

Double Diagnostic Dilemma in Metaplastic Breast Carcinoma

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Abstract

Metaplastic breast carcinoma is a rare and aggressive subtype of breast cancer. It is characterized by the differentiation of epithelial cells into mesenchymal components and often presents as a triple-negative phenotype. Its varied histomorphology can resemble sarcoma or lymphoma, making diagnosis difficult. We will be discussing a case of a 50-year-old woman with a right breast mass and multiple fluorodeoxyglucose (FDG)-avid splenic lesions on PET/CT, which initially suggested a metastatic disease or a disseminated lymphoma. Histopathology of the breast specimen revealed a metaplastic carcinoma with pleomorphic and spindle cell features. The splenic biopsy showed non-tuberculous granulomatous inflammation. This case highlights a diagnostic challenge involving both histological similarities and imaging pitfalls. It emphasizes the importance of tissue diagnosis in FDG-avid lesions to prevent over-staging.

Categories: Nuclear Medicine, Radiology

Keywords: disseminated malignancy, fdg pet/ct, lymphoma, metaplastic breast carcinoma, splenic granuloma

Introduction

While the vast majority of breast neoplasms arise from the glandular epithelium, a rare subset involves a divergent process known as metaplasia. In these cases, the glandular lineage transforms into non-glandular, mesenchymal tissue. Metaplastic breast carcinoma (MBC), a unique variant of invasive ductal carcinoma, is characterized by this cellular transition, often manifesting as squamous differentiation, spindle-cell architecture, or various heterologous mesenchymal components. It accounts for 0.2 % of all breast cancers [1,2].

Clinically, MBC is associated with a poorer prognosis compared to more common variants like invasive ductal carcinoma. It typically presents with larger tumor sizes at diagnosis, a higher histological grade, and an increased propensity for both local recurrence and distant hematogenous metastasis. Furthermore, these tumors are predominantly triple-negative and often necessitate an aggressive multimodal treatment approach.

Fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) has a low sensitivity and specificity in the initial detection of primary breast malignancy and is commonly used for staging and evaluation of response to therapy. Apart from the uptake in tumor cells, FDG activity is also seen in inflammatory and granulomatous conditions [3]. This can result in false-positive interpretations and over-staging.

Case Presentation

Initial presentation and clinical history

A 50-year-old female presented with a rapidly enlarging, palpable lump in her right breast. Initial histopathological evaluation at an external facility revealed a high-grade malignant neoplasm with pleomorphic cells, favouring metaplastic breast carcinoma. The patient was subsequently referred to our tertiary centre for FDG PET/CT staging and further management.

Imaging findings

Fluorodeoxyglucose PET/CT showed an intensely FDG-avid irregular mass in the right breast (maximum standardized uptake value (SUV max) ~17) extending to the skin (Figure 1).

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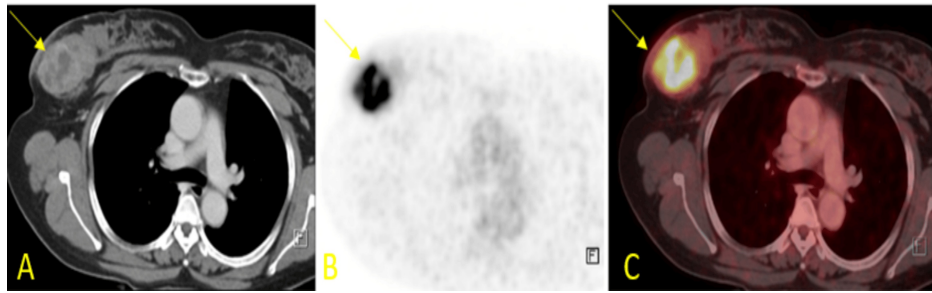


FIGURE 1: Imaging findings - right breast

A. Axial contrast-enhanced CT image showing an irregular heterogeneously enhancing mass lesion (yellow arrow) measuring 5.9 x 5.3 cm in the upper-outer quadrant of the right breast. B. Axial PET image showing increased radiotracer uptake in the right breast lesion (yellow arrow). C. Axial fused PET/CT imaging showing intense fluorodeoxyglucose (FDG) avidity (maximum standardized uptake value (SUV max) 17.0) in the right breast lesion (yellow arrow).

Additional findings included multiple FDG-avid splenic lesions (SUV max up to 11.2) (Figure 2) and abdominal lymphadenopathy (in periportal regions) (Figure 3). No other FDG-avid lesion was found elsewhere in the body. Given the unusually high metabolic activity and the atypical distribution in the splenic and abdominal lymph nodes, the differential diagnosis was narrowed to metastatic metaplastic carcinoma versus a disseminated lymphoma.

