Case report

doi:10.5633/amm.2026.0113

UNUSUAL 18F-FLUOROCHOLINE UPTAKE IN PULMONARY CARCINOID AND EXTRAPULMONARY METASTATIC LESIONS: CASE REPORT AND REVIEW OF LITERATURE

Milica Kotur[1], Miloš Veljković[1,2], Nikola Pantić[1], Lenka Grujičić[1], Isidora Grozdić Milojević[1,2], Dragana Šobić Šaranović[1,2], Vera Artiko[1,2], Strahinja Odalović[1,2]

[1]Center for Nuclear Medicine with PET, University Clinical Center of Serbia, Belgrade, Serbia

[2]Faculty of Medicine, University of Belgrade, Belgrade, Serbia

Contact: Milica Kotur

11000 Višegradska 26, Belgrade, Serbia

E-mail: koturmilica99@gmail.com

AMM Paper Accepted

This case highlights a rare instance of fluorocholine (FCH) uptake in pulmonary carcinoid and suspected extrapulmonary metastatic lesions. A 72-year-old male with a two-year history of pulmonary carcinoid was referred to the Nuclear Medicine Center with PET at the University Clinical Center of Serbia for FCH PET/CT due to elevated serum parathyroid hormone (PTH) levels. The scan demonstrated increased FCH uptake in lymph nodes of the mediastinum and neck, pulmonary lesions in the right lung (with osteolysis of the VII and VIII ribs), and multiple skeletal sites. No increased FCH uptake was detected in the parathyroid glands. Clinically, this case raises important questions regarding potential differences between FCH-avid and non-FCH-avid pulmonary carcinoids in terms of tumor aggressiveness, histological subtype (typical vs. atypical), prognosis, and treatment response.

Keywords: atypical fluorocholine uptake, pulmonary carcinoid, elevated parathyroid hormone

Prikaz bolesnika

doi:10.5633/amm.2026.0113

NEOBIČNA AKUMULACIJA 18F-FLUOROHOLINA U PLUĆNOM KARCINOIDU I EKSTRAPULMONALNIM METASTATSKIM LEZIJAMA: PRIKAZ SLUČAJA I PREGLED LITERATURE

Milica Kotur[1], Miloš Veljković[1,2], Nikola Pantić[1], Lenka Grujičić[1], Isidora Grozdić Milojević[1,2], Dragana Šobić Šaranović[1,2], Vera Artiko[1,2], Strahinja Odalović[1,2]

[1] Centar za Nuklearnu Medicinu sa PET, Univerzitetski klinički centar Srbije, Beograd, Srbija

[2] Medicinski fakultet Univerziteta u Beogradu, Srbija

Kontakt: Milica Kotur

11000 Višegradska 26, Belgrade, Serbia

E-mail: koturmilica99@gmail.com

Ovaj prikaz slučaja predstavlja retku pojavu akumualcije fluoroholina (engl. *Fluorocholine, FCH*) u plućnom karcinoidu i ekstrapulmonalnim promenama koje su suspektne na metastatske depozite. Pacijent starosti 72 godine, koji boluje od plućnog karcinoida dve godine, upućen je u Centar za nuklearnu medicinu sa PET Univerzitetskog kliničkog centra Srbije na *FCH* PET/CT ispitivanje zbog povišenih vrednosti paratireoidnog hormona (PTH) u serumu. Detektovano je pojačano preuzimanje *FCH* u limfnim čvorovima vrata i medijastinuma, mekotkivnom promenama u desnom plućnom krilu sa osteolizom VII i VIII rebra, kao i na više mesta u koštanom sistemu. U paratireoidnim žlezdama nije bilo prisutno pojačano *FCH* preuzimanje. Sa kliničkog aspekta, važno je ispitati da li postoje razlike između plućnih karcinoida koji su *FCH*-avidni i onih koji nisu u pogledu agresivnosti bolesti, histološkog podtipa, prognoze i potencijalnog terapijskog odgovora.

Ključne reči: atipična akumulacija fluoroholina, plućni karcinoid, povišene vrednosti PTH u krvi

AMM Paper Accepted

Introduction

^{18}F-fluorocholine (FCH) is a radiopharmaceutical composed of a choline molecule labeled with the fluorine-18 isotope, and it plays an important role in the diagnosis and evaluation of various diseases using positron emission tomography (PET). The enzyme choline kinase phosphorylates choline into fluorocholine, which subsequently enters a series of chemical reactions and is incorporated into phospholipids — essential components of the cell membrane (1). Nearly all neoplastic cells exhibit a tendency for rapid proliferation, which leads to overexpression of choline-transporters that facilitate the active uptake of choline and analogues like fluoro-choline. (2).

