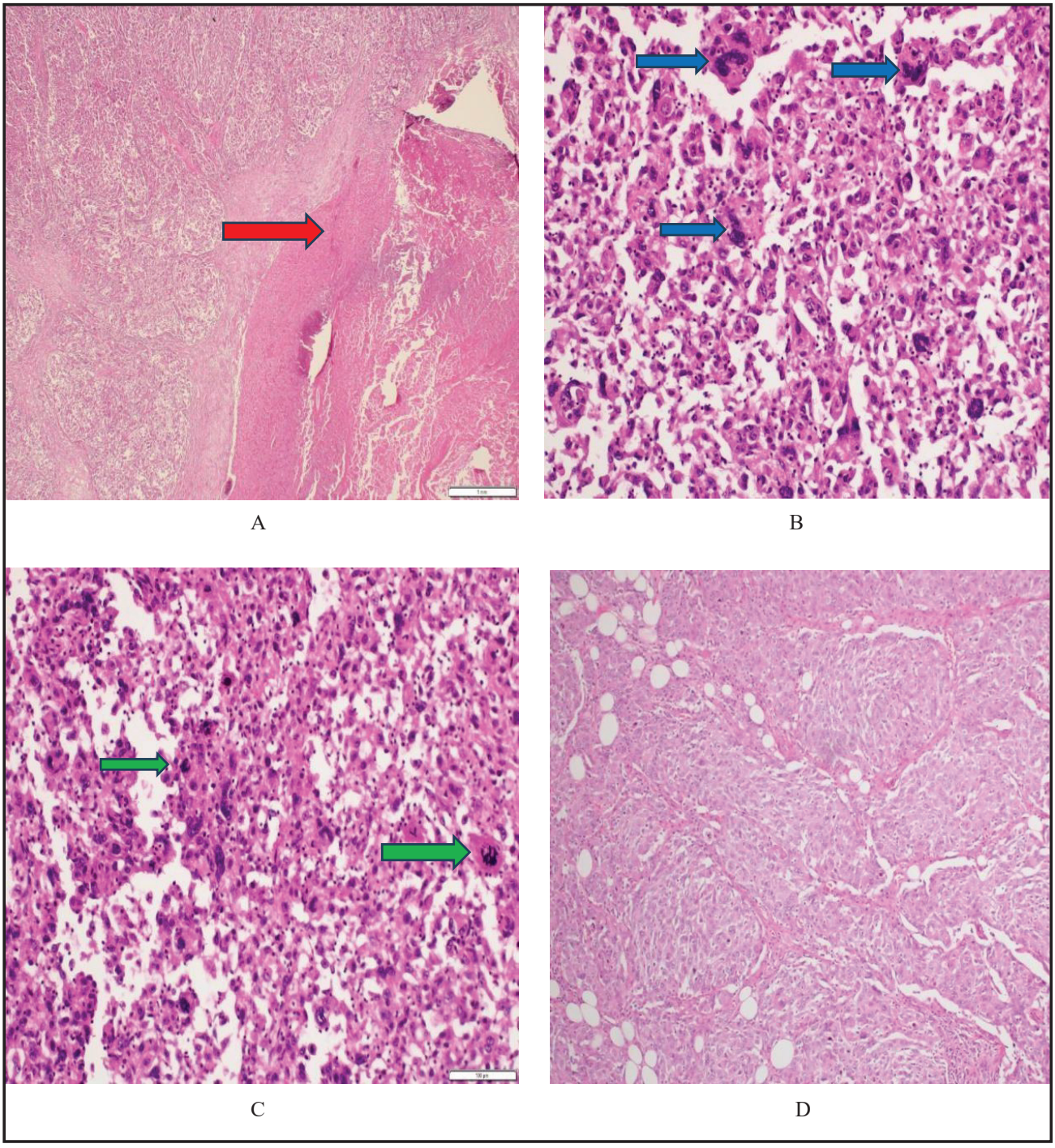

Figure 4. **A)** *Low power (4×) magnification showing the tumor on the left side and large area of necrosis (red arrow) on the right side.* **B)** *High power (20×) magnification of the tumor comprising pleomorphic epithelioid cells having copious eosinophilic cytoplasm and bizarre vesicular nuclei with prominent multinucleated forms (blue arrows).* **C):** *High power (20×) magnification showing tumor with readily identifiable mitotic figures, including atypical forms (green arrows).* **D)** *Low power (4×) magnification showing the tumor with a focal nesting growth pattern.*

the possibility that the lesion could perhaps present metastasis from an undisclosed primary elsewhere may need to be considered.

