

Targeting personalized medicine in a non-Hodgkin lymphoma patient with ^{18}F -FDG and ^{18}F -choline PET/CT

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SUMMARY

Early diagnosis and staging of non-Hodgkin lymphoma (NHL) is essential for therapeutic strategy decision. Positron emission tomography/computed tomography (PET/CT) with fluorodeoxyglucose (FDG), a glucose analogue, labeled with fluor-18 (^{18}F -FDG) has been used to evaluate staging, therapy response and prognosis in NHL patients. However, in some cases, ^{18}F -FDG has shown false-positive uptake due to inflammatory reaction after chemo and/or radiation therapy. In this case report, we present a NHL patient evaluated with ^{18}F -FDG and ^{18}F -choline PET/CT scan imaging pre- and post-therapy. ^{18}F -FDG and ^{18}F -choline PET/CT were performed for the purpose of tumor staging and have shown intense uptake in infiltrative tissue as well as in the lymph node, but with some mismatching in the tumor. Post-treatment ^{18}F -FDG and ^{18}F -choline PET/CT scans revealed no signs of radiotracer uptake, suggesting complete remission of the tumor. ^{18}F -choline may be a complimentary tool for staging and assessment of therapeutic response in non-Hodgkin lymphoma, while non- ^{18}F -FDG tracer can be used for targeted therapy and patient management.

Keywords: ^{18}F -FDG, ^{18}F -choline, PET/CT, non-Hodgkin lymphoma, neoplasm staging.

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Early diagnosis and staging of non-Hodgkin lymphoma (NHL) is an essential process that involves many different technologies.¹ Hybrid positron emission tomography/computed tomography (PET/CT) with fluorodeoxyglucose (FDG), a glucose analogue, labeled with fluor-18 (^{18}F -FDG) has been largely used to evaluate staging, therapy response and prognosis in NHL patients.^{2,3} PET/CT combines morphological and metabolic information of the cancerous tissue, providing more accurate data regarding its different behaviors.^{2,3,4} However, in some cases, ^{18}F -FDG has shown false-positive uptake due to inflammatory reaction after chemo and/or radiation therapy.^{5,6} In order to overcome this problem and increase the accuracy of malignant cell detection, especially to assess response to different therapeutic modalities, non- ^{18}F -FDG PET radiotracers might be an interesting strategy. Thus, in this study, we present the case of a patient diagnosed with NHL assessed through PET/CT scan imaging using ^{18}F -FDG and ^{18}F -choline pre- and post-chemoradiation therapy, in order to determine and improve specific patient management.

A 61-year-old male patient, in good general condition at physical examination, presented an irregular ulcerated lesion in the anterior chest wall. ^{18}F -FDG PET/CT imaging, performed for staging, showed intense uptake in infiltrative tissue into pectoral muscles reaching the sternal body with involvement of supra- and infradiaphragmatic lymph nodes (Figure 1A and E). Further pre-therapy, ^{18}F -choline PET/CT scans were consistent with increased radiotracer uptake in the lesion site as well as in the lymph nodes (Figure 1B and F), but with some mismatching in the tumor (Figure 1F). Histological and immunohistochemistry examinations revealed areas of dense and diffuse infiltrate of large anaplastic cells with strong positivity for CD20 and CD10, and a high proliferative profile with strong and diffuse positivity for Ki-67, that corroborate with the diagnosis of cutaneous large-B cells non-Hodgkin lymphoma (NHL) (Figure 1G and H). The patient was then referred for oncological treatment, thus receiving eight cycles of lymphoma standard (R-chop) chemotherapy followed by conformational radiotherapy (30,6 Gy)

