European Journal of Nuclear Medicine and Molecular Imaging (2023) 50:4112–4113
https://doi.org/10.1007/s00259-023-06348-4

IMAGE OF THE MONTH

[^{68}Ga]Ga-DOTA-FAPI-04 PET/CT depicts metastases from medullary thyroid cancer that [^{68}Ga]Ga-DOTATOC PET/CT missed

Akram Al-Ibraheem[1,2] · Salem Fandi Alyasjeen[1] · Ahmed Saad Abdlkadir[1] · Areej Abu Sheikha[3]

Received: 14 March 2023 / Accepted: 19 July 2023 / Published online: 25 July 2023

This image is the first reported instance of medullary thyroid carcinoma (MTC), in which [^{68}Ga]Ga-DOTA-FAPI-04 provided a more accurate assessment of the disease's metastatic spread than [^{68}Ga]Ga-DOTATOC. A 40-year-old male patient initially presented with a thyroid lesion along with several cervical and thoracic lymph nodes enlargement on CT scan. Additionally, there were sternal bone and liver lesions suggestive of metastases. A left cervical lymph node biopsy confirmed the presence of MTC. The patient received nine cycles of chemotherapy, which only exerted limited local partial control. A follow-up CT scan showed metastatic disease progression. [^{68}Ga]Ga-DOTATOC scan was requested and showed only mild expression of somatostatin receptors in the thyroid and nearby lymph nodes (a–d, arrows). However, there was no significant expression detected in the bones or the liver (a–d, arrow heads). Therefore, this case was not considered a potential candidate for [^{177}Lu]Lu-DOTATATE therapy. In parallel, [^{68}Ga]Ga-DOTA-FAPI-04 was ordered to better evaluate the extent of the disease, which revealed an additional picture of progressive metastatic disease involving the liver, sternum, and iliac bones (e–h, arrows). In addition to the observed discordance (i), biochemical progression was also evident, demonstrating markedly elevated tumor markers (j). Recent studies have shown moderate uptake of the [^{68}Ga]Ga-DOTA-FAPI-04 in MTC [1, 2]. Progressive metastatic MTC usually has limited treatment options [3], a worse prognosis [4], and higher mortality rates [5]. MTC undergoes a progression in which initially well-differentiated lesions express somatostatin receptors (SSTR), but later transition to an undifferentiated state with poor SSTR expression [6]. This shift is accompanied by a significant rise in carcinoembryonic antigen (CEA) tumor marker, which is more useful for serial monitoring of undifferentiated cases than thyrocalcitonin [6]. In these circumstances, molecular imaging with [^{18}F] fluorodeoxyglucose can aid in determining the extent of the disease [7]. This observed discrepancy supports the potential efficacy of [^{68}Ga]Ga-DOTA-FAPI-04 in the management of MTC. The added value of [^{68}Ga]Ga-DOTA-FAPI-04 lies in its potential to provide more accurate staging of multiple cancers and the potential use of fibroblast activation protein inhibitor (FAPI) in radioligand theranostics approach [8, 9]. However, the significance of such evidence is limited as it only represents one case. Therefore, further studies are still needed to approve its implications for both diagnostic and therapeutic purposes.

✉ Akram Al-Ibraheem
aibraheem@khcc.jo; akramalibrahim@gmail.com

Salem Fandi Alyasjeen
salem.yazjeen90@gmail.com

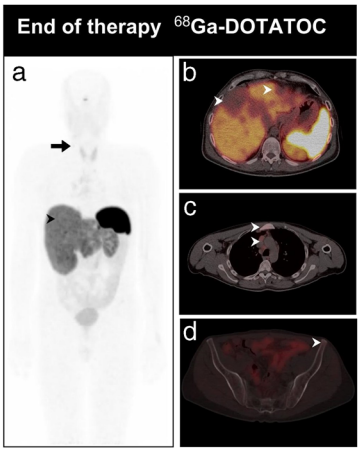
Ahmed Saad Abdlkadir
ahmedshukri92@hotmail.com

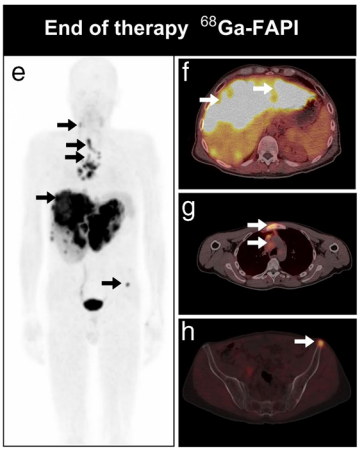
Areej Abu Sheikha
asheikha@khcc.jo

[1] Department of Nuclear Medicine, King Hussein Cancer Center (KHCC), Queen Rania Street Al-Jubeiha, Amman 11941, Jordan

