

CXCR4-targeted PET/CT with Al¹⁸F-NOTA-Pentixather shows superior sensitivity to ¹⁸F-FDG in thyroid follicular lymphoma

Abstract

Primary thyroid follicular lymphoma (FL) is exceedingly rare with frequently low fluorine-18-fluorodeoxyglucose (¹⁸F-FDG) avidity, challenging accurate staging. We report the case of a 49-year-old female who underwent left thyroid lobectomy for a thyroid imaging reporting and data system (TI-RADS) 4a nodule, with histopathology confirming low-grade FL. Postoperative ¹⁸F-FDG positron emission tomography/computed tomography (PET/CT) showed only mild uptake at the surgical bed and cervical lymph nodes, interpreted as reactive change. A subsequent aluminum fluoride-18-1,4,7-triazacyclononane-1,4,7-triacetic acid-Pentixather (Al¹⁸F-NOTA-Pentixather) C-X-C chemokine receptor type 4 (CXCR4)-targeted PET/CT, however, revealed multiple intensely avid cervical and abdominal nodal lesions and spleen involvement. This imaging discrepancy underscores the limitations of ¹⁸F-FDG in low-grade lymphomas and suggests that CXCR4-targeted PET/CT may offer a more accurate reflection of disease burden, with potential implications for staging and therapeutic management.