After the biopsy result and the malignancy was confirmed, the tumor board advised a staging CT scan (Figure 3) to search for any possible metastasis, or another source of primary neoplasm. The CT showed again a heterogeneous enhancing lesion in the left breast with an irregular outline, surrounded by fat stranding. In contrast to Mammogram and Ultrasound Scan, the CT was reported as having enlarged left axillary and subpectoral lymph nodes with absence of fat hila. No evidence of distant metastasis.

In this case, MDT also advised that a PET scan is advisable, but that was not done until after surgery due to maintenance issues.

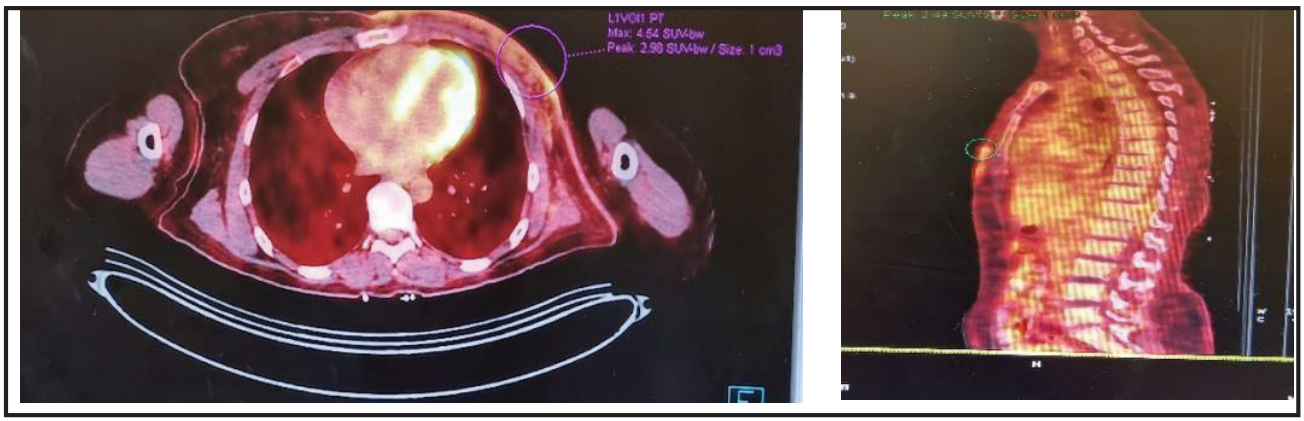

Figure 5. *Positron Emission Tomography-Scan with post-surgical changes and no another active lesion.*

In view of the staging CT report, PET scan delay, and the unpredicted chemotherapy response, the tumor board advised to go ahead with the surgery in the form of modified radical mastectomy (MRM).

The patient was consented later for (MRM) with a full explanation given about the pros and cons of the procedure. The procedure was uneventful, and the patient was discharged the following day with no immediate complications.

The histopathology report (Figure 4) released later showed a single solid lesion measuring 76 × 75 × 67 mm. The deep margin was the closest to the lesion and was 3 mm away.

Sections showed breast tissue with a well-circumscribed malignant neoplasm with nodular growth pattern separated by fibrous septa containing congested blood vessels and measuring 76 mm in maximum dimension. 19 lymph nodes were removed and studied: No evidence of lymph node involvement.

Extensive immunostains were attempted and show the tumor cells are positive for vimentin and CD4. They show multifocal positivity for LCA and CD31. There is weak non-specific positivity for CK14, including background staining with good internal control. They are negative for: Estrogen receptors, Progesterone receptors, Human Epidermal Growth Factor Receptor 2, AE1/3, MNF-116, Cam5.2, CK7, CK5/6, 34BE12, EMA, P63, Chromogranin, Synaptophysin, S100, E-cadherin, Desmin, MyoD1, CD34, CD30, CD20, CD3, CD5, CD8, PAX5, and ALK.