[2] Division of Nuclear Medicine/Department of Radiology and Nuclear Medicine, University of Jordan, Amman 11942, Jordan

[3] Department of Medical Oncology, King Hussein Cancer Center (KHCC), Amman 11941, Jordan





i SUVmax values obtained in each transaxial image

DOTATOC	FAPI
b: SUVmax= 1.8	**f:** SUVmax= 25.5
c: SUVmax up to 4.1	**g:** SUVmax up to 11.8
d: SUVmax= 1.2	**h:** SUVmax= 9.9

j

END OF THERAPY RESULTS FOR TUMOR MARKERS		Normal Reference
Thyrocalcitonin	3925 ng/L	< 19 ng/L
Carcinoembryonic Antigen	134 ng/mL	< 3 ng/mL

Author contribution Akram Al-Ibraheem contributed to the concept and design of this manuscript. Akram Al-Ibraheem, Salem Fandi Alyasjeen, Ahmed Saad Abdlkadir, and Areej Abu Sheikha participated in data acquisition and manuscript revision. Ahmed Saad Abdlkadir drafted the initial manuscript. All authors read and approved the final manuscript.

Data availability The current study data are available from the corresponding author on reasonable request.

Declarations

Ethics approval 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.

Consent to participate Informed consent was obtained from the patient.

Consent for publication Not applicable.

Conflict of interest The authors declare no competing interests.

References

1. Kratochwil C, Flechsig P, Lindner T, Abderrahim L, Altmann A, Mier W, et al. (68)Ga-FAPI PET/CT: tracer uptake in 28 different kinds of cancer. J Nucl Med. 2019;60(6):801–5. https://doi.org/10.2967/jnumed.119.227967.
2. Kuyumcu S, Isik EG, Sanli Y. Liver metastases from medullary thyroid carcinoma detected on (68)Ga-FAPI-04 PET/CT. Endocrine. 2021;74(3):727–8. https://doi.org/10.1007/s12020-021-02800-3.
3. Kim BH, Kim IJ. Recent updates on the management of medullary thyroid carcinoma. Endocrinol Metab (Seoul). 2016;31(3):392–9. https://doi.org/10.3803/EnM.2016.31.3.392.
4. Giovanella L, Treglia G, Iakovou I, Mihailovic J, Verburg FA, Luster M. EANM practice guideline for PET/CT imaging in medullary thyroid carcinoma. Eur J Nucl Med Mol Imaging. 2020;47(1):61–77. https://doi.org/10.1007/s00259-019-04458-6.
5. Roman S, Lin R, Sosa JA. Prognosis of medullary thyroid carcinoma: demographic, clinical, and pathologic predictors of survival in 1252 cases. Cancer. 2006;107(9):2134–42. https://doi.org/10.1002/cncr.22244.
6. Kwekkeboom DJ, Reubi J-C, Lamberts S, Bruining H, Mulder A, Oei H, et al. In vivo somatostatin receptor imaging in medullary thyroid carcinoma. J Clin Endocrinol Metab. 1993;76(6):1413–7.
7. Fortunati E, Argalia G, Zanoni L, Fanti S, Ambrosini V. New PET radiotracers for the imaging of neuroendocrine neoplasms. Curr Treat Options Oncol. 2022;23(5):703–20. https://doi.org/10.1007/s11864-022-00967-z.
8. Ballal S, Yadav MP, Kramer V, Moon ES, Roesch F, Tripathi M, et al. A theranostic approach of [(68)Ga]Ga-DOTA.SA.FAPi PET/CT-guided [(177)Lu]Lu-DOTA.SA.FAPi radionuclide therapy in an end-stage breast cancer patient: new frontier in targeted radionuclide therapy. Eur J Nucl Med Mol Imaging. 2021;48(3):942–4. https://doi.org/10.1007/s00259-020-04990-w.
9. Pang Y, Zhao L, Meng T, Xu W, Lin Q, Wu H, et al. PET imaging of fibroblast activation protein in various types of cancer using (68)Ga-FAP-2286: comparison with (18)F-FDG and (68)Ga-FAPI-46 in a single-center, prospective study. J Nucl Med. 2023;64(3):386–94. https://doi.org/10.2967/jnumed.122.264544.