Intense FAP expression of ovarian metastatic breast cancer detected by [68Ga]RTX-1363 PET/CT [Image abstract]

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Intense FAP Expression of Ovarian Metastatic Breast Cancer Detected by [^{68}Ga]RTX-1363 PET/CT

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Abstract: PET/CT targeting fibroblast activation protein α (FAP) in cancer-associated fibroblasts shows promise in theranostics. Here, we report the case of a 31-year-old woman with hormone receptor–positive/human epidermal growth factor receptor 2–negative breast cancer who presented with rising CA15-3 for further diagnostic workup. Whereas [^{18}F]FDG PET/CT was unremarkable, novel [^{68}Ga]RTX-1363 PET/CT revealed intense tracer accumulation in thoracoabdominal lymph nodes and both ovaries. Follow-up imaging confirmed tumor progression, and diagnostic laparoscopy verified metastatic disease in the ovaries with high FAP expression in the tumor stroma. This case underscores the superior sensitivity of [^{68}Ga]RTX-1363 PET/CT over [^{18}F]FDG PET/CT, enhancing breast cancer diagnostic and therapeutic strategies.

Key Words: [^{68}Ga]RTX-1363, fibroblast activation protein, PET/CT, molecular imaging, ovarian metastases

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Author contributions: Material preparation, data collection, and analysis were performed by L.G., A.D., and C.L. The first draft of the manuscript was written by L.G., A.D., and C.L., and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent was obtained from the patient reported in this case report.

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REFERENCES

1. Kratochwil C, Flechsig P, Lindner T, et al. ^{68}Ga-FAPI PET/CT: tracer uptake in 28 different kinds of cancer. *J Nucl Med*. 2019;60:801–805.
2. Hillier S, Tully K, Kazerounian S, et al. Preclinical characterization of [Cu-64] RTX-1363S: a highly selective and high-affinity FAP inhibitor for PET imaging. *J Nucl Med*. 2024;65:241736.
3. Hesterman J, Hillier S, DiMagno S, et al. First-in-human study of a high affinity FAP imaging agent [Cu-64] LNTH-1363S. *J Nucl Med*. 2024;65:241693.
4. Kasper DL, Fauci AS, Hauser SL, et al. Breast cancer. *Harrison's Manual of Medicine*. 19th ed. New York City, NY: McGraw-Hill Education Location; 2016.
5. Yadav BS, Sharma SC, Robin TP, et al. Synchronous primary carcinoma of breast and ovary versus ovarian metastases. *Semin Oncol*. 2015;42:e13–e24.
6. Demopoulos RI, Touger L, Dubin N. Secondary ovarian carcinoma: a clinical and pathological evaluation. *Int J Gynecol Pathol*. 1987;6:166–175.
7. Tserkezoglou A, Kontou S, Hadjieleftheriou G, et al. Primary and metastatic ovarian cancer in patients with prior breast carcinoma. Pre-operative markers and treatment results. *Anticancer Res*. 2006;26(3B):2339–2344.
8. Bigorie V, Morice P, Duvillard P, et al. Ovarian metastases from breast cancer. *Cancer*. 2010;116:799–804.
9. Tchou J, Zhang PJ, Bi Y, et al. Fibroblast activation protein expression by stromal cells and tumor-associated macrophages in human breast cancer. *Hum Pathol*. 2013;44:2549–2557.
10. Kömek H, Can C, Güzel Y, et al. ^{68}Ga-FAPI-04 PET/CT, a new step in breast cancer imaging: a comparative pilot study with the ^{18}F-FDG PET/CT. *Ann Nucl Med*. 2021;35:744–752.
11. Novruzov F, Mehdi E, Orucova N, et al. Head to head comparison of ^{68}Ga-FAPI-46 PET/CT and 18-FDG PET/CT in breast carcinoma staging: a clinical trial update from Azerbaijan. *J Nucl Med*. 2022;63:2372.
12. Umachanger JK, Zacho HD, Sylvest C, et al. Predicting malignancy in adnexal tumors with FAPI PET/CT and FDG PET/CT: a case report on a borderline ovarian tumor. *Clin Nucl Med*. 2024;50:e124–e126.