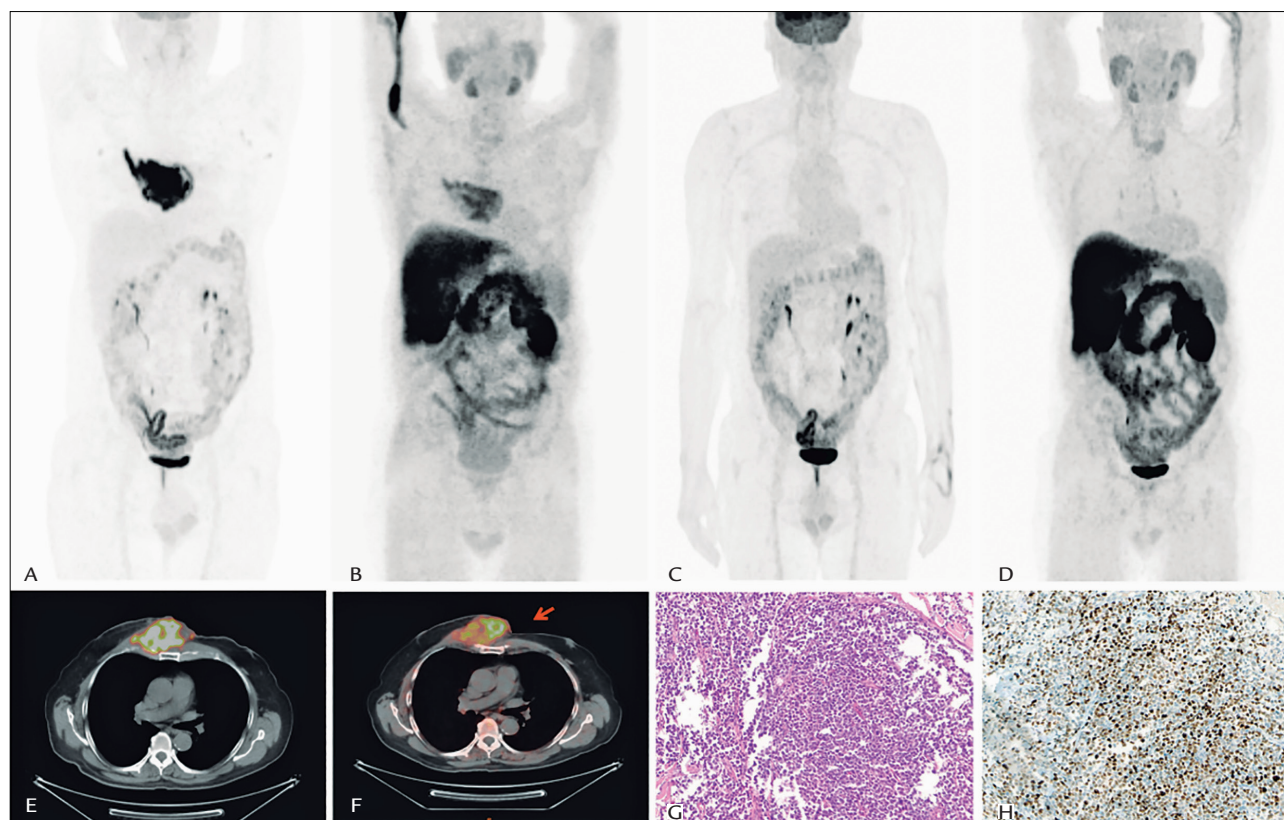


FIGURE 1 A 61-year-old man diagnosed with sternal cutaneous large B-cell non-Hodgkin lymphoma (NHL) (Panel G) underwent PET/CT scans pre- and post-therapy for tumor staging and assessment of response to treatment, respectively, using ^{18}F -FDG and ^{18}F -choline. The ^{18}F -FDG uptake (A and E) showed intense metabolic activity in areas of the tumor with high proliferative pattern (Panel H – strong and diffuse positivity for Ki-67). However, the uptake of ^{18}F -choline (B and F) was more intense in areas of lower glucose consumption of the tumor (arrow).

in the lesion site. Six weeks after chemoradiotherapy, post-treatment ^{18}F -FDG and ^{18}F -choline PET/CT scans were again performed and revealed no signs of radiotracer uptake, suggesting complete remission of the tumor (Figure 1C and D). Remission was confirmed in sixteen-month follow up with conventional imaging (CT).

^{18}F -FDG PET/CT imaging is a well-established imaging technique in clinical oncology.⁷ One of the advantages of using this radiotracer is that it targets glucose phosphorylation, which is increased in malignant tumors due to overexpression of glucose membrane transporters and high glycolytic rate, creating positive tumor to background images.⁸ Although it is considered as highly sensitive in tumor detection, current data indicate that the number of false positive images obtained from ^{18}F -FDG PET/CT is pointed as its most important limitation.⁹

As a non-specific radiotracer for malignant cells, the limitation of the test is based on the fact that ^{18}F -FDG uptake may be shown in areas with no carcinogenic behavior. Thereby, inflammation reaction (common in cancerous tissues), brown adipose tissue or even benign cell

proliferation can create positive images, more likely to be misinterpreted as malignant cell proliferations.^{9,10} A second significant limitation of this method relies on the fibrotic areas in post-therapy healing tissue to take up the radioactive glucose analogue even in cases of complete tumor remission, hence limiting treatment evaluation.¹¹

As a complementary analysis, ^{18}F -choline PET/CT scans were obtained from a patient aiming to create more solid data regarding tumor profile, even though it is most commonly used in management of patients diagnosed with prostate cancer.¹² A previously published paper describes overexpression of choline kinase¹² in malignant cells, an enzyme responsible for phosphorylating choline into phosphatidylcholine, initiating the synthesis of cell membrane phospholipids.^{12,13} Thereby, positive images are shown in response to increased cell proliferation in the lesion area, where more membrane formation is observed.^{14,15}

Axial views obtained with ^{18}F -FDG and ^{18}F -choline PET/CT scanning show different radiotracer uptake in the same region of the tumor, possibly meaning diverse

cell differentiation. Areas of intense ¹⁸F-FDG revealed low ¹⁸F-choline uptake, and vice-versa, revealing a mismatch of metabolic and molecular biology of tumor behavior. On the other hand, both radiotracers were capable to evaluate response to chemoradiation therapy, confirmed with a long follow-up period.

¹⁸F-FDG PET/CT scan is a valuable and established technique in NHL patient management. However, ¹⁸F-choline can be a complimentary tool for tumor staging and assessment of therapeutic response in non-Hodgkin lymphoma. The images obtained in this study showing differential radiotracer uptake by cancer cells in distinct parts of the tumor depict differential metabolic behavior in the lesion. Non-¹⁸F-FDG tracer can be used for targeted therapy and patient management.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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