Tumor type: Pleomorphic undifferentiated epithelioid malignant neoplasm, high grade. Malignancy from another primary cannot be excluded. The slides were again sent to the expert opinion, who confirms the above.

TNM: T3N0M0

As part of the oncological study, PET-Scan was ordered (Figure 5) to look for another source. The patient underwent 18F-FDG whole body positron emission tomography with CT scan. It concludes that there are no Fluorodeoxyglucose avid lesions identified elsewhere with post-surgical changes in the left chest wall and left axillary region.

Multidisciplinary Team discussion advised for standard Triple-Negative Breast Cancer protocol chemotherapy with Epirubicin + Cyclophosphamide (4 Cycles) + Taxol/Carboplatin (12Xw). Then radiotherapy (RT) with Intensity-Modulated Radiotherapy using 6 MV photons to the left chest wall to a dose of 40 Gy/15.

Genetic testing was not performed, as current guidelines do not mandate routine germline testing for pleomorphic carcinoma in the absence of strong clinical or family history indicators. Additionally, this investigation was not pursued because it would not have altered the diagnosis or immediate management in this case.

Discussion

Definition and pathology of pleomorphic carcinoma

Pleomorphic carcinoma of the breast is a rare histologic subtype of invasive breast carcinoma of No Special Type. It is characterized by pleomorphic, bizarre, often multinucleated giant tumor cells showing marked nuclear atypia, eosinophilic cytoplasm, frequent atypical mitoses, and a disorganized architectural pattern [1-3].

Differential diagnosis

Given their cytologic and architectural features, pleomorphic carcinomas enter the differential diagnosis of multiple high-grade malignancies.

- High-grade sarcomas may show similar pleomorphism but usually lack epithelial marker expression.
- Malignant phyllodes tumors can resemble these lesions when stromal overgrowth dominates, although benign or atypical epithelial elements are typically present.

- Metastatic carcinomas from the lung, kidney, or gastrointestinal tract must also be excluded, particularly when breast markers are limited [2,4].

Diagnostic challenges and the role of IHC

In the present case, the pleomorphic cytology and lack of a specific architectural pattern initially raised concern for a metastatic or non-breast primary malignancy. Such diagnostic ambiguity underscores the indispensable role of comprehensive immunohistochemistry and imaging. Typical IHC markers confirming breast origin include broad-spectrum cytokeratins (AE1/AE3), EMA, GATA3, mammaglobin, and GCDFP-15 [5-7]. By contrast, expression of vimentin, desmin, or S100 may suggest mesenchymal or myoepithelial differentiation, assisting in differential diagnosis [8].

We included GATA-3 as part of the immunohistochemical panel for breast-primary–specific markers, but it showed loss of reactivity, which is expected in high-grade triple-negative breast carcinomas. Because the case was referred for expert opinion, claudin-4 immunostaining was also performed and demonstrated strong positivity, highly supportive of epithelial differentiation.

The focal positivity for LCA, CD34, and CD31 was considered non-specific and likely attributable to antigen cross-reactivity. Nevertheless, this finding was not disregarded; therefore, a comprehensive panel of T- and B-cell markers, along with other lymphoma-specific markers such as CD30 and ALK, was undertaken to assess for a possible lymphoma. All these markers were negative.

Given the unusual tumor morphology for primary breast carcinoma, metastatic disease was considered.

The patient subsequently underwent extensive radiological evaluation, including PET and Computed Tomography imaging, which demonstrated no lesions other than the breast mass and ipsilateral axillary lymph nodes, supporting a breast primary. This approach aligns with current oncologic recommendations that all undifferentiated tumors of uncertain origin should be fully staged to exclude metastases from hidden primaries such as lung, kidney, or gastrointestinal tract [9,10].

Although genetic testing can occasionally provide additional context in triple-negative tumors, it was not performed in this case; however, this did not affect diagnostic certainty or therapeutic planning.