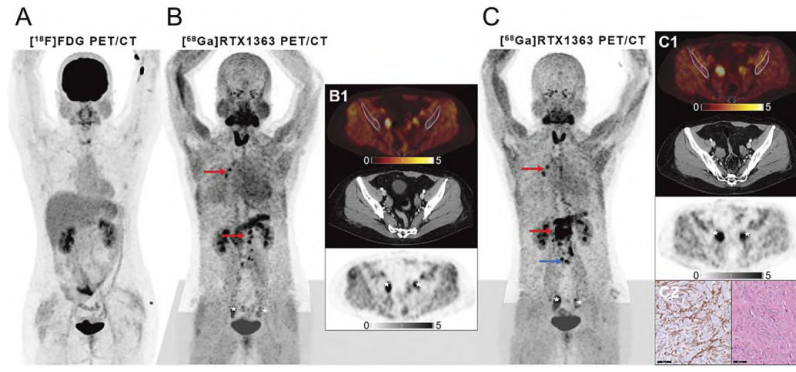

FIGURE 1. Radiolabeled inhibitors of fibroblast activation protein α (FAP) have been developed to target mainly cancer-associated fibroblasts across various tumors.[1] This case features a 31-year-old woman with hormone receptor–positive/human epidermal growth factor receptor 2–negative breast cancer, first diagnosed in 2014. Following primary radical mastectomy, she underwent adjuvant radiochemotherapy and received comprehensive further systemic therapy encompassing antihormonal therapy, denosumab, and bisphosphonates. Despite repeated therapeutic interventions, rising CA15-3 levels were subsequently noted. For further diagnostic workup, [^{18}F]FDG PET/CT was performed with unremarkable results (**A**). For further evaluation, additional imaging with [^{68}Ga]RTX-1363, a novel FAP inhibitor with nanomolar receptor affinity (**B**),[2,3] was conducted 60 minutes after intravenous administration of 168 MBq of the tracer. Compared with [^{18}F]FDG PET/CT, [^{68}Ga]RTX-1363 PET/CT showed intense tracer accumulation in numerous thoracoabdominal lymph nodes (**B**, red arrows) and both ovaries (**B**, B1; asterisks) with SUV_{max} as high as 7.67 (SUV_{peak}, 5.94), consistent with metastatic disease. Breast cancer commonly spreads to lymph nodes, bones, lungs, liver, and brain.[4] Although less common, it also metastasizes to the ovaries,[5] representing 3% to 38% of ovarian neoplasms, with rates differing based on diagnostic techniques and geographic factors.[6–8] At that time point, no treatment was initiated as the multidisciplinary tumor conference recommended follow-up imaging. At 3-month follow-up (**C**), progressive tracer uptake of both ovaries (**C**, C1; asterisks), the aforementioned lymph nodes (**C**, red arrows), and a new osseous lesion in a lumbar vertebral body (**C**, blue arrow) were visualized, in line with continuously rising CA15-3 levels. Subsequently, diagnostic laparoscopy was performed, and the corresponding lesions were resected (right ovary) and biopsied (left ovary) for further workup. Histopathologic and immunohistochemical analysis confirmed metastatic breast cancer lesions in both ovaries (as well as the omentum majus) with a strong desmoplastic reaction and a pronounced FAP expression in the tumor stroma (C2), in line with a previous study by Tchou et al showing a strong FAP expression in breast cancer stromal cells.[9] To further characterize the tumor biology of this interesting case, next-generation sequencing–based multigene panel testing was performed, and a likely pathogen *ATM* variant and variants of unclear significance in the *BAP1* and *BRCA2* genes, as well as an *ESR1::CCDC170* fusion, could be identified. Tumor mutational burden was low (TMB-low with 7.2 mutations per megabase), and the tumor was classified as microsatellite-stable and homologous recombination deficiency-low. In summary, these observations align with current literature, affirming a superiority of FAP-targeted imaging over [^{18}F]FDG PET/CT for pinpointing breast cancer or adnexal lesions.[10–12] Given its unprecedented affinity to FAP, RTX-1363 might prove to be a valuable tool for both diagnostic and therapeutic strategies in breast cancer management.