# FDG PET/CT findings and post-treatment changes of COVID-19 pneumonia in a patient with lymphoma: A case report

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**Abstract.** A 29-year-old male with a history of Hodgkin's lymphoma presented for evaluation of response to chemotherapy with positron emission tomography/computed tomography using fluorine-18-fluoro-2-deoxy-d-glucose ($^{18}$F-FDG PET/CT). Follow-up $^{18}$F-FDG PET/CT imaging demonstrated resolution of previously noted FDG avid axillary lymphadenopathy. However, multiple opacities with increased FDG uptake were noted in the lungs bilaterally, which were suspicious for pulmonary infection, including viral pneumonia. The patient tested positive for coronavirus disease 2019 (COVID-19) virus infection by reverse transcription-polymerase chain reaction (RT-PCR). Additional cycles of chemotherapy were delayed until the patient became negative for COVID-19 virus infection on follow-up RT-PCR test 2 weeks later. The patient received two additional cycles of chemotherapy. Follow-up $^{18}$F-FDG PET/CT post chemotherapy demonstrated a decrease in the size of the previously seen mediastinal lymphadenopathy, reduction of FDG uptake by the previously seen mediastinal lymphadenopathy, and reduction of FDG uptake by the previously seen pulmonary opacities, at 2 months after COVID-19 diagnosis. The findings of this case report demonstrated the importance of recognition of pulmonary abnormalities caused by COVID-19 pneumonia on $^{18}$F-FDG PET/CT imaging for clinical management of patients with lymphoma.

## Introduction

Positron emission tomography/computer tomography (PET/CT) using fluorine-18-fluoro-2-deoxy-d-glucose ($^{18}$F-FDG PET/CT) is a hybrid imaging modality widely used for staging, assessment of response to treatment and restaging of lymphoma (1-4). Because many lymphoma patients have significant immune suppression from anti-lymphoma treatment, lymphoma patients were susceptible to coronavirus disease 2019 (COVID-19) infection (5). It is important to recognize pulmonary changes caused by COVID-19 infection in lymphoma patient without clinical symptoms of COVID-19 pneumonia. There are different patterns of pulmonary abnormalities of COVID-19 pneumonia on chest CT (6-10). The predominant pattern of early stage COVID-19 pneumonia on chest CT is bilateral and multifocal ground-glass opacities. In contrast, the predominant pattern of late stage COVID-19 pneumonia is mixed pattern of consolidation and ground-glass opacities, and some including a reticular pattern associated with bronchiolectasis and irregular interlobular or septal thickening. Recognition of the patterns of pulmonary abnormalities at different stages of COVID-19 pneumonia is important for incidental diagnosis of COVID-19 pneumonia in lymphoma patients who present for staging or restaging of lymphoma with $^{18}$F-FDG PET/CT (11-13). Because initiation of chemotherapy may cause undesirable exacerbation of COVID-19 pneumonia, it is crucial to avoid chemotherapy in lymphoma patients with active COVID-19 infection (5).

Here, we report a case of a lymphoma patient with incidental findings of COVID-19 pneumonia on restaging $^{18}$F-FDG PET/CT. Additional chemotherapy was delayed based on the incidental findings of COVID-19 pneumonia in this patient. Two weeks later, the patient received additional chemotherapy when the patient tested negative for active COVID-19 infection and a complete metabolic response to lymphoma treatment was confirmed by follow up $^{18}$F-FDG PET/CT. The findings from this case report demonstrated the importance of recognizing pulmonary abnormalities of COVID-19 pneumonia on $^{18}$F-FDG PET/CT in clinical management of lymphoma patients during COVID-19 pandemic (5).

## Case report

A 29-year-old man with no past medical history presented with tender right supraclavicular and axillary masses that had been enlarging over a month. The patient endorsed subjective fevers, chills, and night sweats. There were no overlying erythema or skin changers over the masses. The

