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Reassessing a hypermetabolic splenic lesion in breast cancer: PET/CT findings and insights from multimodal imaging and multidisciplinary evaluation

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Abstract

Background [^{18}F]FDG PET/CT is commonly employed for staging and response assessment in breast cancer, yet splenic metastases are exceptionally rare. Hypermetabolic splenic lesions on PET/CT often provoke concern for distant spread but may reflect benign vascular anomalies. Distinguishing treatment-responsive metastases from mimics, such as atypical hemangiomas, poses a diagnostic challenge, particularly when biopsy is impractical.

Case presentation A 39-year-old woman with newly diagnosed HER2-positive invasive ductal carcinoma underwent baseline PET/CT, revealing an intensely FDG-avid splenic nodule (SUVmax 6.5). Abdominal MRI demonstrated a 16 mm lesion without diffusion restriction and progressive post-contrast enhancement, suggestive of an atypical hemangioma. She received nine cycles of neoadjuvant carboplatin, docetaxel, pertuzumab, and trastuzumab. Interim PET/CT and MRI after chemotherapy showed complete metabolic resolution of the splenic focus and nodule shrinkage to 5 mm, with preserved benign imaging features.

Conclusion Multimodal imaging combined with multidisciplinary consensus can help clarify uncertain [^{18}F]FDG PET/CT findings and avoid unnecessary changes in management when percutaneous biopsy is impractical. However, histopathology remains the definitive diagnostic standard, and the diagnosis in this case is presumptive in the absence of tissue confirmation.

Keywords Breast cancer, PET/CT, Metabolic imaging, Spleen, Hemangioma

Introduction

2-[^{18}F]fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography ([^{18}F]FDG PET/CT) plays a pivotal role in staging and response assessment in breast cancer, enabling early detection of occult nodal or distant disease and providing insight into tumor chemosensitivity [1]. While the liver, bones, lungs, and brain represent common sites of distant spread, splenic metastases are exceedingly rare [2, 3]. In a large autopsy study of 1,898 patients with malignant tumors, splenic metastases were observed in 3.0% of cases. Lung cancer (24.6%), cutaneous malignant melanoma (15.8%), and breast cancer (12.3%) were the most frequent primary tumors leading to splenic metastases [4]. Hypermetabolic

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splenic lesions identified on PET/CT thus raise a broad differential, often favoring benign etiologies such as hemangiomas or granulomatous disease over metastatic involvement. However, MRI characterization may remain indeterminate, particularly in the case of atypical vascular lesions.

Here, we describe a case of HER2-positive breast cancer in which an isolated hypermetabolic splenic lesion seen on baseline PET/CT was initially suspicious for metastasis. Subsequent magnetic resonance imaging (MRI) features favored an atypical hemangioma. The lesion's progressive reduction during chemotherapy was ultimately considered suggestive of a PET/CT false positive, highlighting the important role of multidisciplinary interpretation in distinguishing true metastases from benign mimics.

Case presentation

A 39-year-old woman with a strong family history of skin cancers underwent routine breast screening. Her medical history included uterine fibromatosis treated with estrogen–progestin therapy. She was otherwise healthy, a non-smoker, and had no drug allergies. Initial mammography was unremarkable, but a later ultrasound showed a 30 mm hypoechoic mass in the left breast with abnormal lymph nodes in the ipsilateral axillary and supraclavicular regions. Core-needle biopsy confirmed invasive ductal carcinoma, NOS. MRI revealed a 30×20×42 mm irregular, spiculated lesion with necrotic features extending into the axilla, nodal involvement, and a suspicious adjacent 14 mm nodule. No contralateral lesions were found, and BRCA1/2 testing was negative.