FCH PET with computed tomography (CT) is mainly used for the detection of a hyperfunctional parathyroid gland (3, 4). Although ultrasound combined with ^{99m}Tc-methoxyisobutylisonitrile (MIBI) is most commonly used in the evaluation of hyperparathyroidism of various etiologies, an increasing number of studies emphasize that FCH PET/CT offers higher sensitivity, better spatial resolution, lower radiation dose, and shorter acquisition time compared to the ^{99m}Tc-MIBI method in the detection of primary hyperparathyroidism (5-7). Before the introduction of Prostate-Specific Membrane Antigen (PSMA) PET/CT imaging in the diagnosis of prostate cancer, FCH PET/CT was frequently used for detecting metastatic disease in lymph nodes (8, 9). FCH PET/CT also plays a significant role in the initial staging of hepatocellular carcinoma, as well as in the evaluation of response to targeted therapy (10).

Pulmonary carcinoid is a rare tumor, accounting for only 1–2% of all lung neoplasms, and can be histopathologically classified into typical and atypical carcinoids (11-13). Typical carcinoids are well-differentiated and associated with a more favorable prognosis, whereas atypical carcinoids are poorly differentiated, exhibit a more aggressive course, and have a higher tendency to metastasize (12, 14, 15). Carcinoid tumor cells express somatostatin receptors, and the level of receptor expression is associated with the degree of differentiation — typical carcinoids show higher receptor density on the cell surface, while atypical carcinoids demonstrate lower density (16). Nuclear medicine techniques commonly used in the evaluation of pulmonary carcinoids, particularly typical ones, include radiolabeled somatostatin analogs such as ^{111}In-octreotide and ^{68}Ga-DOTATATE (16-18). For the detection of atypical carcinoids, FDG PET/CT is often employed due to their higher proliferative activity (16).

AMM Paper Accepted

While FCH PET/CT is not typically preferred for detecting pulmonary carcinoid tumors due to generally low uptake, occasional cases have shown high choline avidity, suggesting that functional neuroendocrine tumors should also be considered in such findings (19).The purpose of this case report is to highlight the unusual and rare occurrence of FCH uptake in a pulmonary carcinoid, as well as in extrapulmonary metastatic lesions.

Case presentation

A 72-year-old male patient was referred to the Center for Nuclear Medicine with PET at the University Clinical Center of Serbia for an FCH PET/CT examination due to elevated serum parathyroid hormone (PTH) levels (116 ng/L). A review of medical records revealed that has had a diagnosis of pulmonary carcinoid for the past two years. At the time of diagnosis, a chest X-ray revealed a tumor mass, located in the lower lobe of the right lung.