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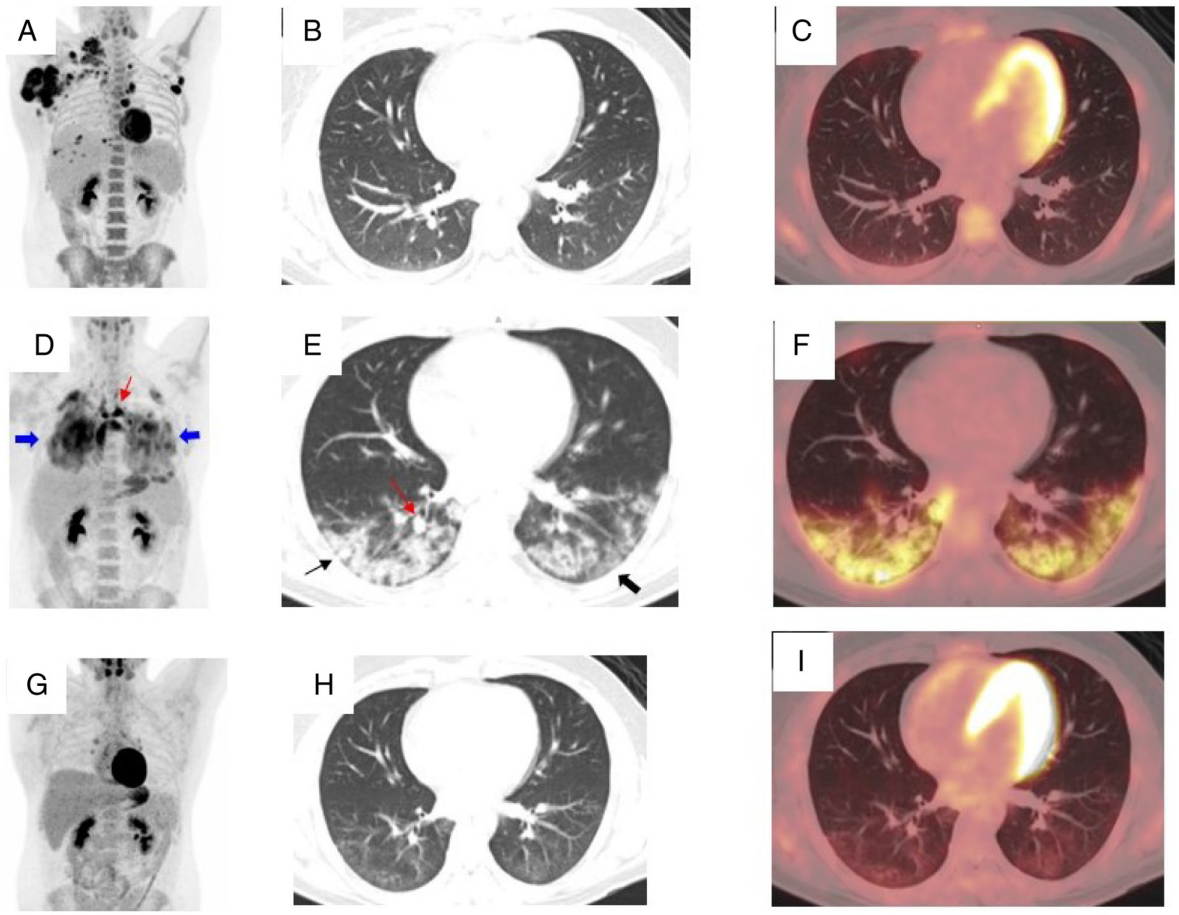


Figure 1. Incidental finding of COVID-19 pneumonia in a patient with lymphoma who presented for evaluation of lymphoma treatment. (A) MIP image of the initial staging $^{18}$F-FDG PET/CT demonstrated multiple hypermetabolic nodal lesions in the right axilla, right subpectoral region, left axilla and mediastinum, along with possible pleural metastases. (B) Axial CT and (C) hybrid PET/CT images were negative for pulmonary air space opacities. (D) MIP image showing interval decrease of FDG uptake in previously seen lymphadenopathy, suggesting good response to chemotherapy. However, there were diffuse increased FDG uptake in the bilateral lungs (thick blue arrow) and new foci of abnormal increased FDG uptake in the mediastinum (thin red arrow). (E) Axial CT and (F) hybrid PET/CT images of the chest demonstrated abnormal increased FDG uptake by numerous new pulmonary airspace opacities. The pulmonary opacities were bilateral, peripheral, multilobar, either ground-glass (thick black arrow) or consolidative (thin black arrow), and some with a rounded morphology (thin red arrow), which are all classic CT manifestations of COVID-19 pneumonia. (G) MIP image of follow-up FDG PET demonstrated interval decrease of diffuse abnormal FDG uptake in the bilateral lungs and foci of FDG uptake in the mediastinum. (H) Axial CT and (I) hybrid PET/CT images demonstrated interval resolution of residual FDG avid mediastinal lymphadenopathy and near complete resolution of previously seen FDG-avid peripheral pulmonary opacities, with very faint FDG uptake by the small residual ground glass opacities. (G, H and I) These images were acquired 2 month after the patient tested negative for COVID-19 and 1 month after two cycles of AVD. $^{18}$F-FDG PET/CT, positron emission tomography/computed tomography using fluorine-18-fluoro-2-deoxy-d-glucose; AVD, a chemotherapy combination that includes Adriamycin or doxorubicin, vinblastine, and dacarbazine or DTIC; MIP, maximum intensity projection.