Hell J Nucl Med 2026;29(2): 139-140

Published online: 31 August 2026

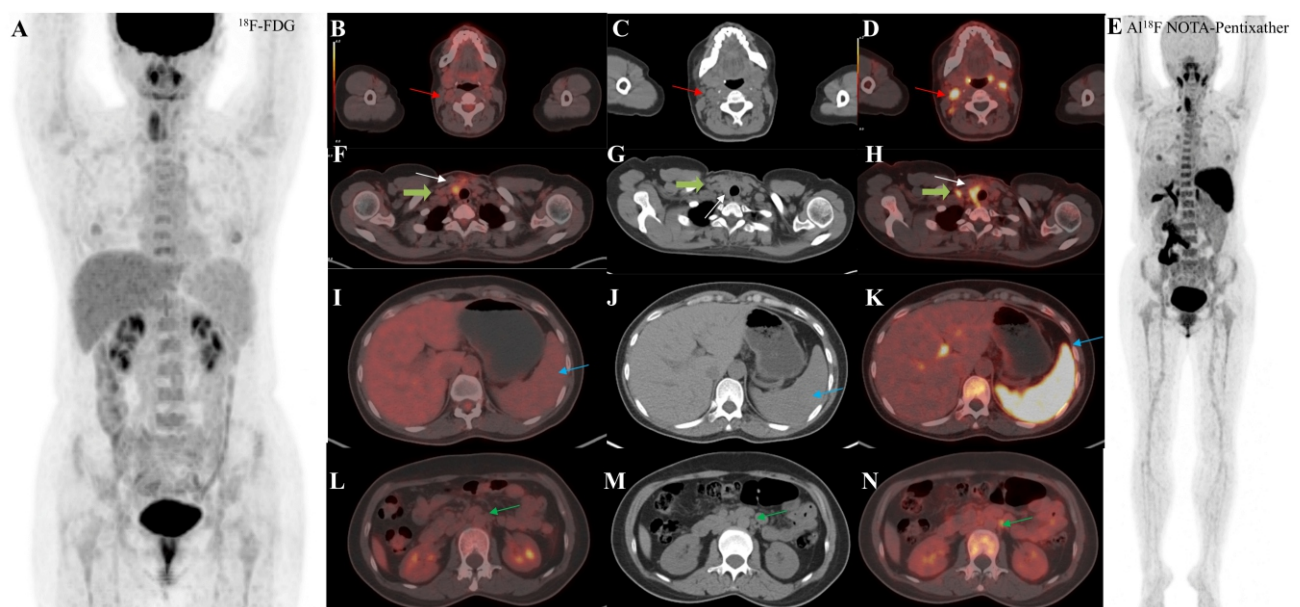


Figure 1. A 49-year-old female presented with a painless left neck nodule (TI-RADS 4a) and subsequently underwent left thyroid lobectomy and isthmectomy. Histopathological and immunohistochemical analysis confirmed the diagnosis of low-grade follicular lymphoma, positive for CD20, CD10, BCL-6, and partially positive for BCL-2, with Ki-67 of ~30%. One month post-surgery, ¹⁸F-FDG PET/CT was performed for staging. The ¹⁸F-FDG PET/CT showed mild uptake in the surgical bed and scattered cervical lymph nodes, with no definitive evidence of distant disease (A, B, F, I, L). These findings were interpreted as postoperative or reactive changes. Given clinical suspicion, the patient subsequently underwent Al¹⁸F-NOTA-Pentixather PET/CT. This scan revealed strikingly intense uptake in multiple lymph nodes in the submandibular, upper cervical, supraclavicular, and parapharyngeal regions, as well as diffusely increased uptake in the spleen and abdominal lymph nodes (D, E, H, K, N). Axial fused PET/CT images (B, D), axial CT images (C, G), and fused images (F, H) demonstrate the cervical and parapharyngeal nodal involvement (red arrows: submandibular node; green/white arrows: parapharyngeal nodes). Hepatic lesion (blue arrow) on fused and CT images (I, J, K). Abdominal nodal lesion (green arrow) on fused, CT, and fused images (L, M, N).

Primary thyroid lymphoma constitutes fewer than 5% of thyroid malignancies, with FL being one of the rarer subtypes (~3%-5%) [1, 2]. Low-grade FL often exhibit low glycolytic activity, leading to false-negative or underwhelming ¹⁸F-FDG PET/CT results. As highlighted in this case, ¹⁸F-FDG PET/CT demonstrated only mild uptake which was interpreted as postoperative or reactive changes.

The chemokine receptor CXCR4 is overexpressed in various B-cell lymphomas [3, 4]. Al¹⁸F-NOTA-Pentixather has proven superior in targeting this receptor, providing higher lesion detection sensitivity compared to ¹⁸F-FDG. In this case, CXCR4 imaging was pivotal in revealing the true extent of disease which was underestimated on ¹⁸F-FDG PET/CT. The discordant imaging findings prompted a reassessment of disease burden, highlighting the potential role of Al¹⁸F-NOTA-Pentixather PET/CT in accurate staging and guiding therapeutic decisions.

In conclusion, this case illustrates the superiority of CXCR4-targeted Al¹⁸F-NOTA-Pentixafer PET/CT over ¹⁸F-FDG PET/CT for staging low-grade thyroid FL, a tumor type characterized by low glycolytic activity. C-X-C chemokine receptor type 4-targeted imaging should be considered when ¹⁸F-FDG results are equivocal in patients with low-grade B-cell lymphomas.

The authors declare that they have no conflicts of interest.

Bibliography

1. Bacon CM, Diss TC, Ye H et al. Follicular lymphoma of the thyroid gland. *Am J Surg Pathol* 2009; 33: 22-34.
2. Naswa N, Sharma P, Nazar AH et al. ¹⁸F-FDG PET/CT for initial assessment and response monitoring in a case of high grade primary lymphoma of the thyroid gland: a case report and review of literature. *Indian J Nucl Med* 2014; 29: 94-6.
3. Luo Y, Cao X, Pan Q et al. ⁶⁸Ga-Pentixafer PET/CT for imaging of chemokine receptor 4 expression in Waldenström macroglobulinemia/lymphoplasmacytic lymphoma: comparison to ¹⁸F-FDG PET/CT. *J Nucl Med* 2019; 60: 1724-9.
4. Pan Q, Luo Y, Zhang Y et al. Preliminary evidence of imaging of chemokine receptor-4-targeted PET/CT with [⁶⁸Ga]pentixafer in non-Hodgkin lymphoma: comparison to ¹⁸F-FDG. *EJNMMI Res* 2020; 10: 89.

Caiqiong Zhou¹ MD, Yanqing Diao² MD

1. Department of Endocrinology, Chengdu Fifth People's Hospital, Chengdu, Sichuan, China. 2. Department of Nutrition, Chengdu Fifth People's Hospital, Chengdu, Sichuan, China.

Corresponding author: Yanqing Diao MD, Department of Nutrition, Chengdu Fifth People's Hospital, Chengdu, Sichuan, China. Tel: +86-15390037897, E-mail: yanqingdiao@yeah.net