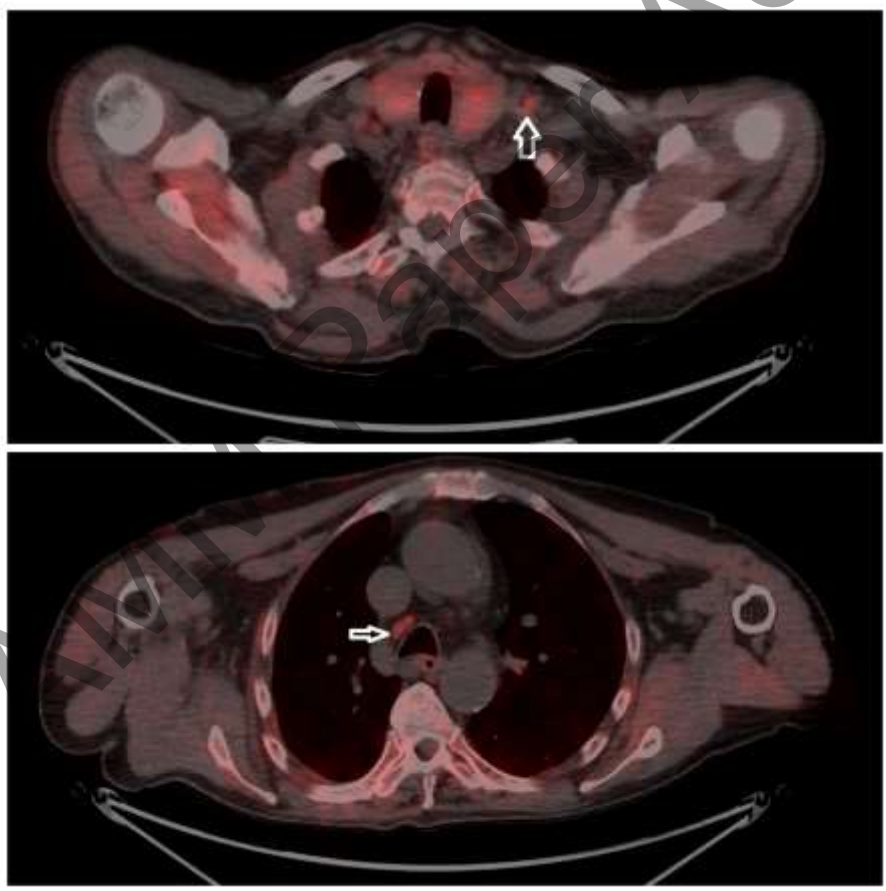
Approximately two months prior to the FCH PET/CT examination, a multislice (MS)CT scan of the chest and abdomen was performed, which revealed a persistent tumor mass in the lower lobe of the right lung, measuring 95 × 110 × 90 mm. The lesion exhibited partial infiltration of the intermediate bronchus and complete obstruction of the segmental bronchus supplying the lower lobe. Additionally, another tumor mass was detected, measuring 47 × 70 × 51 mm, located posterior to the previously described mass, adjacent to the posterior chest wall, with osteolysis of the posterior portion of the VII and VIII ribs. Furthermore, enlarged mediastinal lymph nodes were reported, as well as a heterodense lesion in the VII segment of the liver, which was characterized as highly suspicious for a metastatic deposit.

Initial bronchoscopy revealed an unclassified carcinoid tumor after a chest X-ray detected a mass in the right lung, with the diagnosis confirmed by Tru-cut biopsy of a posterior chest wall lesion performed one month after MSCT. Histopathological analysis identified an atypical pulmonary carcinoid, with a Ki-67 proliferation index between 3% and 5%, a mitotic count of 2–3 per 2 mm², and the presence of small foci of necrosis. Additionally, elevated serum chromogranin A (CgA) levels were recorded (1003.1 ng/mL). The medical documentation indicates that the patient has not expressed interest in treatment since the diagnosis was established.

The FCH PET/CT scan, covering the region from the vertex to the proximal third of the femurs, was performed on a Discovery PET/CT Elite system (GE Healthcare) 45 minutes after the

AMM Paper Accepted

administration of 180 MBq of FCH. Increased FCH uptake was observed in the following regions: a left supraclavicular lymph node measuring 7 mm in diameter (Figure 1); mediastinal lymph nodes, including a right paratracheal node measuring 8 mm (Figure 1), and bilateral hilar nodes (Figure 2). A 14 mm nodular lesion was detected within the lumen of the lobar bronchus (Figure 3). This lesion was contiguous with a soft tissue mass located posterobasally in the lower lobe of the right lung, measuring 11 × 82 mm, previously described on CT (Figure 3). Additionally, another soft tissue lesion, located more cranially, was identified near the posterior chest wall at the level of the VII and VIII right ribs, measuring 5 × 74 mm, also previously described on CT (Figure 4). This lesion caused osteolysis of the posterior portions of the aforementioned ribs. Increased FCH uptake was also noted in multiple skeletal sites: the right scapula (Figure 5), the second thoracic vertebra (Figure 5), the body of the sternum (Figure 6), and the inferior ramus of the right pubic bone (Figure 7). Despite elevated serum PTH levels, no increased FCH accumulation was detected in the parathyroid glands.



Article in Press Accepted

Figure 1. Left supraclavicular (above) (SUVmax 2.5) and right paratracheal (down) lymph nodes (SUVmax 3.0) with moderately increased FCH uptake, suspicious for metastases from pulmonary carcinoid.

