



Early ^{18}F -FDG PET/CT in COVID-19

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Summary

We report the case of who has been hospitalized complaining about fever in the last 4 days. Laboratory data revealed lymphocytopenia and leucopenia with an elevation of C-reactive protein and positive real-time reverse transcription-polymerase chain reaction (RT-PCR). Six days before this hospitalization, when the patient was asymptomatic, ^{18}F -FDG PET/CT images were performed for the therapeutic control of liver metastases of colorectal cancer. Lung abnormality findings at ^{18}F -FDG PET/CT images, unrelated to cancer metastases, but suspicious for viral infection, may suggest the presence of COVID-19 disease in its early phase before symptoms onset. Since PET/CT is more sensitive than CT scan in detecting host's reaction, the added value of this technique could be monitoring disease progression and could be used as a biomarker of lung disease activity and therefore as an important tool for a better understanding of the factors that contribute to the progression of lung disease.

Key words: ^{18}F -FDG PET/CT; COVID-19; infection lung; lymphadenopathy; SARS-CoV-2.

Coronavirus disease 2019 (COVID-19) is an infectious disease, caused by a severe acute respiratory syndrome coronavirus (SARS-CoV-2), recently declared the cause of a global public health emergency of international concern (PHEIC) by the World Health Organization (WHO).¹ We report the case of who has been hospitalized complaining about fever in the last 4 days. Laboratory data revealed lymphocytopenia and leucopenia with an elevation of C-reactive protein and positive real-time reverse transcription-polymerase chain reaction (RT-PCR). Six days before this hospitalization, when the patient was asymptomatic, ^{18}F -FDG PET / CT images were performed for the therapeutic control of liver metastases of colorectal cancer. A review of the images showed multiple peripheral ground-glass opacities (GGO) with consolidative opacities in the right lung (Fig. 1a,b,c). These lesions were hypermetabolic (Fig. 1d,e,f) with a maximum standardized uptake value (SUV max) of 2.4. Furthermore, even if COVID-19 does not seem to be associated with lymphadenopathy and nodal enlargement on CT is an uncommon finding, in this patient a nodal right interlobar (Fig. 2a) ^{18}F -FDG faint uptake (Fig. 2b) was detected. ^{18}F -FDG PET / CT images also showed the presence of metastases in the liver but no affected lymph nodes anywhere in the body except in the chest. Lung abnormality

findings, unrelated to cancer metastases, but suspicious for viral infection, may suggest the presence of COVID-19 disease in its early phase before symptoms onset. The reference standard for diagnosis is the RT-PCR of viral nucleic acid but accounting the possibility of false-negative results, and recent studies addressed the importance of clinical diagnosis based on clinical symptoms, laboratory tests and CT.²⁻⁴ Patients present respiratory symptoms, less frequently gastrointestinal symptoms. Usually, predominant imaging findings on CT consist of bilateral GGOs with or without consolidation in peripheral lungs. Setti et al. reported 5 cases of asymptomatic cancer patients who performed ^{18}F -FDG-PET/CT. Lungs' involvement (GGOs or consolidative opacities and faint nodal uptake) suspicious for viral infection was shown in these patients, and the diagnosis of SARS-CoV-2 infection was subsequently confirmed. 2/5 patients presented mild respiratory symptoms and fever after one follow-up week.⁵ Even in the reported case, the patient was oncological but the lymph nodes seen in the images were not connected to the primary tumour; in fact, they reduced over time and with adequate therapies show that they were not correlated to cancer. Qin et al. also reported PET/CT imaging findings from four patients with a clinical diagnosis of COVID-19 and without molecular

