




^{18}F -FDG PET/CT findings of COVID-19: a series of four highly suspected cases

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Abstract

Purpose The aim of this case series is to illustrate the ^{18}F -FDG PET/CT findings of patients with acute respiratory disease caused by COVID-19 in Wuhan, Hubei province of China.

Methods We describe the ^{18}F -FDG PET/CT results from four patients who were admitted to the hospital with respiratory symptoms and fever between January 13 and January 20, 2020, when the COVID-19 outbreak was still unrecognized and the virus infectivity was unknown. A retrospective review of the patients' medical history, clinical and laboratory data, as well as imaging findings strongly suggested a diagnosis of COVID-19.

Results All patients had peripheral ground-glass opacities and/or lung consolidations in more than two pulmonary lobes. Lung lesions were characterized by a high ^{18}F -FDG uptake and there was evidence of lymph node involvement. Conversely, disseminated disease was absent, a finding suggesting that COVID-19 has pulmonary tropism.

Conclusions Although ^{18}F -FDG PET/CT cannot be routinely used in an emergency setting and is generally not recommended for infectious diseases, our pilot data shed light on the potential clinical utility of this imaging technique in the differential diagnosis of complex cases.

Keywords COVID-19 · SARS-CoV-2 · Infection · Acute respiratory disease · ^{18}F -FDG PET/CT · Ground-glass opacities · Consolidative opacities

An outbreak of acute respiratory disease caused by a novel coronavirus of zoonotic origin (SARS-CoV-2) occurred

during December 2019 in Wuhan, Hubei province of China. Additional cases have been subsequently identified both in other parts of China and worldwide [1, 2]. World Health Organization officially names the disease COVID-19 [3]. Common clinical manifestations of COVID-19 include fever, cough, shortness of breath, myalgia, and fatigue [4, 5]. Although detection of viral RNA remains the gold standard for diagnosis, false-negative results are not uncommon. The possible reasons may include the lack of standard operation procedures (SOPs) and validation across different laboratories for viral identification, different viral loads at different anatomical sites and high mutation rates. Consequently, clinical diagnosis is generally based on exposure history, clinical symptoms, results of blood and biochemical tests, and findings on chest computed tomography (CT)—which typically consist of ground-glass opacities (GGOs) or bilateral pulmonary consolidations in multiple lobular and sub-segmental areas [4, 6].

In general, the identification of pulmonary GGOs or patients presenting with persistent fever should prompt additional diagnostic testing for differential diagnosis—including ^{18}F -

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FDG PET/CT imaging. Here, we report the ^{18}F -FDG PET/CT findings from four patients who were admitted to the Wuhan Union Hospital with lung GGOs and fever between January 13 and January 20, 2020—when the COVID-19 outbreak was still unrecognized and the virus infectivity was unknown. A retrospective review of the patients' medical history, clinical and laboratory data, as well as imaging findings (Table 1) strongly suggested a diagnosis of COVID-19.

Case 1 A 57-year-old man living in Wuhan presented with sore throat and fever (39.0 °C) lasting for 3 days. Laboratory testing revealed a white blood cell (WBC) count within the reference range and a slight elevation of high-sensitivity C-reactive protein (hsCRP; 6.65 mg/L, reference range 0–5 mg/L). A search for common respiratory pathogens, including *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, adenovirus, respiratory syncytial virus, and Coxsackie B-virus specific IgM, yielded negative results. A chest CT scan conducted in another hospital 2 days before revealed the presence of a GGO in the right lung, which required further diagnostic workout (differential diagnosis between a tumor and an infectious disease). ^{18}F -FDG PET/CT identified peripheral GGOs with an

increased ^{18}F -FDG uptake (SUVmax range 2.2–4.6) in the right upper lung (Fig. 1a, b, arrows) and left lower lung (Fig. 1c; arrows). Unfortunately, SARS-CoV-2 nucleic acid testing was not performed. Antiviral, anti-inflammatory, and symptomatic treatment for 2 weeks led to complete resolution of symptoms.