AMM Paper Accepted

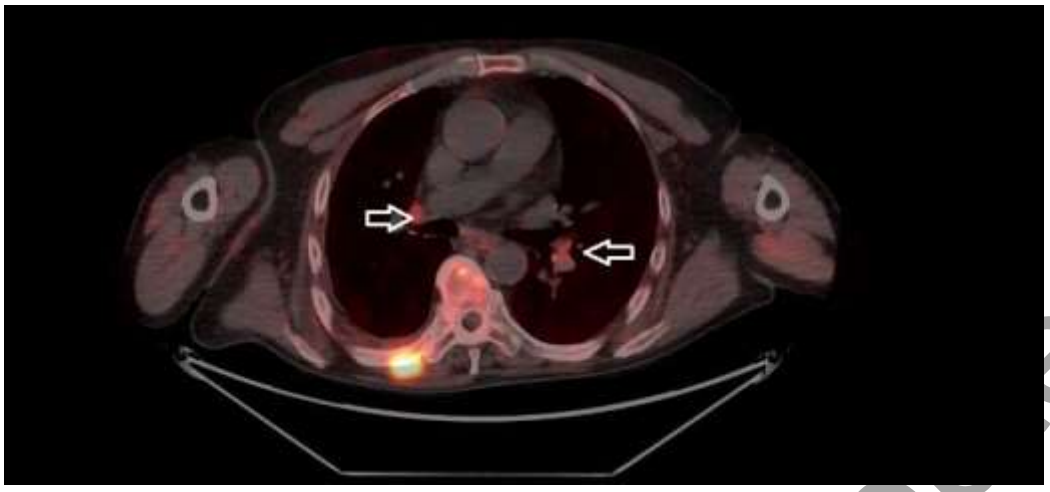


Figure 2. The arrows demonstrate increased FCH uptake in bilateral hilar lymph nodes (SUVmax up to 3.7), suspicious for metastatic spread of pulmonary carcinoid.

AMM Paper Accepted

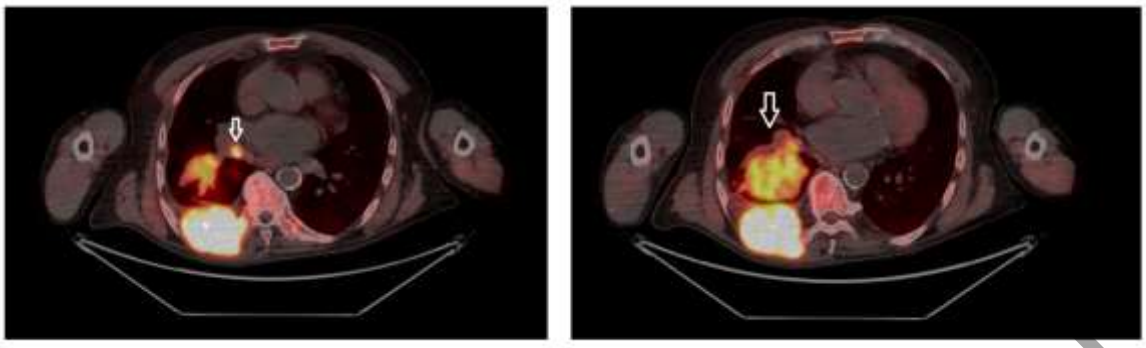


Figure 3. The left image shows a nodular lesion within the lumen of the right lower lobe bronchus with increased FCH uptake (white arrow) (SUVmax 10.4), while the right image shows a soft-tissue mass continuous with the nodular lesion seen on the left (SUVmax 10.4), also demonstrating increased FCH uptake — consistent with pulmonary carcinoid.