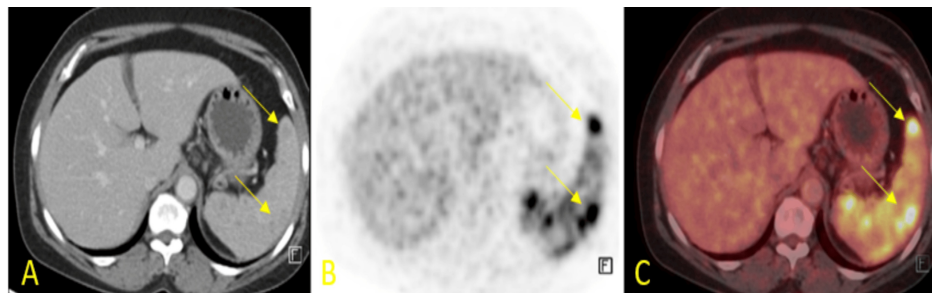


FIGURE 2: Imaging findings - spleen

A. Axial contrast-enhanced CT image showing multiple hypodense lesions (yellow arrows) in the spleen. B. Axial PET image showing increased radiotracer uptake in the splenic lesions (yellow arrows). C. Axial fused PET/CT imaging showing intense Fluorodeoxyglucose (FDG) avidity (maximum standardized uptake value (SUV max) 11.2) in the splenic lesions (yellow arrows).

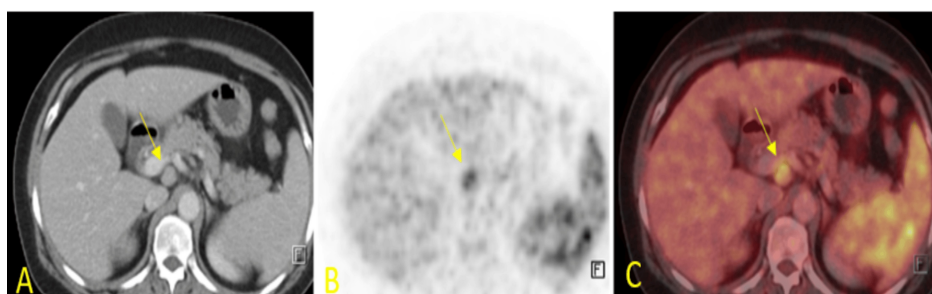


FIGURE 3: Imaging findings - lymph node

A. Axial contrast-enhanced CT image showing an enlarged lymph node (yellow arrow) measuring 11 x 12 mm in the periportal region. B. Axial PET image showing increased radiotracer uptake in the periportal lymph node (yellow arrow). C. Axial fused PET/CT imaging showing fluorodeoxyglucose (FDG) avid (maximum standardized uptake value (SUV max 3.2)) periportal lymph node.

Diagnostic workup and histopathology

Due to the prognostic implications of systemic spread, a multidisciplinary decision was made to perform a

repeat biopsy of the breast mass and a targeted biopsy of the splenic lesions.

Breast Histopathology

Histopathological examination of the breast mass identified a high-grade malignant tumor made up of pleomorphic and spindle-shaped cells with significant nuclear atypia (Figure 4A). Immunohistochemical (IHC) staining confirmed the diagnosis by revealing a characteristic multi-lineage expression profile. The tumor demonstrated a triple-negative phenotype, testing negative for estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2/neu). The biphasic nature of the malignancy was evidenced by positivity for epithelial markers (pan-cytokeratin) alongside intense, diffuse staining for mesenchymal/stromal markers (vimentin and CD10). The myoepithelial marker p63 showed the invasive nature of the tumor, establishing the diagnosis as metaplastic spectrum. To refine the differential diagnosis, the pan-endothelial marker erythroblast transformation-specific-related gene (ERG) and the lymphoid marker CD45 were both negative, successfully ruling out angiosarcoma and lymphoma, respectively (Figure 4B, 4C, 4D).

