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Unusual metastatic pattern in male breast invasive ductal carcinoma: Cutaneous and skeletal muscle metastases identified on [^{18}F]FDG PET/CT

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ABSTRACT
A 67-year-old man presented with multiple cutaneous nodules involving the face, trunk, and extremities. Biopsy of the largest lesion on the upper anterior chest wall demonstrated metastatic carcinoma of unknown primary origin. [^{18}F]FDG PET/CT demonstrated an unusual metastatic pattern with diffuse hypermetabolic cutaneous, subcutaneous, muscular, and osseous involvement. Among these lesions, a hypermetabolic right breast nodule was identified and targeted for biopsy, establishing the diagnosis of triple-negative invasive ductal carcinoma. This case represents an exceedingly rare presentation of male breast cancer with extensive skin and muscle metastases. It highlights the critical diagnostic value of [^{18}F]FDG PET/CT in resolving unknown-primary malignancies and guiding definitive tissue sampling in atypical metastatic disease.

Keywords: Malignancy workup; Oncology; Dermatology; Triple-negative breast cancer; Theranostics

INTRODUCTION
Male breast cancer (MBC) is an uncommon malignancy and is typically diagnosed at an advanced stage [1-4]. Triple-negative breast cancer (TNBC) in men is particularly rare and associated with aggressive behavior and early metastatic spread. Cutaneous and skeletal muscle metastases are exceedingly uncommon initial manifestations and may obscure identification of the primary tumor [3-8]. We report a rare case of male TNBC presenting with diffuse cutaneous, muscular, and osseous metastases, in which [^{18}F]FDG PET/CT played a pivotal role in localizing the primary lesion and guiding definitive diagnosis.

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CASE PRESENTATION

A 67-year-old man presented with multiple cutaneous nodules distributed across the face, trunk, and extremities (Figure 1A). His medical history was notable for polycystic kidney disease and prior surgical repair of an abdominal aortic aneurysm. On physical examination, the lesions were firm, indurated, and variable in size, with occasional central umbilication, and were scattered diffusely with greater clustering on the face and upper trunk. A punch biopsy was obtained from the largest nodule on the upper anterior chest wall (Figure 1A, red arrow). Histopathologic evaluation revealed metastatic carcinoma. Immunohistochemistry (IHC) demonstrated positivity for Cytokeratin 7 (CK7) and Vimentin, focal CK20 positivity, weak GATA3 expression, and negativity for TTF-1, P63, S100, and CDX2. This IHC profile was inconclusive for establishing the primary tumor site. Although CK7 and CK20 expression patterns may provide diagnostic clues, they are not specific to a single primary malignancy. Similarly, weak GATA3 expression was insufficient to definitively establish breast origin in this case. The negative expression of TTF-1 and CDX2 helped narrow the differential diagnosis but did not identify the primary site. Consequently, whole-body [^{18}F]FDG PET/CT was performed to investigate the malignancy of unknown primary origin and identify a potential target for biopsy. The maximum intensity projection demonstrated numerous hypermetabolic foci diffusely distributed throughout the body, creating an unusual and striking metastatic pattern (Figure 1B).

The [^{18}F]FDG PET/CT demonstrated innumerable hypermetabolic foci throughout the axial and appendicular skeleton without corresponding structural abnormalities, consistent with diffuse osseous metastatic involvement (Figure 2A). Additionally, numerous [^{18}F]FDG-avid cutaneous and subcutaneous nodules were observed, accompanied by scattered hypermetabolic foci within multiple skeletal muscles (Figure 2B, first row) and hypermetabolic lymph nodes, including hilar and mediastinal nodes (Figure 2B, second row), collectively forming an atypical and extensive metastatic pattern. Other findings included a hepatic cyst (Figure 2B, third row) and polycystic kidneys (Figure 2B, Fourth row), both of which showed no abnormal [^{18}F]FDG uptake. Of particular significance, one of the hypermetabolic soft-tissue nodules was localized to the right breast (Figure 2B, second row, green arrow). This lesion subsequently underwent core-needle biopsy. Histopathologic evaluation confirmed invasive ductal carcinoma of no special type. IHC demonstrated negativity for estrogen receptor (ER), progesterone receptor (PR), and HER2, with a Ki-67 proliferation index of 70%, establishing the diagnosis of TNBC. IHC assessment of PD-L1 expression also demonstrated positivity in 50% of tumor cells and 5% of tumor-infiltrating immune cells. Based on these findings and the overall clinical assessment, the patient subsequently received systemic chemotherapy in combination with pembrolizumab immunotherapy.

