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IMAGE OF THE MONTH

Rabbit fever: granulomatous inflammation by *Francisella tularensis* mimics lung cancer in dual tracer ^{18}FDG and ^{68}Ga-FAPI PET/CT

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A 39-year-old hunter presented with chills, headache, limb pain, tachycardia, hypertension, ventricular extrasystoles, elevated inflammatory values, and persistent chest pain. A CT scan revealed a mass on the left hilus (A). Due to suspicion of lymphoma or lung cancer 1 week later, an ^{18}FDG (B–D) plus a ^{68}Ga-labeled fibroblast activation protein inhibitor (^{68}Ga-FAPI) PET/CT scan (E–G) were performed. The hilar mass increased in size (B, E) and demonstrated both intense ^{18}FDG uptake (SUVmax 24.5) (C, D) and ^{68} Ga-FAPI accumulation (SUVmax 23.2) (F, G) strongly indicating malignancy. However, subsequent EBUS-TBNA and EUS-B yielded necrotizing granulomatosis (H). Finally, a bone-hard mass on the left hilus discharging creamy pus was resected by VATS. Pathological and microbiological workup evidenced *Francisella tularensis* infection by FISHseq analysis (Fluorescence in situ hybridization combined with 16S rRNA gene amplification and sequencing [1]), ELISA, and Western blot. Postoperative bronchoscopy demonstrated re-established bronchus patency (I). After antibiotic therapy with gentamicin and ciprofloxacin, no recurrence was detectable on CT control 20 weeks later (J).

^{18}FDG PET/CT is one of the diagnostic mainstays in oncology and standard imaging in patients with lung mass. However, its specificity is impaired due to inflammation-induced uptake. In tularemia, a granulomatous inflammation, ^{18}FDG PET/CT revealed an uptake pattern indicative for lung cancer in more than 50% of all cases [2]. ^{68}Ga-FAPI emerged as an alternative tracer for tumor imaging, as FAP is expressed in > 90% of epithelial cancers [3, 4]. ^{68}Ga-FAPI shows high uptake and tumor-to-background ratio in primary lung cancer and in metastatic lesions of other tumor types located in the lung [5–9]. Although promising data on this new radiotracer are increasing, false-positive results in non-malignant diseases with FAP uptake have been reported [10]. Also, chronic infections like tuberculosis might occasionally demonstrate increased ^{68}Ga-FAPI [11]. On the other hand, in a head-to-head comparison (sub)acute inflammation in lymph nodes after COVID-19 vaccination induces no ^{68}Ga-FAPI accumulation besides a positive FDG signal [12].

Our case adds tularemia to the scope of potential granulomatous inflammation-induced pitfalls in hybrid imaging coming along with increased high FDG uptake but also high FAP expression. However, given an already known diagnosis of granulomatous disease like tularemia, ^{68}Ga-FAPI PET/CT might be suitable to assess extent and activity of chronic inflammation.

This article is part of the Topical Collection on Image of the month

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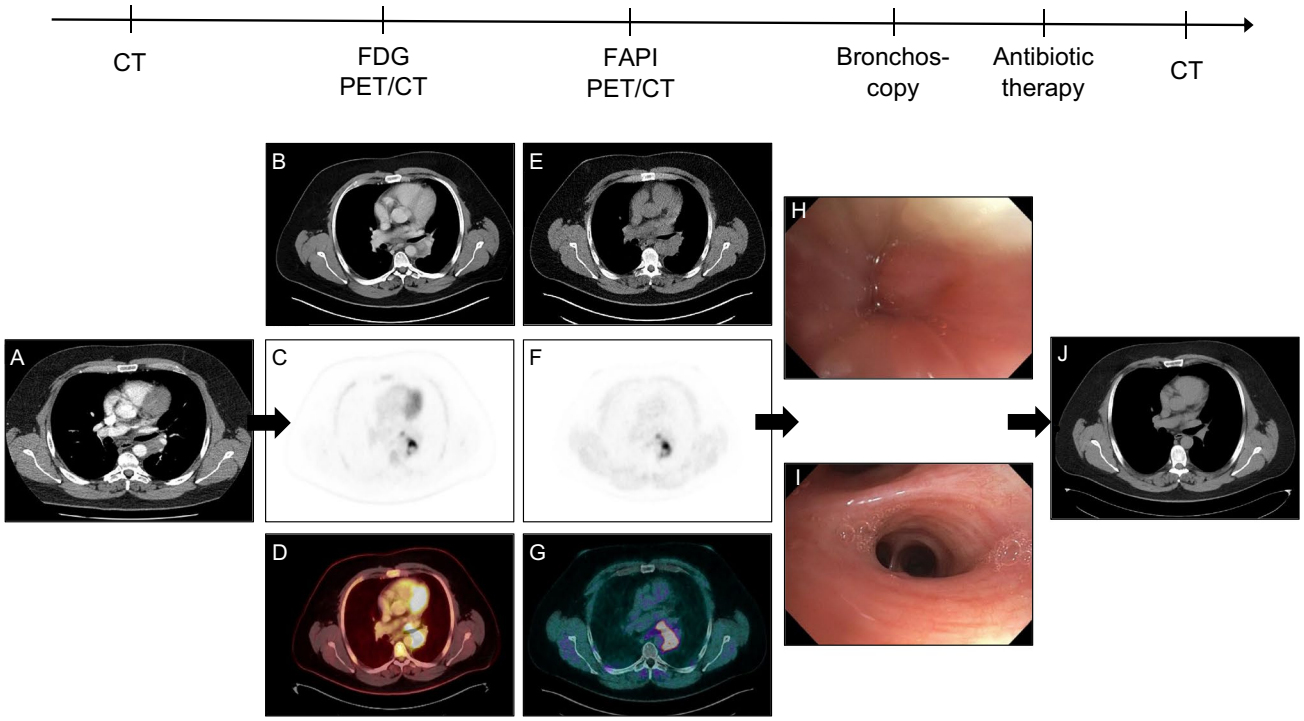