AMM Paper Accepted

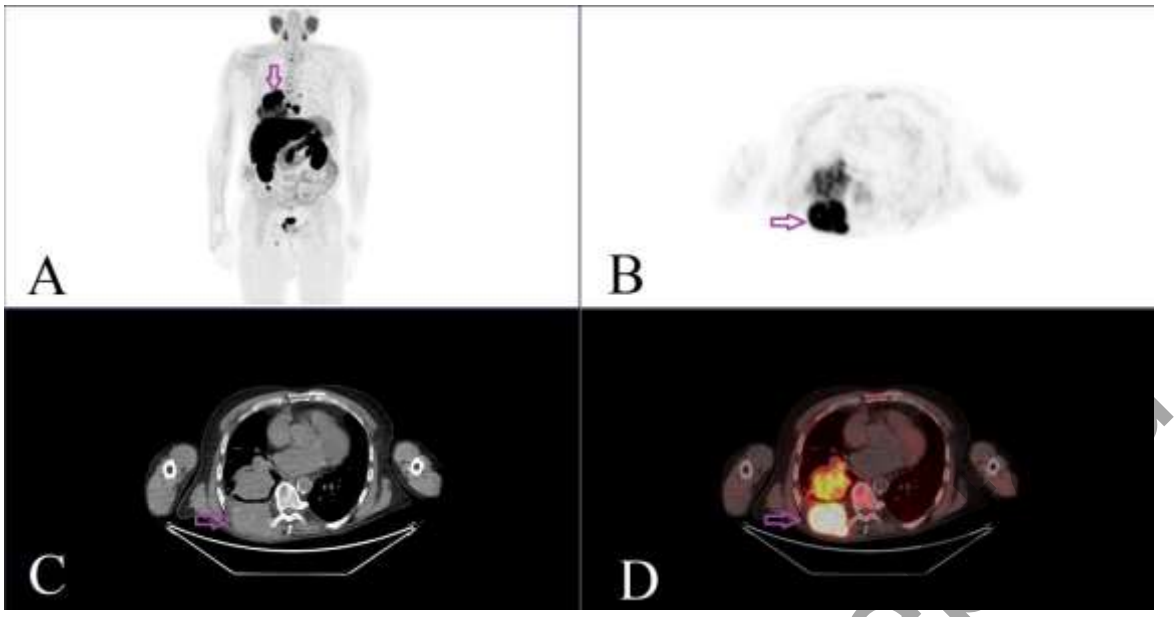


Figure 4. The arrow indicates increased FCH uptake in a tumor lesion (part of a pulmonary carcinoid) causing osteolysis of the VII and VIII ribs (SUVmax 15.7) (A – on MIP; B – on PET; C – on low-dose CT; D – on PET/CT).

AMM Paper Accepted

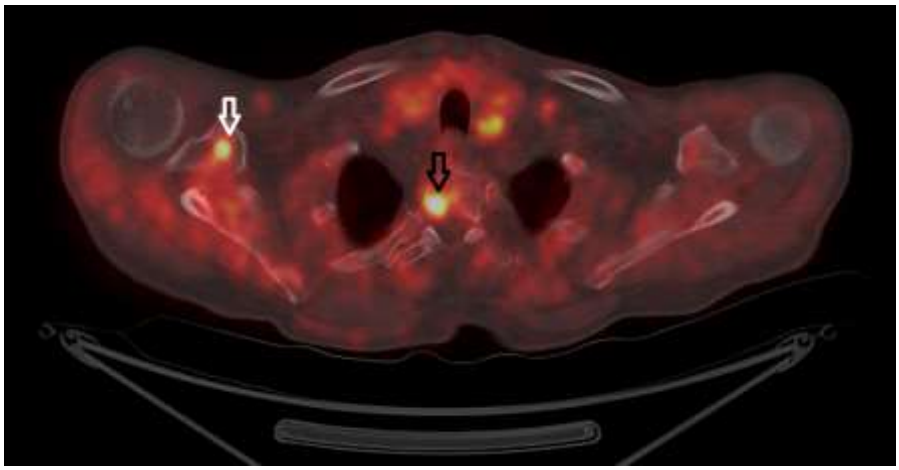


Figure 5. The white arrow indicates increased FCH uptake in the right scapula (SUVmax 5.6), while the black arrow shows increased uptake in the Th2 vertebral body (SUVmax 17.6) — both highly suspicious for metastases from pulmonary carcinoid.

AMM Paper Accepted

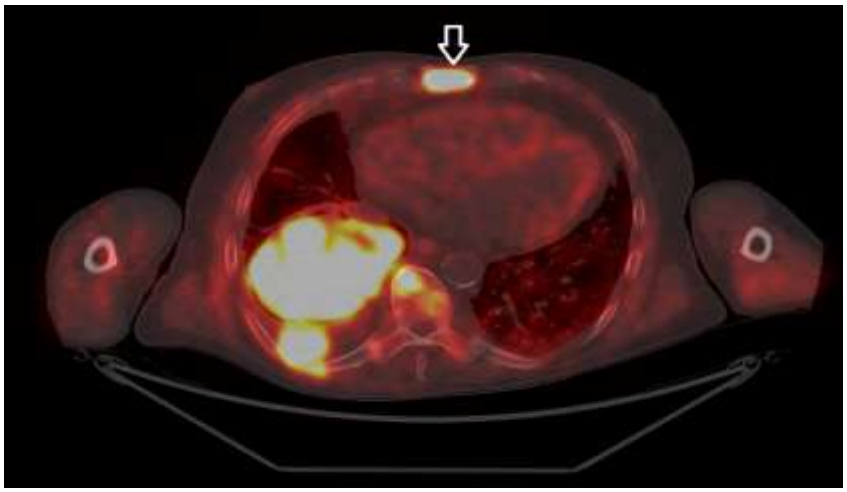


Figure 6. Increased FCH uptake in the body of the sternum (SUVmax 12.0) — highly suspicious for a metastatic lesion from pulmonary carcinoid.