DISCUSSION

MBC is a rare but clinically significant malignancy, accounting for approximately 1% of all breast cancer cases, with evidence suggesting a gradual increase in incidence over recent decades [1]. Its risk factors parallel those observed in women and include advancing age, family history, certain medical conditions, elevated lifetime estrogen exposure, and lifestyle-related influences [2]. Compared with women, MBC is more frequently associated with adverse prognostic features, including presentation at a more advanced stage, higher rates of lymphovascular invasion, and a greater likelihood of primary distant metastasis [3]. Invasive ductal carcinoma accounts for over 90% of all MBC cases, representing the predominant histologic subtype in this population [4]. Notably, most MBCs are ER–positive [2]. TNBC, although less common than other molecular subtypes, has a higher propensity for distant

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metastases, particularly involving visceral organs, which contributes to its overall poorer prognosis relative to other subtypes [5–7]. Our case represents a rare instance of male TNBC presenting with an exceedingly uncommon metastatic pattern involving both skin and skeletal muscles [8–12]. Skeletal muscle metastases are uncommon despite the extensive vascular supply and substantial mass of skeletal muscle in the human body. Their reported frequency varies considerably according to the study population and diagnostic method. In a retrospective imaging study, skeletal muscle metastases were identified in 61 of 5,170 patients with metastatic malignancies (1.2%), whereas another CT-based study reported a prevalence of 0.33% among patients with malignancy. However, these figures reflect the prevalence of skeletal muscle metastases across cancer types and should not be interpreted as breast cancer-specific estimates [13,14]. A 2024 review of striated muscle metastases summarized published cases and discussed potential biological mechanisms underlying the relative resistance of skeletal muscle to metastatic colonization [15]. In breast cancer, skeletal muscle involvement is an unusual manifestation of disseminated disease and may be overlooked when more typical metastatic sites, such as bone, liver, and lung, dominate the clinical presentation.

Cutaneous metastases are also a recognized manifestation of advanced breast cancer in women, including those with TNBC, although their occurrence as the initial manifestation of an occult primary is less common [16, 17]. A 2025 case report and literature review further highlights the clinical and diagnostic challenges associated with cutaneous metastases from TNBC [17]. In men, breast cancer itself accounts for less than 1% of breast cancer diagnoses, and TNBC represents an uncommon subtype of male breast cancer. Consequently, the presentation of male TNBC with diffuse cutaneous metastases accompanied by widespread skeletal muscle involvement is exceptionally unusual. A recent report of male TNBC presenting with cutaneous metastasis also emphasizes the scarcity of this presentation in the literature [18]. Although direct comparisons of the frequency of this combined metastatic pattern between men and women are limited by the rarity of reported cases, the present case illustrates an especially uncommon presentation in a male patient.

In the this case, the diagnostic challenge of an unknown primary was resolved through [^{18}F]FDG PET/CT, which identified a hypermetabolic lesion in the right breast among the disseminated cutaneous and subcutaneous nodules, guiding targeted biopsy and confirming the breast as the primary site. This case illustrates that molecular-targeted imaging, while occasionally non-specific, can nonetheless identify lesions—either intentionally or incidentally—that serve as actionable targets, guiding both diagnostic evaluation and subsequent therapeutic interventions [19–24].