A baseline [^{18}F]FDG PET/CT (GE Discovery Molecular Insights—DMI PET/CT, GE Healthcare) performed 60 min post-injection of 3.7 MBq/kg. [18F]FDG showed intense uptake (maximum standardized uptake value/SUVmax 14.5) in the primary breast lesion. Adjacent to the primary lesion, a small hypermetabolic focus (SUVmax 8.5) was identified, compatible with a satellite lesion. Several metabolically active lymph nodes were observed in the axillary, supraclavicular, and retropectoral regions (SUVmax 5.5–8.6), as shown in Fig. 1. Notably, a hypermetabolic lesion (SUVmax 6.5) was detected at the anterior pole of the spleen, corresponding on CT to a 16 mm hypodense nodule—raising concern for a solitary distant metastasis. An abdominal MRI revealed a round, 16 mm

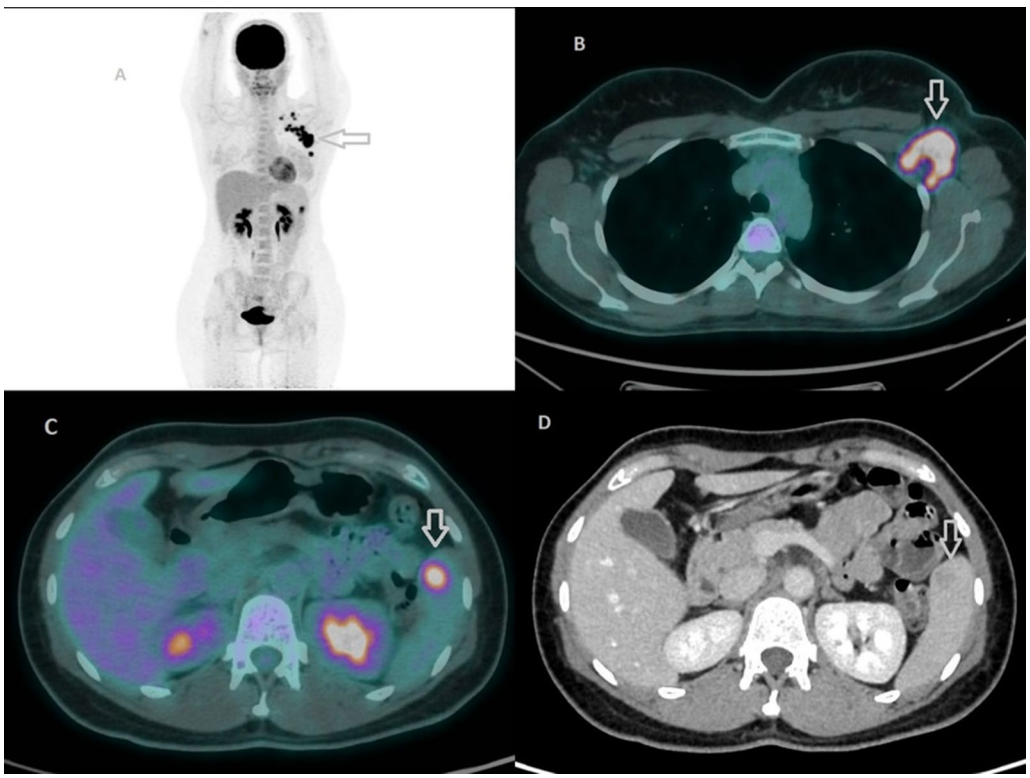

Fig. 1 **A** Maximum intensity projection (MIP) and **B** fused PET/CT axials from the [^{18}F]FDG PET/CT scan demonstrate intense radiotracer uptake in multiple axillary, supraclavicular, and retropectoral metabolically active lymph nodes (arrow). [18F]FDG PET/CT axial slices show a hypermetabolic lesion at the anterior pole of the spleen **C**, corresponding on CT to a 16 mm hypodense nodule, with hypodense core and rim-enhancement **D** (arrow)

vascular lesion at the anterior-inferior pole of the spleen. The lesion showed no restricted diffusion and demonstrated progressive post-contrast filling—radiologically suggestive of an atypical hemangioma rather than a metastasis (Fig. 2). Given the known overlap between imaging features of benign and malignant splenic lesions, particularly in hypervascular tumors, the finding remained uncertain.