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Ethical approval This is a case presentation of the ongoing ^{68}Ga-FAPI PET observational trial conducted at the University Hospital Essen (NCT04571086). Evaluation of data was approved by the ethics committee of the University Duisburg-Essen (20–9485-BO and 19–8991-BO).

All studies involving human participants were conducted in accordance with the ethical standards of the relevant committee and the 1964 Helsinki Declaration and its later amendments.

Consent to participate Written informed consent was obtained from individual participant included in the study.

Conflict of interest The authors declare no competing interests.

References

1. Hajduczenia MM, Klefisch FR, Hopf AGM, Grubitzsch H, Stegemann MS, Pfäfflin F, et al. New perspectives for prosthetic valve endocarditis - impact of molecular imaging by FISHseq diagnostics. Clin Infect Dis. 2022. https://doi.org/10.1093/cid/ciac860.
2. Martinet P, Khatchatourian L, Saidani N, Fangous MS, Goulon D, Lesecq L, et al. Hypermetabolic pulmonary lesions on FDG-PET/CT: tularemia or neoplasia? Infect Dis Now. 2021;51:607–13. https://doi.org/10.1016/j.idnow.2021.06.307.
3. Lindner T, Loktev A, Giesel F, Kratochwil C, Altmann A, Haberkorn U. Targeting of activated fibroblasts for imaging and therapy. EJNMMI Radiopharm Chem. 2019;4:16. https://doi.org/10.1186/s41181-019-0069-0.

4. Puré E, Blomberg R. Pro-tumorigenic roles of fibroblast activation protein in cancer: back to the basics. Oncogene. 2018;37:4343–57. https://doi.org/10.1038/s41388-018-0275-3.
5. Zhou X, Wang S, Xu X, Meng X, Zhang H, Zhang A, et al. Higher accuracy of [(68) Ga]Ga-DOTA-FAPI-04 PET/CT comparing with 2-[(18)F]FDG PET/CT in clinical staging of NSCLC. Eur J Nucl Med Mol Imaging. 2022;49:2983–93. https://doi.org/10.1007/s00259-022-05818-5.
6. Liao Y, Ni Y, He R, Liu W, Du J. Clinical implications of fibroblast activation protein-α in non-small cell lung cancer after curative resection: a new predictor for prognosis. J Cancer Res Clin Oncol. 2013;139:1523–8. https://doi.org/10.1007/s00432-013-1471-8.
7. Shi J, Hou Z, Yan J, Qiu W, Liang L, Meng M, et al. The prognostic significance of fibroblast activation protein-α in human lung adenocarcinoma. Ann Transl Med. 2020;8:224. https://doi.org/10.21037/atm.2020.01.82.
8. Loktev A, Lindner T, Mier W, Debus J, Altmann A, Jäger D, et al. A tumor-imaging method targeting cancer-associated fibroblasts. J Nucl Med. 2018;59:1423–9. https://doi.org/10.2967/jnumed.118.210435.
9. Hirmas N, Hamacher R, Sraieb M, Ingenwerth M, Kessler L, Pabst KM, et al. Fibroblast activation protein positron emission tomography and histopathology in a single-center database of 324 patients and 21 tumor entities. J Nucl Med. 2022. https://doi.org/10.2967/jnumed.122.264689.
10. Kessler L, Ferdinandus J, Hirmas N, Zarrad F, Nader M, Kersting D, et al. Pitfalls and common findings in (68)Ga-FAPI PET: a pictorial analysis. J Nucl Med. 2022;63:890–6. https://doi.org/10.2967/jnumed.121.262808.
11. Sun R, Huang Z, Wei J, Zeng C, Chen X. 68Ga-FAPI and 18F-FDG PET/CT findings in a patient with pancreatic tuberculosis mimicking malignant tumor. Clin Nucl Med. 2022;47:653–4. https://doi.org/10.1097/rlu.0000000000004099.
12. Demmert TT, Maric I, Pomykala KL, Lueckerath K, Siveke J, Schaarschmidt BM, et al. Novel (68)Ga-FAPI PET/CT offers oncologic staging without COVID-19 vaccine-related pitfalls. J Nucl Med. 2022. https://doi.org/10.2967/jnumed.122.264872.