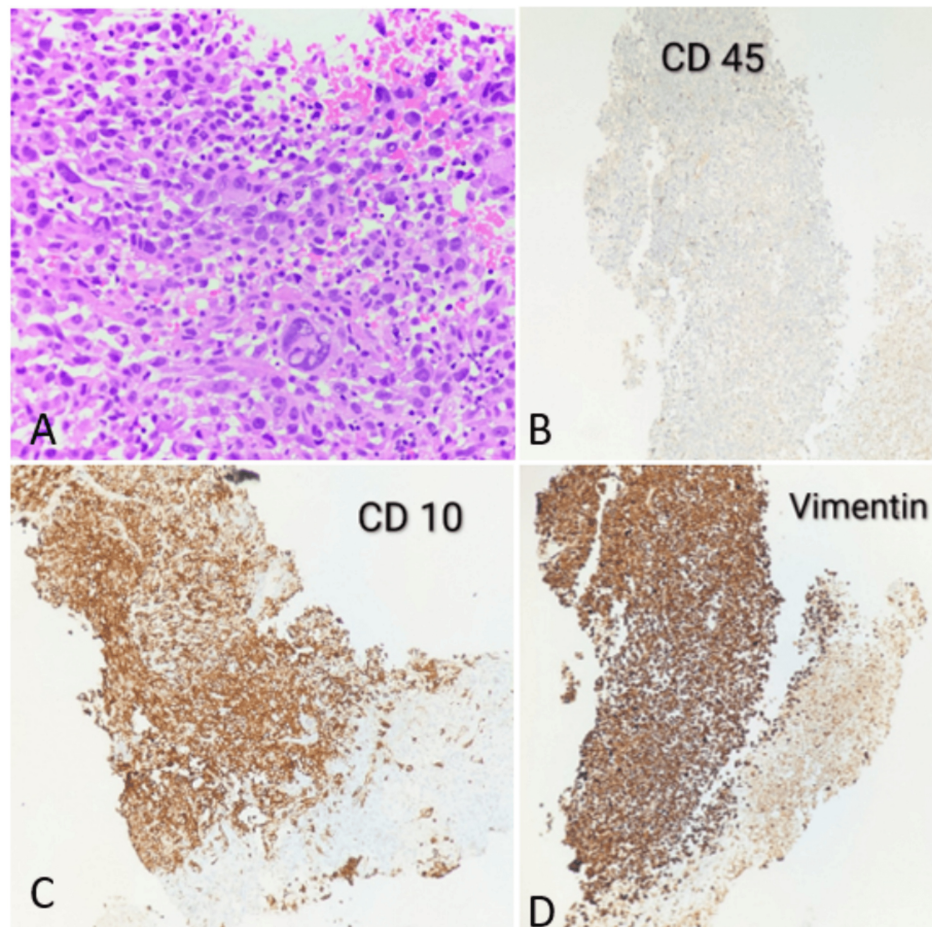


FIGURE 4: Breast histopathology

A. Hematoxylin and eosin stain (10x magnification) of breast biopsy shows a linear core of breast parenchyma with infiltration by markedly pleomorphic malignant cells arranged in sheets with atypical mitotic figures. B. CD 45 Immunohistochemistry stain (10x magnification): negative (rules out lymphoma). C. CD 10 Immunohistochemistry stain (10x magnification): positive (stromal marker). D. Vimentin immunohistochemistry stain (10x magnification): positive (mesenchymal marker associated with aggressive and high-grade tumors).

Splenic Histopathology

Surprisingly, histopathological examination of the splenic lesions revealed granulomatous inflammation with no evidence of malignant cells (Figure 5). Further laboratory testing for *Mycobacterium tuberculosis* was negative.