The patient was clinically staged as cT2N3 HER2-positive breast cancer (ER+, PR+, Grade 3), and the multidisciplinary tumor board recommended neoadjuvant chemotherapy with six cycles of carboplatin (AUC 6) and docetaxel (75 mg/m^2), along with fixed-dose pertuzumab and trastuzumab every 21 days.

Follow-up [^{18}F]FDG PET/CT (four months after therapy initiation) demonstrated a marked metabolic and morphological response: the primary lesion had shrunk to 12 mm with a corresponding SUVmax reduction to 1.3, and previously involved lymph nodes no longer showed abnormal uptake (Fig. 3). Critically, the previously hypermetabolic splenic lesion was no longer visible on PET/CT. Concurrent MRI showed further shrinkage of the splenic nodule to 5 mm, with preserved benign imaging characteristics (i.e., hypointense on all sequences and hypovascular after contrast administration, likely of nonspecific significance), as depicted in Fig. 4.

Given these findings—and supported by reports in the literature indicating that atypical hemangiomas may exhibit [^{18}F]FDG uptake and also regress under systemic therapy—the multidisciplinary team concluded that the splenic lesion most likely represented a benign, atypical hemangioma rather than a metastasis. The initial [^{18}F]FDG uptake was thus interpreted as a possible false positive. The patient continued to tolerate therapy well, with persistent but improving cutaneous edema. To maximize tumor downstaging before surgery, neoadjuvant chemotherapy was extended to nine total cycles, with the last dose administered on June 11, 2025. Breast MRI and US showed persistent response to treatment.

Discussion

In this case report, we highlight the dual-edged utility of [^{18}F]FDG PET/CT in the management of breast cancer, illustrating both its strengths in staging and response assessment and its pitfalls related to specificity. The role of [^{18}F]FDG PET/CT in breast cancer has been increasingly recognized, particularly for phenotypes characterized by high glycolytic activity—namely triple-negative and "HER2-enriched" subtypes [1, 5, 6]. The Phergain study prospectively demonstrated that changes in [^{18}F]FDG uptake during neoadjuvant therapy can guide adaptive treatment strategies, improving pathological complete response rates in HER2-positive disease [7]. This study underscored the prognostic importance of metabolic response on interim PET and validated [^{18}F]FDG PET/CT as a decision-making tool during treatment.

However, [^{18}F]FDG PET/CT is not without limitations. Focal FDG-avid splenic lesions encompass a wide differential, including benign vascular entities such as cavernous or capillary hemangiomas, sclerosing angiomatoid nodular transformation (SANT), and less common vascular neoplasms like hemangioendothelioma [8, 9]. Other considerations include inflammatory or granulomatous disorders (e.g., sarcoidosis, tuberculosis, other mycobacterial or fungal infections), infectious abscess, hematologic involvement by lymphoma or leukemia, and metastatic disease. Several benign entities (notably SANT and atypical hemangiomas) can show variable FDG uptake and overlapping cross-sectional features, which complicate noninvasive diagnosis [10, 11]. Histopathology remains the reference standard for definitive diagnosis, but percutaneous splenic biopsy carries bleeding and sampling-error risks and may be impractical for small lesions—therefore, tailored integration of imaging