AMM Paper Accepted

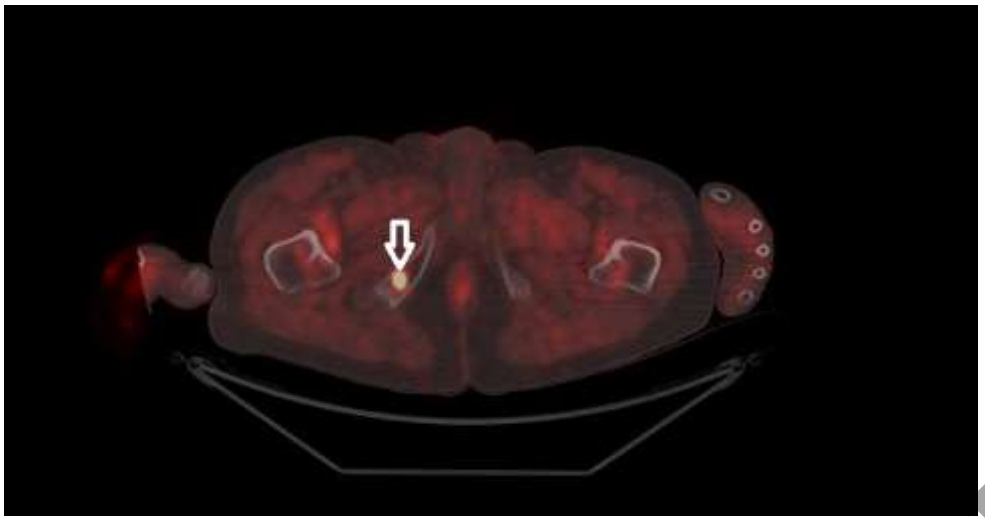


Figure 7. Increased FCH uptake in the right ischial bone (SUVmax 9.8) — suspicious for metastatic involvement.

Discussion

This case presents an uncommon example of FCH uptake in a pulmonary carcinoid tumor, as well as in extrapulmonary lesions that are most likely of metastatic origin. Tumor masses located in the lower lobe of the right lung, osteolysis of the VII and VIII ribs, and enlarged mediastinal lymph nodes—previously identified on MSCT—were confirmed by FCH PET/CT, demonstrating significant radiotracer accumulation. However, the FCH PET/CT scan also revealed additional lesions suspicious for metastases. These included lesions with FCH increased in the right scapula, the body of the sternum including the xiphoid process, the second thoracic vertebra, and the inferior ramus of the right pubic bone. In addition, a left supraclavicular lymph node with elevated uptake was detected. Interestingly, the heterodense lesion in segment VII of the liver, previously described on MSCT, was not visualized on the low-dose CT component of the FCH PET/CT scan.

Although the patient was referred for FCH PET/CT imaging due to elevated serum PTH levels, no increased FCH accumulation was observed in the parathyroid glands. A thorough review of the medical documentation, along with long-term follow-up by physicians from various specialties, did not identify a definitive cause of hyperparathyroidism. It is important to consider the possibility of ectopic PTH secretion as part of a paraneoplastic syndrome. However, pulmonary carcinoid tumors typically secrete ACTH or its precursors, while ectopic PTH production is more commonly

AMM Paper Accepted

associated with squamous cell carcinoma of the lung, malignancies of the head and neck region, as well as esophageal, vulvar, vaginal, cervical, and other solid tumors (20).

As previously mentioned, FCH PET/CT is most commonly used for the detection of primary hyperparathyroidism, hepatocellular carcinoma, and prostate cancer, while FCH uptake in other malignancies, including pulmonary carcinoid tumors, is a rare occurrence (19). The study presented by Van der Hiel et al. one of the few reported cases of FCH uptake in pulmonary carcinoid tumors. The authors described three cases of FCH accumulation in pulmonary carcinoid, two of which were atypical and one typical carcinoid. These cases, including ours, suggest that pulmonary carcinoid tumors, regardless of being typical or atypical, may demonstrate FCH uptake. When comparing the histopathological findings of the atypical carcinoid in our patient with those from the Van der Hiel et al. study, certain similarities and differences can be noted. The Ki-67 proliferation index in our case ranged from 3% to 5%, whereas in their patients it varied as follows: less than 1%, between 1% and 5%, and 10%. The mitotic index in their patients was <2 per 2 mm², 6 per 2 mm², and 2 per 2 mm², partially consistent with our finding of 2 per 2 mm². Small foci of necrosis were observed in our patient's histopathological specimen, while their series included patients both with and without necrosis. Based on these data, it is difficult to identify a common characteristic that could reliably serve as a predictive parameter for FCH accumulation, given the variability of all three analyzed features among the total of four cases.

