

# Case Report: Pulmonary Actinomyces Infection Mimics Lung Cancer on [<sup>68</sup>Ga]Ga-FAPI PET/CT

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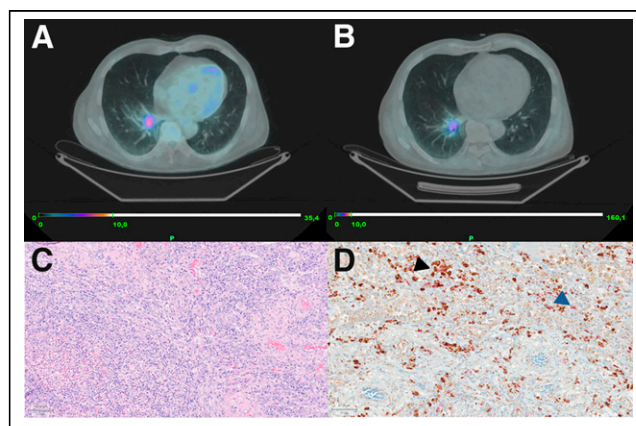
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**A**ctinomycosis is a rare gram-positive infection, generally granulomatous. The diagnosis can be complex and sometimes can be achieved only at the chronic stage. *Actinomyces* normally colonize the mouth, urogenital tract, and gastrointestinal tract, whereas pulmonary infections occur primarily as a complication of secretion aspiration (1).

A 70-y-old patient who had undergone previous surgery for prostate cancer, was a former smoker, and had a family history of lung cancer presented with hemoptysis. A thoracic high-resolution CT scan detected a 45-mm heterogeneous pulmonary nodule (with surrounding ground-glass opacification) in the inferior right lobe, suggestive of malignancy and no significant adenopathies. Subsequent [<sup>18</sup>F]F-FDG PET/CT showed significant uptake in the nodule, with SUV<sub>max</sub> of 12.7 (Fig. 1A). For the suspected lung cancer, the patient was then enrolled in a prospective monocentric interventional study (EudraCT number 2021-006570-23 [CE AVEC: 51/2022/Fam/AOUBo]; the study protocol was approved by a Committee on Ethics, and all subjects signed a written informed-consent form). The patient underwent [<sup>68</sup>Ga]Ga-fibroblast activation protein inhibitor (FAPI)-46 PET/CT 23 d later. The images showed only mild uptake (SUV<sub>max</sub>, 5.9 at 60 min after injection; Fig. 1B) in the pulmonary nodule, slightly increasing on delayed scanning (SUV<sub>max</sub>, 8.9 at 160 min). No lymph node uptake was detected.

Bronchoscopy was performed, and the frozen-section procedure showed reactive bronchial cells with granulocyte infiltration and lymphocytes; however, the results of microbiology and biochemical blood testing were negative. Subsequent CT confirmed the lung finding, with necrotic center features, not responding to antibiotic therapy. One month after [<sup>68</sup>Ga]Ga-FAPI-46 PET/CT, the patient was hospitalized for recurrent hemoptysis, low hemoglobin level, and weight loss. After multidisciplinary evaluation, the patient was referred for right inferior lobectomy. The definitive histopathologic diagnosis excluded the presence of neoplastic cells; on the contrary, it showed acute bronchopneumonia and chronic abscess with gram-positive colonies, consistent with actinomycosis. Immunohistochemistry was also performed (Figs. 1C and 1D) with FAPI (53066; Abcam) and IRF-4 (EP190 [Ventana; Roche]) double staining: FAPI antibody reacts with fibroblasts and plasma cells, whereas IRF-4 is a specific immunostain for plasma cells.

Although actinomycosis is well known to mimic lung cancer on [<sup>18</sup>F]F-FDG PET/CT (2,3), this is a clear example of how the new tracer [<sup>68</sup>Ga]Ga-FAPI-46 can also be misleading in infection.



**FIGURE 1.** (A) Lung nodule on transaxial [<sup>18</sup>F]F-FDG PET fused with attenuation-corrected CT. (B) Lung nodule on transaxial [<sup>68</sup>Ga]Ga-FAPI-46 PET fused with attenuation-corrected CT (60-min uptake time). PET intensity scales are based on SUV body weight (g/mL). (C) Hematoxylin- and eosin-stained sections at  $\times 4$  magnification. Acute and chronic pneumonia with abscess formation is seen. Lesion is seen with rich acute and chronic inflammation, plasma cells, and fibroblasts. (D) Brown color represents fibroblast activation protein positivity in plasma cells and fibroblasts (black arrowhead), and red color represents IRTA1 nuclear immunoreactivity in plasma cells (blue arrowhead). Magnification is  $\times 10$ .

However, [<sup>18</sup>F]F-FDG and [<sup>68</sup>Ga]Ga-FAPI-46 uptake proved to be different, with [<sup>68</sup>Ga]Ga-FAPI-46 uptake being slightly milder.

Although a few other cases of granulomatous diseases mimicking malignancies on [<sup>68</sup>Ga]Ga-FAPI PET/CT have been described (4), full knowledge of this promising tracer's features and pitfalls (5) has yet to be acquired.

## DISCLOSURE

This research project was funded by FIN-RER 2020 Program of Emilia-Romagna Region. No other potential conflict of interest relevant to this article was reported.

## REFERENCES

- Valour F, Sénéchal A, Dupieux C, et al. Actinomycosis: etiology, clinical features, diagnosis, treatment, and management. *Infect Drug Resist.* 2014;7:183–197.
- Aydin Y, Arslan R, Filik M. Pulmonary actinomycosis mimicks lung cancer. *Rev Soc Bras Med Trop.* 2022;55:e0195.
- Kogure S, Yamamoto N, Watanabe F, Yuasa U, Tokui T, Shomura S. Pulmonary actinomycosis which was clinically suggested lung cancer; report of a case [in Japanese]. *Kyobu Geka.* 2011;64:254–257.
- Meetschen M, Sandach P, Darwiche K, et al. Rabbit fever: granulomatous inflammation by *Francisella tularensis* mimics lung cancer in dual tracer <sup>18</sup>F-FDG and <sup>68</sup>Ga-FAPI PET/CT. *Eur J Nucl Med Mol Imaging.* 2023;50:2567–2569.
- Hotta M, Rieger AC, Jafarvand MG, et al. Non-oncologic incidental uptake on FAPI PET/CT imaging. *Br J Radiol.* 2023;96:20220463.

Received Nov. 28, 2023; revision accepted Feb. 13, 2024.

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Published online Mar. 7, 2024.

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DOI: 10.2967/jnumed.123.267155