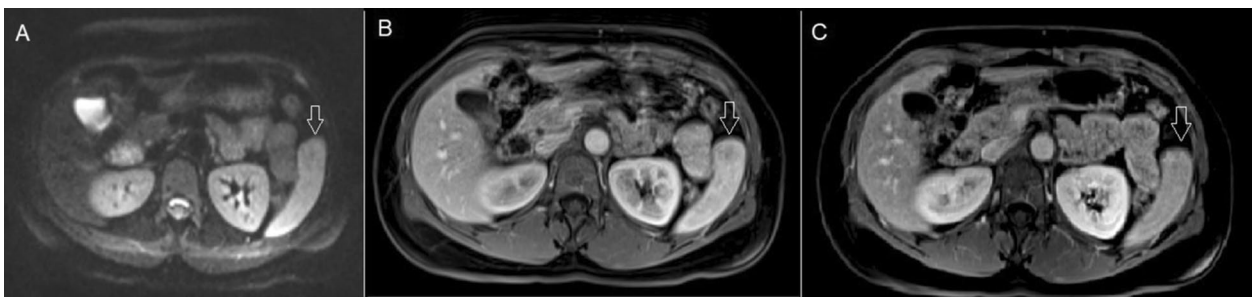

Fig. 2 **A** Axial diffusion-weighted MRI showing homogeneous high signal in the spleen without focal restricted diffusion (arrow). **B** Early post-contrast axial T1-weighted image demonstrates an ovoid hypointense lesion at the anterior splenic pole (arrow). **C** Delayed post-contrast axial T1-weighted image reveals progressive filling on the tardive acquisition (arrow)

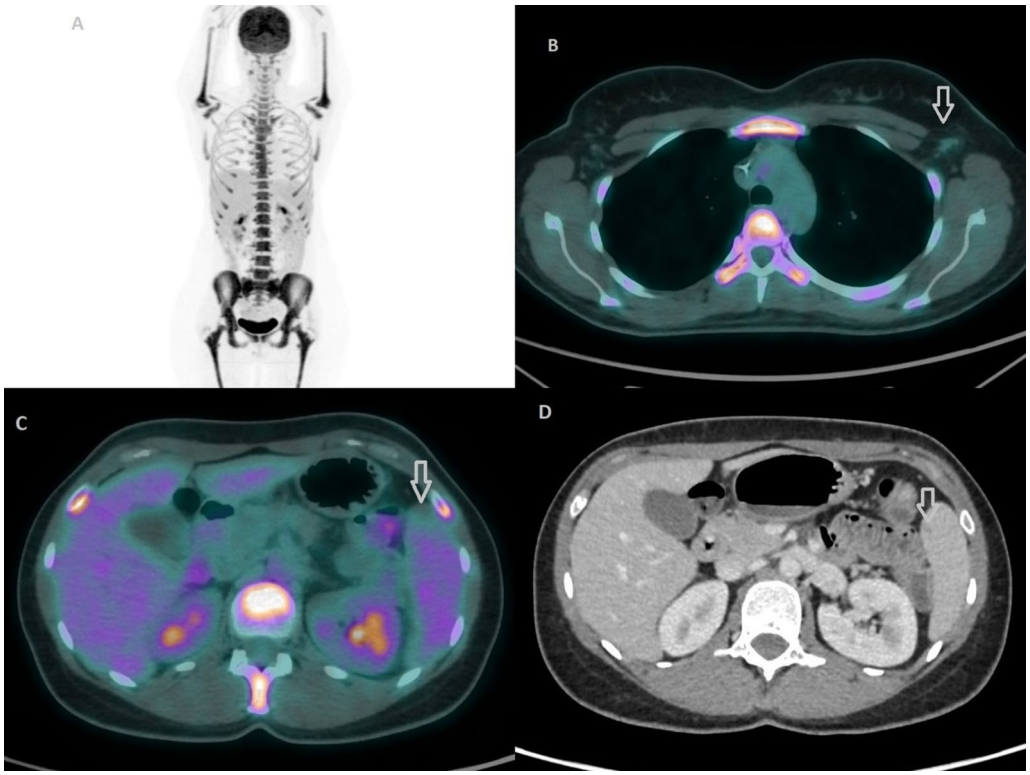

Fig. 3 **A** Follow-up [^{18}F]FDG PET/CT demonstrates marked metabolic and morphological response. **B** PET/CT axials show that the primary lesion has shrunk and previously involved lymph nodes no longer show abnormal uptake (arrows); notably, an intense tracer uptake was evident in the bone marrow, as for chemotherapy-induced activation. **C** Fused axial PET/CT shows that the previously hypermetabolic splenic lesion was no longer visible (arrow); **D** abdominal CE-CT also showed a meaningful reduction in size of the splenic lesion