patient had an elevated white blood cell count (26.48x10$^9$/l), normal RBC (4.58x10$^9$/l), hemoglobin (11.9 g/dl), and slightly elevated platelets (490x10$^9$/l). Lymphadenitis of infectious etiology such as tuberculosis and lymphoma were among differential diagnoses. The patient completed a one week course of treatment with amoxicillin, without improvement of lymphadenopathy. The patient underwent biopsy of a right supraclavicular lymph node that confirmed the diagnosis of nodular sclerosis classical Hodgkin's lymphoma.

$^{18}$F-FDG PET/CT was performed in a protocol similar to that previously described (14). Briefly, PET acquisition was obtained from mid-thigh to base of skull (5 min/bed) using a Siemens Biograph scanner, starting at 60 min post intravenous injection of 397.75 MBq (10.75 mCi) of $^{18}$F-FDG. The non-contrast CT scans (200 mAs, 120 kV, 0.5 sec rotation time, 5 mm slice, in a caudal-to-cranial direction) were used for attenuation correction and localization. Transaxial, coronal and sagittal PET images were reviewed in conjunction with fused non-contrast CT. Whole body biodistribution of radiotracer activity was assessed by visual assessment and semi-quantitative analysis was performed to determine radiotracer concentration (standardized uptake value, SUV), in reference to blood pool radiotracer activity measured from descending aorta and liver radiotracer activity measured from right hepatic lobe.

On the whole body PET/CT images (base of skull to mid-thigh), there was FDG-vid lymphadenopathy with multiple hypermetabolic nodal lesions in the right axilla, right subpectoral region, left axilla, and mediastinum, along with possible pleural metastases (Fig. 1A-C). The patient underwent chemotherapy for treatment of lymphoma with ABVD (a chemotherapy combination that includes Adriamycin or doxorubicin, bleomycin, vinblastine and dacarbazine or DTIC). After completion of two cycles of ABVD, the

patient underwent interim $^{18}$F-FDG PET/CT for assessment of treatment response (2,4). There was interval resolution of multiple previously noted FDG avid mediastinal nodes and decrease of FDG uptake by a few mediastinal lymph nodes (decrease of the SUVmax of index left para-aortic lymph node from 9.0 to 4.0), suggesting a good treatment response. However, there were bilateral, multilobar, basal predominant peripheral FDG-avid ground-glass and consolidative opacities, some with a rounded morphology (Fig. 1D-F). Multiple new FDG avid lymph nodes were detected in the right hilum and mediastinum, including 1.5 cm subcarinal lymph node with SUVmax 9.4 and 1 cm right paratracheal lymph node with SUVmax 9.9. The findings were highly suspicious for COVID-19 pneumonia. On clinical evaluation, the patient had fever and fatigue. The patient tested positive for COVID-19 coronavirus infection the next day by Roche SARS-COV-2 polymerase chain reaction (PCR) test.

Additional cycles of chemotherapy were postponed due to COVID-19 pneumonia. One month after diagnosis of COVID-19 pneumonia, the patient received 4 cycles of chemotherapy with AVD (a chemotherapy combination that includes Adriamycin or doxorubicin, vinblastine, and dacarbazine or DTIC). Bleomycin was discontinued per the Response Adapted Treatment in Hodgkin Lymphoma trial (Rathl Trial) based on good response to initial two cycles of ABVD demonstrated by FDG PET/CT imaging. On follow-up $^{18}$F-FDG PET/CT images obtained two months after diagnosis of COVID-19 and 4 cycles of chemotherapy with AVD, there was interval resolution of residual mediastinal nodes related to lymphoma such as a residual left para-aortic lymph node and decrease of focal FDG uptake by the lymph nodes in the mediastinum related to COVID-19 pneumonia (decrease of the SUVmax of index subcarinal lymph node from 9.4 to 3.8), along with decrease of diffuse FDG uptake in the bilateral lungs, indicating complete metabolic response of lymphoma to chemotherapy and improvement of COVID-19 pneumonia (Fig. 1G-I).