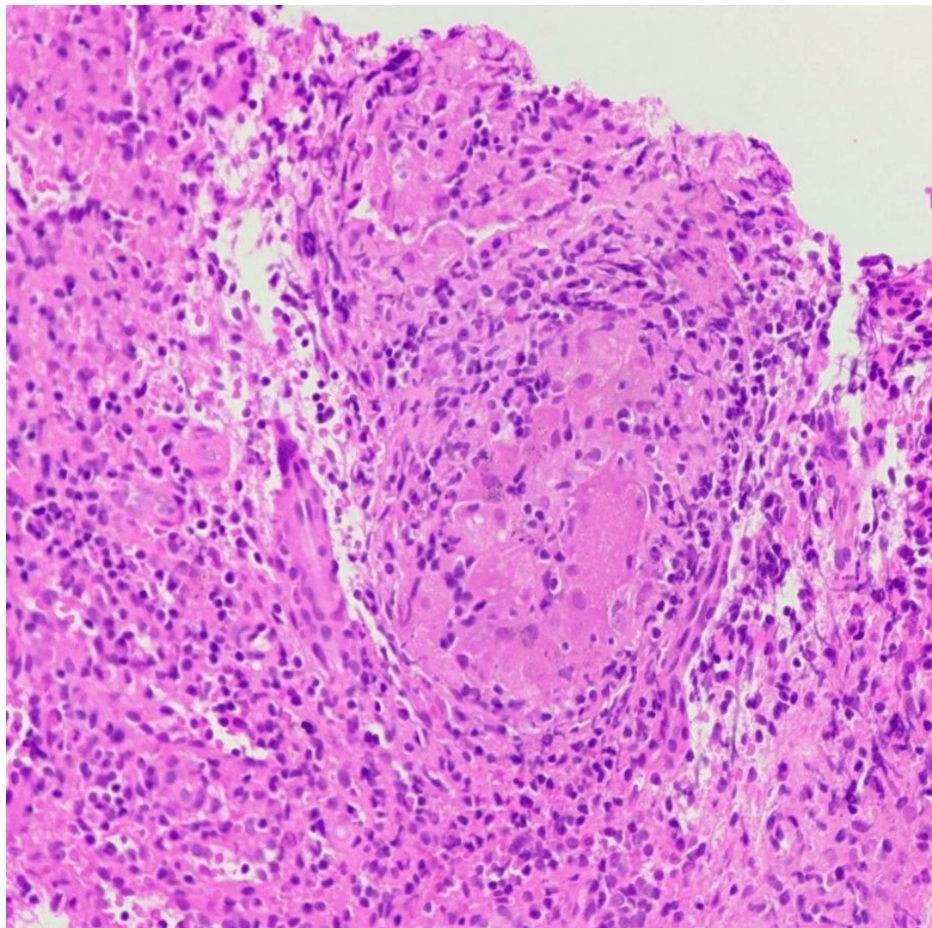


FIGURE 5: Splenic histopathology

Hematoxylin and eosin stain (10x magnification) of spleen biopsy shows ill-defined granulomas composed of epithelioid histiocytes and foamy macrophages.

A final diagnosis of metaplastic breast carcinoma with coexisting reactive granulomas of the spleen was established.

Treatment

The management of the patient was coordinated through a multidisciplinary tumor board. By ruling out distant metastasis, the patient's clinical stage was established as cT4bN0M0.

The board prioritized treatment of the primary metaplastic breast carcinoma with a conservative approach for the abdominal findings based on the following diagnostic evidence.

Histopathology: Splenic biopsy confirmed granulomatous inflammation with no evidence of malignancy.

Infection Screening: Clinical and laboratory parameters did not support an infectious etiology; specifically, screening for tuberculosis (acid-fast bacillus (AFB) staining, GeneXpert® (Cepheid, Sunnyvale, USA), mycobacteria growth indicator tube (MGIT), and Mantoux) was negative.

Systemic Evaluation: The patient was asymptomatic for systemic sarcoidosis, and the serum angiotensin-converting enzyme (ACE) level was normal (25 U/L).

Patient is now on a neoadjuvant chemotherapy (NACT) regimen consisting of four cycles of doxorubicin and cyclophosphamide, followed by four cycles of docetaxel, each cycle given every 21 days, after which the patient is planned for a modified radical mastectomy (MRM).

Given that neither malignancy nor active infection was present, no anti-tubercular or steroid therapy was initiated for the spleen lesions. The lesions are currently being monitored via serial follow-up during the course of systemic therapy.

Discussion

Metabolic characteristics and differential diagnosis

The intensity of tracer uptake in breast malignancies is highly variable and depends on the underlying tumor biology. Many common breast tumors (like invasive lobular carcinoma) exhibit lower FDG avidity due to lower tumor cell density, a more diffuse growth pattern, or a lower expression of glucose transporter proteins like GLUT1.

In contrast, metaplastic breast carcinomas and high-grade lymphomas share an inherently aggressive biology that drives distinctly high SUV values (ranging from 6.2 to 18.9)[4]. In our case, the patient's primary lesion demonstrated an SUV of 17.0. Such extreme metabolic activity in MBC is because of its high-grade (Grade 3), triple-negative phenotype and p53 mutations [4]. High tumor cell density and rapid growth are responsible for high SUV in high-grade lymphomas.

The presence of similarly intense FDG avidity in the spleen (SUV max 11.2) blurred the diagnostic lines in our case. In inflammatory and granulomatous states, activated immune cells undergo a significant metabolic shift, upregulating glucose transporter receptors (specifically GLUT1 and GLUT3) to meet the high energy demands of the inflammatory response [3,5]. This intense FDG avidity within granulomatous lesions can mimic the appearance of metastatic disease and frequently leads to false-positive interpretations on PET/CT.