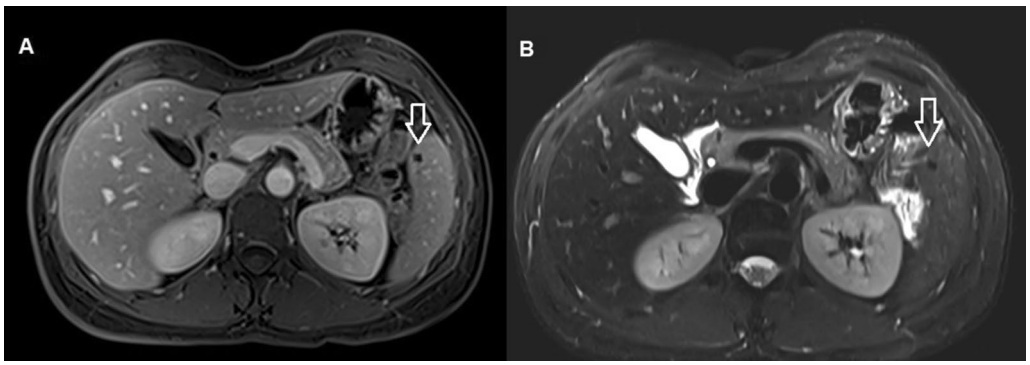

Fig. 4 Follow-up MRI shows further shrinkage of the splenic nodule, with preserved benign imaging characteristics, and hypointensity at both axial T1-weighted fat-suppressed post-contrast **A** and axial T2-weighted fat-suppressed sequences **B**, likely of nonspecific significance

features, clinical context, and multidisciplinary review is often required when tissue is not available.

A major drawback of [^{18}F]FDG PET/CT is its limited specificity. [^{18}F]FDG uptake is not tumor-specific, and many benign processes—including inflammation, infection, and vascular lesions—can exhibit significant tracer accumulation. Large retrospective series and case reviews have similarly emphasized that splenic involvement by breast cancer is an uncommon event, with a pooled prevalence well below 1% across thousands of PET/CT studies [12, 13]. Consequently, the evidence of an FDG-avid splenic nodule in a breast cancer patient almost always prompts consideration

of benign etiologies, with vascular anomalies such as hemangiomas ranking high on the differential.

In this context, MRI and contrast CT provide complementary morphologic and enhancement information to PET metabolic data. Typical cavernous hemangiomas usually appear markedly T2-hyperintense and demonstrate peripheral nodular enhancement with progressive centripetal fill-in on delayed phases (CT or MRI), while they may be variably FDG-avid [14]. SANT, although rare, often shows a characteristic spoke-wheel or star-shaped enhancement with a central fibrous scar and persistent delayed enhancement. In addition, on MRI, SANT may be heterogeneous with lower T2 signal centrally [15]. On PET/CT, both SANT and atypical vascular lesions can show increased [^{18}F]FDG uptake, limiting specificity [10, 11]. Thus, enhancement pattern, diffusion behavior, and clinical context are the most useful MRI/CT discriminators, while PET adds sensitivity for metabolic activity but not reliable lesion-type specificity. In this regard, quantitative PET-derived parameters may help in distinguishing benign from malignant lesions. In particular, an SUV threshold of 2.3 has been reported to differentiate benign from malignant lesions, although this finding has not been validated in larger cohorts [8]. In our patient, in fact, the increased and focal tracer uptake (SUVmax 6.5) in the splenic lesion was misleading, as it suggested a neoplastic rather than a benign origin.

Our patient's baseline staging PET/CT revealed an isolated hypermetabolic splenic lesion (SUVmax 6.5) with corresponding CT findings of a 16 mm hypodense nodule possessing a central low-density core and peripheral rim enhancement—features that are often worrisome for metastasis. Given the uncommon nature of splenic metastases in breast cancer, we pursued multimodal imaging. MRI characterization demonstrated no diffusion restriction and progressive contrast filling on delayed sequences, radiologically favoring an atypical hemangioma. Indeed, focal [^{18}F]FDG uptake in atypical hemangiomas has been documented in both vertebral and hepatic locations, further complicating interpretation [16, 17]. In these reports, benign vascular tumors displayed intense [^{18}F]FDG avidity akin to malignant lesions, likely reflecting the high endothelial cell turnover or inflammatory milieu within the lesion. What made our case particularly challenging was the combination of intense [^{18}F]FDG uptake with CT features mimicking metastatic disease—a presentation that even experienced observers found disconcerting.