Case 2 A 56-year-old man with a recent history of surgery for lung repair and rib fracture internal fixation following a traumatic event presented to hospital with an 8-day history of intermittent fever (up to 39.1 °C, more frequent in early morning and the afternoon) accompanied by fatigue and dizziness. Cough and sputum production were absent. Laboratory testing revealed mild leukopenia (WBC count $3.33 \times 10^9/\text{L}$; reference range $3.5\text{--}9.5 \times 10^9/\text{L}$) with 75.5% neutrophils and 17.5% lymphocytes (normal range 20–40%). Inflammatory indices, including hsCRP (23.6 mg/L) and erythrocyte sedimentation rate (73 mm/h; reference range < 15 mm/h), were increased, but a search for known respiratory pathogens yielded negative findings. ^{18}F -FDG PET/CT imaging (January 13, 2020) revealed multiple FDG-positive GGOs and consolidative opacities in both lungs (SUVmax range

Table 1 General characteristics and PET/CT findings of four cases with COVID-19

Patient number	1	2	3	4
Sex	Man	Man	Woman	Woman
Age, years	57	56	61	48
Clinical symptoms	Fever, sore throat	Fever, fatigue, dizziness	Back pain, dry cough	Fever, chill, dry cough, myalgia, and fatigue
History of staying in Wuhan	Yes	Yes	Yes	Yes
WBC ($\times 10^9/\text{L}$) (reference range $3.5\text{--}9.5 \times 10^9/\text{L}$)	Normal	3.33	3.47	Normal
Lymphocytes (%) (reference range 20–40%)	Normal	17.5%	Normal	Normal
HsCRP (mg/L) (reference range 0–5 mg/L)	6.65	23.6	Not available	12.2
Respiratory pathogens*	Negative	Negative	Not available	Negative
PET/CT findings				
Number of affected lobes	2 (RUL, LLL)	5 (all lobes)	3 (RUL, RLL, LLL)	3 (RML, RLL, LLL)
Lung CT features	GGO	GGO and consolidative opacities	GGO	GGO with interlobular septal thickening
SUVmax	4.6	7.9	12.2	9.3
LN involvement	Absent	Right subclavian region, mediastinum	Right supraclavicular region, mediastinum	Right subclavian region, mediastinum, right hilar region
LN SUVmax	–	7	5.4	5.5
Concomitant diseases**	Absent	Absent	Absent	Absent

*The following respiratory pathogens were investigated: *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, adenovirus, respiratory syncytial virus, and Coxsackie B-virus specific IgM

**Including malignancies and other infectious diseases

WBC, white blood cell; hsCRP, high-sensitivity C-reactive protein; LN, lymph node; RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe; GGO, ground-glass opacities; SUV, standardized uptake value