CONCLUSION

This case underscores the diagnostic challenge posed by malignancy of unknown primary and demonstrates the critical role of [^{18}F]FDG PET/CT in identifying the occult breast lesion, guiding targeted biopsy, and establishing the definitive diagnosis. Early use of whole-body molecular imaging may facilitate accurate diagnosis in atypical metastatic presentations.

REFERENCES

1. Zheng G, Leone JP. Male breast cancer: an updated review of epidemiology, clinicopathology, and treatment. J Oncol. 2022 May 24;2022:1734049.
2. Pullen RL Jr. Breast cancer in males. Nursing. 2025 Mar 1;55(3):18-26.
3. Graf M, Gerken M, Klinkhammer-Schalke M, Schrodi S, Pauer A, Geiss K, Ortmann O, Sturm-Inwald EC. Clinical, therapeutic and prognostic differences between male and female patients with breast cancer-a comparison of 2510 men and 307,634 women in a registry-based study in Germany. J Cancer Res Clin Oncol. 2025 Jun 3;151(6):181.

4. Ray SK, Mukherjee S. Clinical aspect of male breast cancer: a burgeoning and unaddressed issue. Mol Biol Rep. 2025 May 13;52(1):452.
5. Dent R, Hanna WM, Trudeau M, Rawlinson E, Sun P, Narod SA. Pattern of metastatic spread in triple-negative breast cancer. Breast Cancer Res Treat. 2009 May;115(2):423-8.
6. Li Y, Su P, Wang Y, Zhang H, Liang Y, Zhang N, Song X, Li X, Li J, Yang Q. Impact of histotypes on preferential organ-specific metastasis in triple-negative breast cancer. Cancer Med. 2020 Feb;9(3):872-881.
7. Qavi Q, Alkistawi F, Kumar S, Ahmed R, Saad Abdalla Al-Zawi A. Male triple-negative breast cancer. cureus. 2021 Apr 18;13(4):e14542.
8. Araújo E, Barbosa M, Costa R, Sousa B, Costa V. A first sign not to be missed: cutaneous metastasis from breast cancer. Eur J Case Rep Intern Med. 2020 Jan 8;7(1):001356.
9. Salemis NS. Skeletal muscle metastasis from breast cancer: management and literature review. Breast Dis. 2015;35(1):37-40.
10. Kim YW, Seo KJ, Lee SL, Kwon KW, Hur J, An HJ, Ko YH, Kim JS, Won HS. Skeletal muscle metastases from breast cancer: two case reports. J Breast Cancer. 2013 Mar 1;16(1):117-21.
11. Ogiya A, Takahashi K, Sato M, Kubo Y, Nishikawa N, Kikutani M, Tadokoro Y, Tanaka K, Uematsu T, Watanabe J, Kasami M. Metastatic breast carcinoma of the abdominal wall muscle: a case report. Breast Cancer. 2015 Mar;22(2):206-9.
12. Khandelwal AR, Takalkar AM, Lilien DL, Ravi A. Skeletal muscle metastases on FDG PET/CT imaging. Clin Nucl Med. 2012 Jun;37(6):575-9.
13. Surov A, Hainz M, Holzhausen HJ, Arnold D, Katzer M, Schmidt J, Spielmann RP, Behrmann C. Skeletal muscle metastases: primary tumours, prevalence, and radiological features. Eur Radiol. 2010 Mar;20(3):649-58.
14. Ong N, George M, Dutta R, Ng CH. CT imaging features of skeletal muscle metastasis. Clin Radiol. 2019 May;74(5):374-7.
15. Saunders AAE, Thomson RE, Goodman CA, Anderson RL, Gregorevic P. Striated muscle: an inadequate soil for cancers. Cancer Metastasis Rev. 2024 Dec;43(4):1511-27.
16. Rafiei Z, Saber Tanha A, Tayyebi Meibodi N, Zahed Anaraki S, Askari E. Cutaneous and subcutaneous prostate-specific membrane antigen-avid lesions. Clin Nucl Med. 2025 Mar 1;50(3):e164-5.
17. Flindris S, Margioula-Siarkou C, Margioula-Siarkou G, Gouta C, Styliara E, Navrozoglou I, Petousis S, Dinas K. Cutaneous metastasis of triple negative breast cancer: a case report and review of literature. Cureus. 2025 Mar 2;17(3):e79926.
18. Ajai Mokan Dasan SL, Pandey N, Sukhoroslov M, Rudikoff D, Mazhar N. Triple-negative male breast cancer presenting as cutaneous metastasis: a diagnostic rarity. Case Rep Oncol Med. 2025 Nov 20;2025:4393243.
19. Hugentobler A, Gilbeau L, Talbot JN, Gauthé M. 18F-Fluorocholine PET/CT of incidental male breast cancer. Clin Nucl Med. 2017 Jan;42(1):e56-7.
20. Gill HS, Tade F, Greenwald DT, Yonover PM, Savir-Baruch B. Metastatic male breast cancer with increased uptake on 18F-Fluciclovine PET/CT scan. Clin Nucl Med. 2018 Jan;43(1):23-4.
21. Sindoni A, Perin T, Borsatti E. Re: 18F-Fluorocholine PET/CT of incidental male breast cancer. Clin Nucl Med. 2018 Jan;43(1):75-6.
22. McEachen JC, Kuo PH. Male primary breast cancer found on FDG-PET/CT. Clin Nucl Med. 2008 Sep;33(9):630-2.
23. Hooda Z, Lu Y, Mehran RJ, Moran C, Barcenas CH. Rosai-Dorfman disease mimicking metastasis to the spleen from breast cancer. Clin Nucl Med. 2025 May 1;50(5):450-1.
24. Piciu A, Piciu D, Polocoser N, Kovendi AA, Almasan I, Mester A, Morariu DS, Cainap C, Cainap SS. Diagnostic performance of F18-FDG PET/CT in male breast cancers patients. Diagnostics (Basel). 2021 Jan 13;11(1):119