Treatment strategies

Because of the scarcity of reported cases, there is no standardized treatment protocol for pleomorphic carcinoma of the breast. Management is typically extrapolated from that of TNBC or poorly differentiated NST carcinomas [11]. Surgical excision with clear margins remains the cornerstone of therapy; MRM is frequently chosen due to large tumor size and uncertain nodal status [12,13]. In our case, a MRM was an appropriate choice, both due to tumor size and uncertain preoperative nodal status.

The role of adjuvant systemic therapy remains ill-defined. Most pleomorphic carcinomas are ER-negative, PR-negative, and HER2-negative, aligning them with the TNBC subtype [2,12]. Consequently, standard TNBC chemotherapy regimens are typically recommended. Recent studies in TNBC suggest that platinum-based regimens and immune checkpoint inhibitors (e.g., pembrolizumab) improve outcomes and may represent future therapeutic avenues for pleomorphic variants [3,14]. These principles were applied in our case. As the tumor was a TNBC, MDT recommended standard chemotherapy Doxorubicin (Adriamycin) + Cyclophosphamide followed by Paclitaxel with platinum.

Because of the extreme rarity of pleomorphic carcinoma, no specific evidence-based guidelines exist for post-operative RT. MDT recommended RT as per the size of the tumor, the age of the patient.

Prognostic implications

Despite initial responsiveness, pleomorphic carcinomas demonstrate high recurrence rates and poorer overall survival compared with conventional invasive ductal carcinoma [1,11,12]. In the available scarce published series, survival is significantly lower than that of standard NST carcinoma, even after controlling for stage [1,15]. The patient has shown no evidence of recurrence after 4 years of follow-up.

Lessons to be learnt

Finally, this case contributes to the limited literature on pleomorphic breast carcinoma and reinforces the need for national and international tumor registries dedicated to rare breast cancer subtypes. Such registries would enable aggregation of data, facilitate molecular characterization, and guide evidence-based therapeutic strategies in this challenging entity.

Conclusion

Pleomorphic carcinoma of the breast poses significant diagnostic challenges due to its marked cytologic atypia and potential overlap with sarcomatoid or metastatic malignancies. Accurate classification relies on a comprehensive immunohistochemical workup integrated with appropriate imaging to exclude alternative primaries. Given the tumor's rarity and the absence of standardized treatment protocols, management must be individualized and guided through close collaboration among pathologists, radiologists, surgeons, and oncologists. This case underscores the essential role of multidisciplinary evaluation when approaching uncommon and diagnostically complex breast tumors.

What is new

- This case report describes an extremely rare breast cancer entity.
- It adds value to the need for more of such cases, so we can understand this cancer in a better way and may change the current classification.

List of Abbreviations

AC-T	Adriamycin (Doxorubicin) and Cyclophosphamide, followed by a Taxane
CT	Computed Tomography
ER	Estrogen Receptor
FDG	Fluorodeoxyglucose
IMRT	Intensity-Modulated Radiation Therapy
MDT	Multidisciplinary Team
PET	Positron Emission Tomography
PET-CT	Positron Emission Tomography-Computed Tomography
PR	Progesterone Receptor
UOQ	Upper Outer Quadrant
USS	Ultrasound Scan

Conflict of interests

The authors declare that there is no conflict of interest regarding the publication of this article.

Funding

None.

Consent for publication

The patient was called and she approved the publication of the case including the images and the information. She gave verbal consent by phone as she lives in a different city. The conversation was documented in her file.

Ethical approval

Ethical approval is not required at our institution to publish an anonymous case report.

Author contributions

Rudainy Kaddoura: Principal investigator; conceptualized the study, collected and analyzed data, and led manuscript writing and literature review.Hiba Al Mahruqi: Assisted in study design, data analysis, and manuscript preparation.Salim Al Rahbi: Supported literature review. Supervised the surgery part.Zakiya Al Ajmi: Supervised the pathology part, provided and edited the required imaging.

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Summary of the case

1	Patient (gender, age)	39 years, female
2	Final diagnosis	Breast undifferentiated carcinoma
3	Symptoms	Breast mass
4	Medications	Chemotherapy
5	Clinical procedure	Surgery followed by chemo
6	Specialty	General surgery, breast surgery, breast oncology