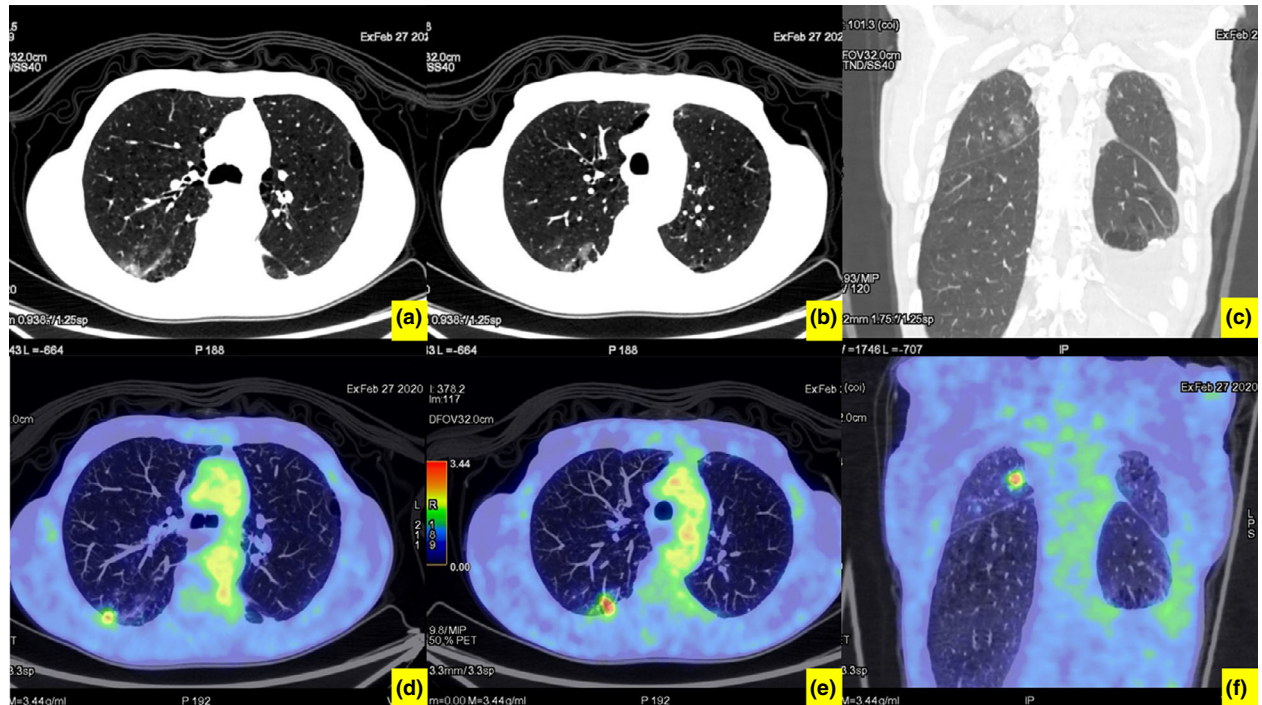


Fig. 1. High-resolution CT transaxial (a, b) coronal (c) and ^{18}F -FDG PET/CT transaxial (d, e) coronal (f) images.

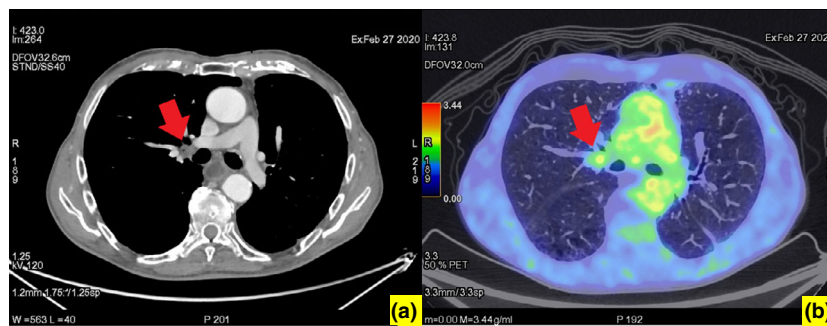


Fig. 2. High-resolution CT transaxial (a) and ^{18}F -FDG PET/CT transaxial (b) images.

confirmation of SARS-CoV-2 infection, thus recommending this imaging technique for the differential diagnosis of complex cases. All patients presented ^{18}F -FDG-positive GGOs, and three showed increased nodal ^{18}F -FDG uptake without corresponding lymphadenopathy.⁴ Lastly, in another study, a patient with SARS-CoV-2 infection confirmed by RT-PCR showed increased accumulation of ^{18}F -FDG in lymph nodes as well as bone marrow and lungs.⁶ ^{18}F -FDG PET-CT is an imaging method to evaluate inflammatory and infectious pulmonary disease. Glucose transporters are overexpressed in activated inflammatory cells, and their affinity for deoxyglucose is increased by cytokines and growth factors released in

the inflammatory site. The uptake of FDG is proportional to the cellular metabolic rate. Studies demonstrated that ^{18}F -FDG PET/CT is useful to assess and quantify the activity of inflammatory pulmonary diseases considering that its uptake can be detected 'when neutrophils are activated and sequestered within the lungs before their trans-endothelial migration into airways'. Inflammatory cells, primarily neutrophils, when activated, exploiting anaerobic glycolysis, require increased glucose that resulted in a high ^{18}F -FDG uptake. At an early stage, ^{18}F -FDG PET/CT could play an additional role in evaluating patients with non-specific clinical symptoms or before their onset and in the presence of a false-negative

finding. Joob et al. did not share the same enthusiasm for the potential benefits provided by ¹⁸F-FDG PET/CT for the diagnosis of COVID-19 considering it 'a risk of disease spreading due to long period of ¹⁸F-FDG PET/CT procedure in investigation unit'.³ Since PET/CT is more sensitive than CT scan in detecting host's reaction, the added value of this technique could be monitoring disease progression and could be used as a biomarker of lung disease activity and therefore as an important tool for a better understanding of the factors that contribute to the progression of lung disease.

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