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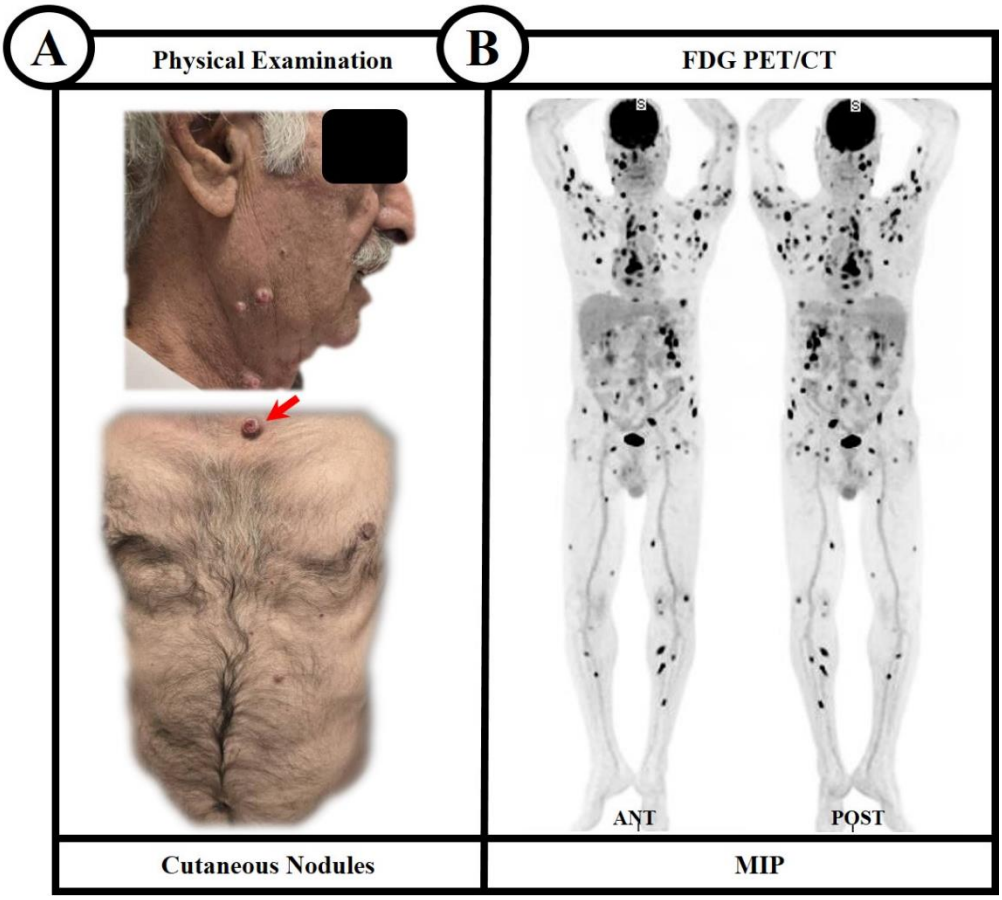