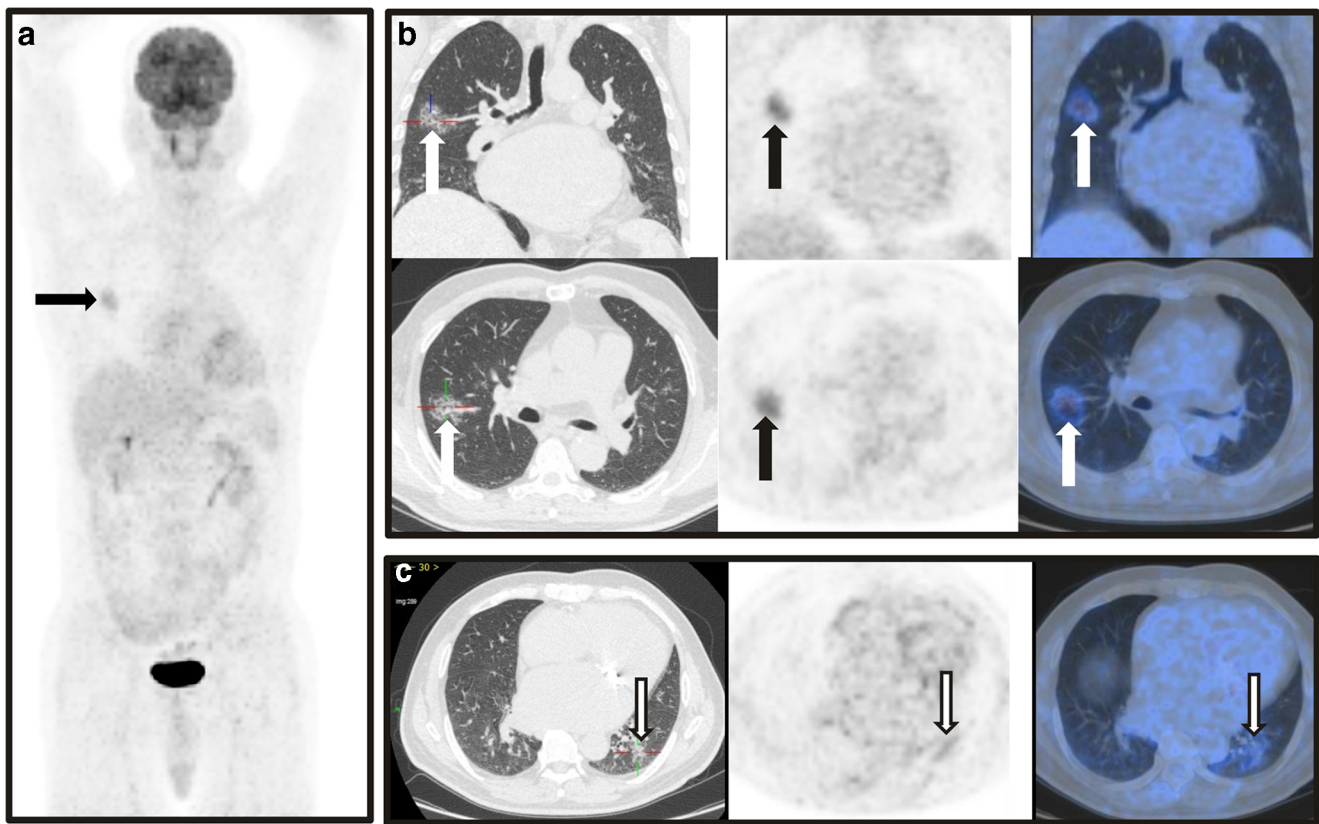


Fig. 1 Peripheral GGOs with an increased ^{18}F -FDG uptake in the right upper lung and left lower lung

1.8–7.9; Fig. 2a, b, arrows). There were also multiple FDG-avid lymph nodes in the mediastinum and the subclavian region (SUVmax range 4.1–7.0; Fig. 2c, arrows). Unfortunately, SARS-CoV-2 nucleic acid testing was not performed. The lesions on ^{18}F -FDG PET/CT were smaller than those detected on previous CT imaging (January 7, 2020) and regressed further after treatment (January 21, 2020; Fig. 2d, arrows).

Case 3 A 61-year-old woman living in Wuhan complained of back pain and dry cough over a week. Laboratory testing revealed a mild leucopenia ($\text{WBC } 3.47 \times 10^9/\text{L}$). Chest CT identified an 8-mm light shadow in the right upper lung lobe and a 9-mm solid nodule in the left lower lung lobe, which initially led to a suspicion of malignancy. A week thereafter, ^{18}F -FDG PET/CT revealed multiple peripheral FDG-avid GGOs (SUVmax range 3.7–12.2) in the right lung (Fig. 3a, b, arrows). Multiple FDG-positive lymph nodes were also identified in the mediastinum and the right subclavian region (SUVmax range 3.4–5.4; Fig. 3c, arrows). We did not perform SARS-CoV-2 nucleic acid testing. An 18-day treatment with antiviral and anti-inflammatory drugs led to symptom improvement.

Case 4 A 48-year-old woman working in the Wuhan Union Hospital presented with an 8-day history of fever ($37\text{--}38^\circ\text{C}$)

accompanied by chills, dry cough, myalgia, and fatigue. WBC count was within the reference range, but she had increased hsCRP levels (12.2 mg/L). A search for known respiratory pathogens yielded negative findings. Chest CT imaging (January 15, 2020, Fig. 4d) led to the identification of a blurry shadow in the right lower lung lobe. A subsequent ^{18}F -FDG PET/CT scan (January 20, 2020) revealed the presence of peripheral FDG-avid GGOs with interlobular septal thickening in both lungs (SUVmax range 3.7–9.3; Fig. 4a, b, arrows). When compared with previous chest CT results, there was evidence of disease progression as shown by a higher number of lesions, which were also characterized by an increased extent and density. There were also multiple FDG-positive lymph nodes in the mediastinum and right hilar region (SUVmax range 3.8–5.5; Fig. 4c, arrows). Real-time fluorescent polymerase chain reaction (RT-PCR) for the detection of SARS-CoV-2 nucleic acid yielded negative findings in two independent measurements. A follow-up chest CT (February 1, 2020) performed after antiviral and anti-infective treatment revealed a significant improvement in the picture (Fig. 4d).