Staging challenges

The systemic pattern on PET/CT in this case strongly mimicked high-grade lymphoma, which involves the spleen in 30-40% of patients at the time of diagnosis. In lymphoma, splenic involvement often leads to upstaging, necessitating an immediate escalation to more aggressive chemotherapy [6].

In contrast, breast carcinoma, including metaplastic carcinoma, most often spreads to bone, liver, and lungs, with splenic metastasis being relatively rare [7]. Metaplastic carcinomas typically present as a larger tumor with lower rates of axillary lymphadenopathy compared to invasive ductal carcinomas. They predominantly exhibit a triple-negative phenotype (ER/PR/HER2-negative), a molecular profile characterized by increased glucose transporter (GLUT1) expression and high metabolic turnover, which is responsible for its high FDG activity [8].

Histopathological similarities

Metaplastic breast carcinomas show significant diversity and are divided into three groups based on their components: epithelial type, which presents as pure squamous cell carcinoma (SCC) or a mixed adenocarcinoma and squamous cell carcinoma; biphasic type, which displays a combined carcinomatous (adenocarcinoma/SCC) and sarcomatoid/spindle cell components; and the monophasic type, characterized exclusively by sarcomatoid or spindle cell morphology [9].

These patterns can closely mimic sarcoma or lymphoma, particularly in small biopsy specimens, requiring immunohistochemical markers for origin confirmation.

Conclusions

While PET/CT is a powerful tool for staging, this case serves as a reminder that intense metabolic activity is not always synonymous with malignancy. The rare nature of metaplastic breast carcinoma, combined with the metabolic mimicry of granulomatous inflammation, can easily lead to a false-positive diagnosis of Stage IV disease. FDG-avid lesions in atypical locations, such as the spleen, should be interpreted with caution, and histopathological confirmation is crucial. By correlating imaging findings with detailed IHC markers, we can avoid the trap of over-staging, ensuring that a potentially curable breast cancer isn't mismanaged as an incurable systemic spread.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Acquisition, analysis, or interpretation of data: Moniga Shree Murugesan, Minmini Selvam, Venkata Sai, Gayathri Kuppusamy, Subalakshmi Balasubramanian

Drafting of the manuscript: Moniga Shree Murugesan

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Supervision: Venkata Sai

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

References

1. Türkan H, Gökgöz MŞ, Parlak NS: Metaplastic breast cancer. *J Breast Health*. 2016, 12:47-9. [10.5152/tjbh.2015.2505](#)
2. Günhan-Bilgen I, Memiş A, Ustün EE, Zekioglu O, Ozdemir N: Metaplastic carcinoma of the breast: clinical, mammographic, and sonographic findings with histopathologic correlation. *AJR Am J Roentgenol*. 2002, 178:1421-5. [10.2214/ajr.178.6.1781421](#)
3. Mbakaza O, Vangu MW: (18)F-FDG PET/CT imaging: normal variants, pitfalls, and artifacts musculoskeletal, infection, and inflammation. *Front Nucl Med*. 2022, 2:847810. [10.3389/fnume.2022.847810](#)
4. Dong A, Wang Y, Lu J, Zuo C: Spectrum of the breast lesions with increased 18F-FDG uptake on PET/CT. *Clin Nucl Med*. 2016, 41:543-57. [10.1097/RLU.0000000000001203](#)
5. Vaidyanathan S, Patel CN, Scarsbrook AF, Chowdhury FU: FDG PET/CT in infection and inflammation--current and emerging clinical applications. *Clin Radiol*. 2015, 70:787-800. [10.1016/j.crad.2015.03.010](#)
6. Saboo SS, Krajewski KM, O'Regan KN, Giardino A, Brown JR, Ramaiya N, Jagannathan JP: Spleen in haematological malignancies: spectrum of imaging findings. *Br J Radiol*. 2012, 85:81-92. [10.1259/bjr/31542964](#)
7. Donato H, Candelária I, Oliveira P, Gonçalves M, Caseiro-Alves F: Imaging findings of metaplastic carcinoma of the breast with pathologic correlation. *J Belg Soc Radiol*. 2018, 102:46. [10.5334/jbsr.1386](#)
8. Kim HJ, Kim SY, Huh S: Multimodality imaging findings of metaplastic breast carcinomas: a report of five cases. *Ultrasound Q*. 2018, 34:88-93. [10.1097/RUQ.0000000000000340](#)
9. Tse GM, Tan PH, Putti TC, Lui PC, Chaiwun B, Law BK: Metaplastic carcinoma of the breast: a clinicopathological review. *J Clin Pathol*. 2006, 59:1079-83. [10.1136/jcp.2005.030536](#)