Figure 1. (**A**) Multiple firm cutaneous nodules diffusely distributed over the face, trunk, and extremities; the red arrow indicates the initial biopsy site on the upper anterior chest wall. (**B**) Maximum intensity projection of the [^{18}F]FDG PET/CT demonstrating innumerable hypermetabolic foci throughout the body, producing an unusual and diffuse metastatic pattern

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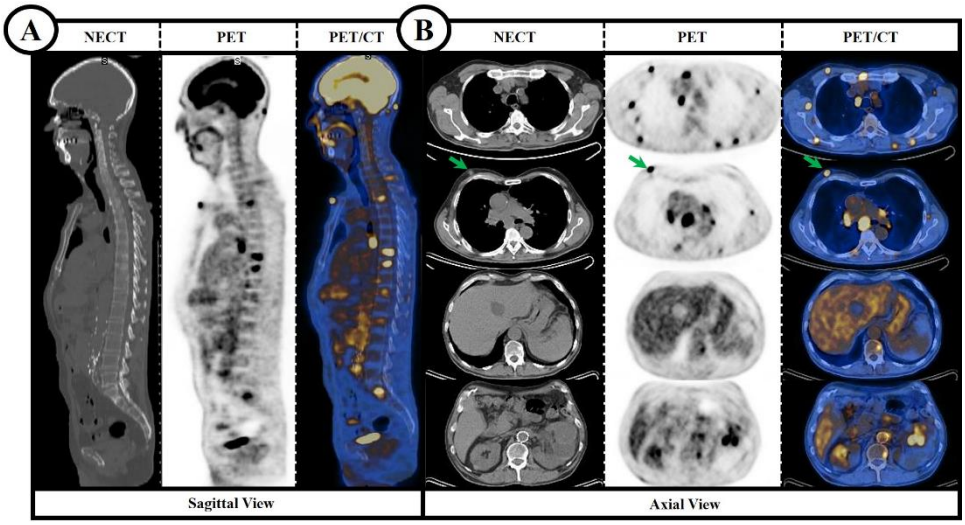


Figure 2. (**A**) Diffuse hypermetabolic involvement of the axial and appendicular skeleton without corresponding structural abnormalities, consistent with widespread osseous metastases. (**B**) Multiple [^{18}F]FDG-avid cutaneous, subcutaneous, muscular, and nodal lesions; a hypermetabolic right breast soft-tissue nodule (green arrow) was identified and subsequently confirmed as triple-negative invasive ductal carcinoma on biopsy. The third and fourth rows depict hepatic and renal cysts, respectively, both without abnormal FDG uptake