The therapeutic course provided an opportunity to further clarify the lesion's nature. Following the first six cycles of neoadjuvant carboplatin, docetaxel, pertuzumab, and trastuzumab, repeat PET/CT demonstrated complete metabolic resolution of the splenic focus alongside reduction of the nodule to 5 mm on CT and preserved benign imaging characteristics on MRI. Such volume reduction of benign splenic lesions post-therapy has been sporadically noted in the literature: one case series reported shrinkage of a splenic hemangioma following systemic chemotherapy for lymphoma [18]. However, to our knowledge, this is the first documented case of an atypical hemangioma in the spleen of a breast cancer patient evaluated in a true multimodal fashion—PET, CT, and MRI—both before and after neoadjuvant chemotherapy, with a demonstrated complete metabolic response.

The observed treatment-associated involution of the splenic lesion could be attributed to non-specific effects of cytotoxic and targeted therapies on the vascular endothelium, inflammatory stroma, or associated macrophages within the hemangioma [19]. Such phenomena underscore the necessity of caution when interpreting post-therapy reductions in size or metabolic activity, as benign lesions may mimic true tumor response. In our patient, multidisciplinary review—bringing together nuclear medicine physicians, radiologists, oncologists, and surgeons—was pivotal in integrating imaging findings with clinical context, thereby avoiding overtreatment based on a false-positive PET result.

Despite these insights, several limitations must be acknowledged. First, the diagnosis of atypical hemangioma remains presumptive, as histologic confirmation was not available. Although percutaneous biopsy of small splenic lesions carries risks of hemorrhage and sampling error, tissue diagnosis remains the gold standard. Second, while [^{18}F]FDG PET/CT remains widely accessible, its lack of specificity in differentiating benign from malignant vascular splenic lesions suggests a potential role for more selective radiotracers. Novel agents such as fibroblast activation protein inhibitor (FAPI) analogues have demonstrated low-background splenic uptake and high tumor-to-background ratios in breast cancer, offering promise for improved specificity [20, 21]. Preliminary studies of HER2-targeted agents labeled with positron emitters (e.g., ^{89}Zr-trastuzumab) have also shown utility in assessing HER2 expression in metastatic lesions while sparing benign tissues [22]. These targeted tracers could potentially reduce false-positive findings in the spleen by exploiting receptor-based uptake rather than glycolytic activity alone.

Moreover, advanced MRI techniques—such as dynamic contrast-enhanced perfusion imaging, diffusion tensor imaging, and MR elastography—may provide additional tissue characterization metrics to distinguish benign vascular anomalies from metastatic deposits. Radiomics and machine learning approaches using multiparametric MRI

and PET features may further refine diagnostic accuracy [23].

Conclusions

This case underscores the importance of multimodal imaging and multidisciplinary collaboration in evaluating FDG-avid splenic lesions in breast cancer. Given the limited specificity of PET/CT, careful correlation with MRI and, when possible, histologic confirmation is essential to avoid mistaking benign lesions for metastases. A conservative approach—integrating imaging review, multidisciplinary discussion, and selective biopsy—can help prevent unnecessary overtreatment until more specific radiotracers or robust biomarkers become available.

Supplementary Information

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Supplementry Material (PDF 438 KB)

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Author contributions
Contributions LF, LS, SS and CDR participated in the study design, drafting of the article, analysis, and interpretation of data. LF and LS were the chief investigator and responsible for the data analysis. RD had full access to all of the data in the study and takes responsibility for the integrity of the data. LF and SS were major contributors in writing the manuscript. All authors read and approved the final manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

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Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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