## Discussion

Typical CT findings of COVID-19 pneumonia include bilateral ground-glass opacities with or without consolidation or intralobular lines ('crazy-paving') in a peripheral, and lower lung zone distribution. FDG avid multifocal ground-glass opacities with rounded morphology or FDG-avid focal consolidations with central ground-glass attenuation (reverse halo sign) are also typical manifestations on FDG PET/CT imaging. Non-peripheral, non-rounded groundglass opacities with diffuse, unilateral, multifocal or perihilar distribution is indeterminate for COVID-19 pneumonia and can also be seen with other infectious or non-infectious processes. Lobar consolidation and discrete centrilobular nodules are atypical for COVID-19 pneumonia (10).

In this patient, the findings of bilateral, multilobar, basal predominant peripheral FDG-avid ground-glass and consolidative opacities were similar to the findings on the case report by Playe *et al* (11) and different from the findings of bilateral tree-in-bud opacities and several peripheral and subpleural ground-glass opacities with mild FDG activity on the case report by Boulvard Chollet *et al* (12). Additionally, there were new subcentimeter FDG-avid lymph nodes in the right hilum and mediastinum, in addition to multiple peripheral, multilobar, FDG-avid ground-glass and consolidative opacities in bilateral lungs. On the follow-up $^{18}$F-FDG PET/CT images, there were interval resolution of residual FDG avid mediastinal lymphadenopathy and near complete resolution of previously seen FDG-avid peripheral pulmonary opacities, with very faint FDG uptake by the small residual ground glass opacities. To the best of our knowledge this is the first case report regarding changes of pulmonary and mediastinal abnormalities in lymphoma patient with COVID-19 pneumonia prior to and after additional chemotherapy. It is imperative to consider both inflammatory lymphadenopathy associated with COVID-19 pneumonia and residual or recurrent lymphoma in patients with incidental findings of COVID-19 pneumonia.

Early diagnosis of COVID-19 pneumonia through recognition of pulmonary abnormalities on FDG PET/CT is important for the treatment of lymphoma patients who are often immunocompromised and might be more vulnerable to complications caused by COVID-19 pneumonia (5), particularly for the treatment of the lymphoma patients with unexpected SARS-Cov-2 co-infection despite double reverse transcription-PCR negativity (12). In addition to challenges in the timely completion of the staging and restaging studies, clinicians might encounter the challenges of making complex treatment decisions in management of patients with hematologic malignancies during the COVID-19 pandemic (5). It was recommended to hold treatment of COVID-19 positive multiple myeloma patients for at least 2 to 3 weeks and antineoplastic therapy should be reintroduced only after complete convalescence, ensuring safety (5). It might be also appropriate to hold chemotherapy for 2 to 3 weeks in lymphoma patients with incidental CT findings of pulmonary abnormalities associated with COVID-19 pneumonia, in order to ensure safety. As illustrated in this case report, incidental diagnosis of COVID-19 pneumonia in this patient helped oncologists to decide to postpone chemotherapy in order to avoid exacerbation of COVID-19 pneumonia. The patients tolerated chemotherapy well that was received one month after incidental diagnosis of COVID-19 pneumonia, and a complete metabolic response to chemotherapy that was confirmed by follow up $^{18}$F-FDG PET/CT imaging. Moreover, incidental diagnosis of COVID-19 pneumonia facilitated accurate interpretation of restaging $^{18}$F-FDG PET/CT imaging by distinguishing FDG avid nodal disease of lymphoma from FDG avid lymphadenopathy related to COVID-19 pneumonia.

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## Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Authors' contributions

JM, AK and FP contributed to conception and design, and acquisition, analysis and interpretation of data. JM and FP contributed to drafting, and revision of the manuscript. AK contributed to revising the manuscript critically for important intellectual content. JM, AK and FP have confirmed the authenticity of all the raw data, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work were appropriately investigated and resolved. All authors have read and approved the final manuscript.

## Ethics approval and consent to participate

All procedures performed in the study involving human participants were performed in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The case report protocol was approved by the Institutional Review Board (IRB# STU 102014-055) of the University of Texas Southwestern Medical Center, Dallas, TX, USA. The requirement for informed consent to participate was waived based on the approved protocol of the retrospective case report.

## Patient consent for publication

The requirement for patient consent for publication was waived based on the protocol of the retrospective case report approved by the Institutional Review Board (IRB# STU 102014-055) of the University of Texas Southwestern Medical Center (Dallas, TX, USA).

## Competing interests

The authors declare that they have no competing interests.

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