In non-small cell lung carcinomas, increased choline kinase activity has been observed; however, in neuroendocrine tumors, due to their very low proliferation rate, the high choline accumulation is unlikely to be explained by this mechanism. On the other hand, it is known that small cell lung carcinoma cells express CTL1—a protein similar to choline transporter 1—which facilitates more efficient uptake of choline from the extracellular environment (19). It remains unclear whether certain pulmonary carcinoids exhibit increased CTL1 expression or possess higher proliferative activity that could lead to enhanced choline kinase activity. These questions remain unresolved and warrant further investigation.

Conclusion

This rare case of FCH accumulation in a pulmonary carcinoid may serve as a basis for future research exploring the potential role of this radiotracer in the detection of such malignancies. From a clinical perspective, it would be valuable to investigate whether there are differences

AMM Paper Accepted

between FCH-avid and non–FCH-avid carcinoids in terms of disease aggressiveness, histological subtype (typical vs. atypical), prognosis, and potential therapeutic response. Further studies could help clarify whether FCH PET/CT has a role as an adjunct diagnostic tool in the evaluation and individualized management of patients with pulmonary carcinoid tumors.

Acknowledgement

The study was supported by Grant No 451-03-137/2025-03/ 200110 Ministry of Science, Technological Development and Innovation.

AMM Paper Accepted

References

1. Zeisel SH, Blusztajn JK. Choline and human nutrition. Annu Rev Nutr. 1994;14:269-296. doi:10.1146/annurev.nu.14.070194.001413. PMID: 7946521

2. Podo F. Tumour phospholipid metabolism. NMR Biomed. 1999;12(7):413-439. doi:10.1002/(sici)1099-1492(199911)12:7<413::aid-nbm587>3.0.co;2-u. PMID: 10654290

3. Treglia G, Piccardo A, Imperiale A, Strobel K, Kaufmann PA, Prior JO, et al. Diagnostic performance of choline PET for detection of hyperfunctioning parathyroid glands in hyperparathyroidism: a systematic review and meta-analysis. Eur J Nucl Med Mol Imaging. 2019;46:751-765. doi:10.1007/s00259-018-4123-z. PMID: 30094461.

4. Cuderman A, Senica K, Rep S, Hocevar M, Kocjan T, Jensterle Sever M, et al. 18F-Fluorocholine PET/CT in Primary Hyperparathyroidism: Superior Diagnostic Performance to Conventional Scintigraphic Imaging for Localization of Hyperfunctioning Parathyroid Glands. J Nucl Med. 2020;61(4):577-583. doi:10.2967/jnumed.119.229914. PMID: 31562221.

5. De Feo ML, Colagrande S, Biagini C, Tonarelli A, Bisi G, Vaggelli L, et al. Parathyroid glands: combination of (99m)Tc MIBI scintigraphy and US for demonstration of parathyroid glands and nodules. Radiology. 2000;214(2):393-402. doi:10.1148/radiology.214.2.r00fe04393. PMID: 10671586

6. Damle NA, Tripathi M, Behera A, Aggarwal S, Bal C, Aggarwal S, et al. Utility of (18)F-choline photon emission tomography/computed tomography in the diagnosis of parathyroid adenoma [published correction appears in Indian J Nucl Med. 2016 Oct-Dec;31(4):324. doi: 10.4103/0972-3919.190809. PMID: 27385893

7. Nocuń A, Kędra M, Stefaniak B, Chrapko B. Parathyroid hyperplasia detected by F-18-Choline PET/CT, negative on Tc-99m-MIBI SPECT/CT and F-18-Deoxyglucose PET/CT scans. Nucl Med Rev Cent East Eur. 2017;20(1):60-61. doi:10.5603/NMR.2017.0005. PMID: 28218350

8. Roland A, Drouet C, Boulahdour H, Cochet A, De Bari B. Unusual uptakes on 18F-fluorocholine positron emission tomography/computed tomography (PET/CT): a retrospective study of 368

AMM Paper Accepted

prostate cancer patients referred for a biochemical recurrence or an initial staging. Quant Imaging Med Surg. 2021;11(1):172-182. doi:10.21037/qims-19-981. PMID: 33392020

9. Bjöersdorff M, Puterman C, Oddstig J, Amidi J, Zackrisson S, Kjölhede H, et al. Detection of lymph node metastases in patients with prostate cancer: Comparing conventional and digital [18 F]-fluorocholine PET-CT using histopathology as a reference. Clin Physiol Funct Imaging. 2022;42(6):381-388. doi:10.1111/cpf.12770. PMID: 35866190

10. Wallace MC, Sek K, Francis RJ, Samuelson S, Ferguson J, Tibballs J et al. Baseline and Post-treatment 18F-Fluorocholine PET/CT Predicts Outcomes in Hepatocellular Carcinoma Following Locoregional Therapy. Dig Dis Sci. 2020;65(2):647-657. doi:10.1007/s10620-019-05781-6. PMID: 31440998

11. Fink G, Krelbaum T, Yellin A, Bendayan D, Saute M, Glazer M et al. Pulmonary carcinoid: presentation, diagnosis, and outcome in 142 cases in Israel and review of 640 cases from the literature. Chest. 2001;119(6):1647-1651. doi:10.1378/chest.119.6.1647. PMID: 11399686

12. Martini N, Zaman MB, Bains MS, et al. Treatment and prognosis in bronchial carcinoids involving regional lymph nodes. J Thorac Cardiovasc Surg. 1994;107(1):1-7. PMID: 8283871

13. Bertino EM, Confer PD, Colonna JE, Ross P, Otterson GA. Pulmonary neuroendocrine/carcinoid tumors: a review article. Cancer. 2009;115(19):4434-4441. doi:10.1002/cncr.24498. PMID: 19562772

14. Filosso PL, Rena O, Donati G, Casadio C, Ruffini E, Papalia E, et al. Bronchial carcinoid tumors: surgical management and long-term outcome. J Thorac Cardiovasc Surg. 2002;123(2):303-309. doi:10.1067/mtc.2002.119886. PMID: 11828290

15. Thakur S, Florisson D, Telianidis S, Yaftian N, Lee J, Knight S, et al. Pulmonary carcinoid tumours: A multi-centre analysis of survival and predictors of outcome following sublobar, lobar, and extended pulmonary resections. Asian Cardiovasc Thorac Ann. 2021;29(6):532-540. doi:10.1177/02184923211010090. PMID: 33853389

16. Jindal T, Kumar A, Venkitaraman B, Meena M, Kumar R, Malhotra A, et al. Evaluation of the role of [18F]FDG-PET/CT and [68Ga]DOTATOC-PET/CT in differentiating typical and atypical

AMM Paper Accepted

pulmonary carcinoids. Cancer Imaging. 2011;11(1):70-75. doi:10.1102/1470-7330.2011.0010. PMID: 21697027

17. Herrmann K, Czernin J, Wolin EM, Gupta P, Barrio M, Gutierrez A, et al. Impact of 68Ga-DOTATATE PET/CT on the management of neuroendocrine tumors: the referring physician's perspective. J Nucl Med. 2015;56(1):70-75. doi:10.2967/jnumed.114.148247. PMID: 25500825

18. Därr R, Zöphel K, Eisenhofer G, Abolmaali N, Gastmeier J, Wieczorek K, et al. Combined use of 68Ga-DOTATATE and 18F-FDG PET/CT to localize a bronchial carcinoid associated with ectopic ACTH syndrome. J Clin Endocrinol Metab. 2012;97(7):2207-2208. doi:10.1210/jc.2012-1402. PMID: 22529105

19. Van der Hiel B, Stokkel MP, Buikhuisen WA, Janssen H, van Velthuysen MF, Rhodius RJ, et al. 18F-Choline PET/CT as a new tool for functional imaging of non-proliferating secreting neuroendocrine tumors. J Endocrinol Metab. 2015;5(4):267-271. doi: http://dx.doi.org/10.14740/jem300w

20. Ahmadieh H, Arabi A. Endocrine paraneoplastic syndromes: a review. Endocrinol Metab Int J. 2015;1(1):15-25. doi: 10.15406/emij.2015.01.00004

AMM Paper Accepted