Discussion

Because COVID-19 is believed to have an interpersonal human-to-human transmission [2], either home residence or

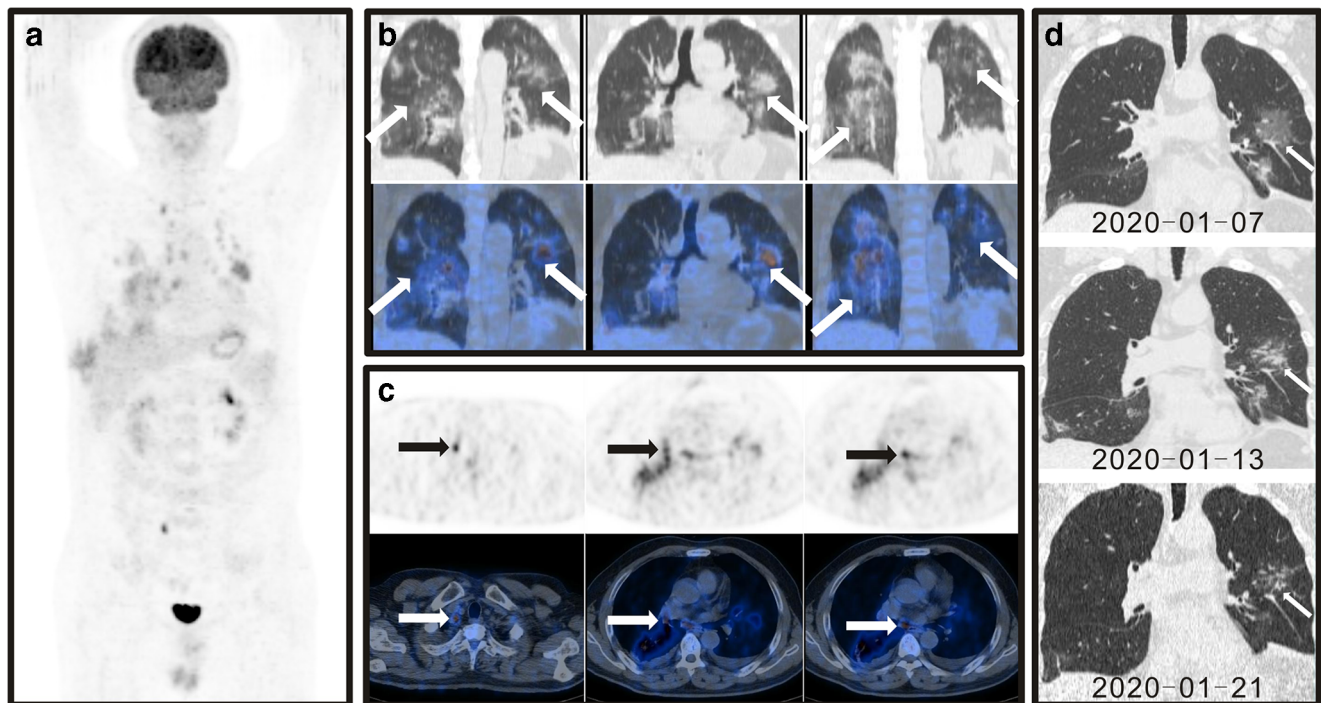


Fig. 2 Multiple FDG-positive GGOs and consolidative opacities in both lungs as well as multiple FDG-avid lymph nodes in the mediastinum and the subclavian region

a travel history to Wuhan—coupled with exposure to known or suspected cases—is paramount to raise clinical suspicion. The clinical, laboratory, and imaging characteristics of the four patients described in the current report are consistent with a diagnosis of COVID-19. Herein, we therefore describe for the first time the ^{18}F -FDG PET/CT findings of four patients with COVID-19.

In accordance with previously published observations [5, 6], our cases were characterized by the presence of peripheral GGOs and/or consolidative opacities in more than two pulmonary lobes. Notably, all of these lesions showed a high tracer uptake. Although a bilateral involvement of the lung

parenchyma can be observed in several benign and malignant lung diseases [7], tumors presenting as GGOs are unlikely to be FDG-avid [8]. The high tracer uptake that characterized COVID-19 pulmonary infections reflects a significant inflammatory burden, similar to that elicited by the Middle East respiratory syndrome or the H1N1 pandemic influenza virus [9, 10]. Although COVID-19 infections do not seem to be accompanied by lymphadenopathy [6], our ^{18}F -FDG PET/CT findings revealed an increased nodal FDG uptake in three of four cases. Although no obvious nodal enlargement was evident, our imaging data indicate for the first time that COVID-19 may cause lymphadenitis—in line with previous

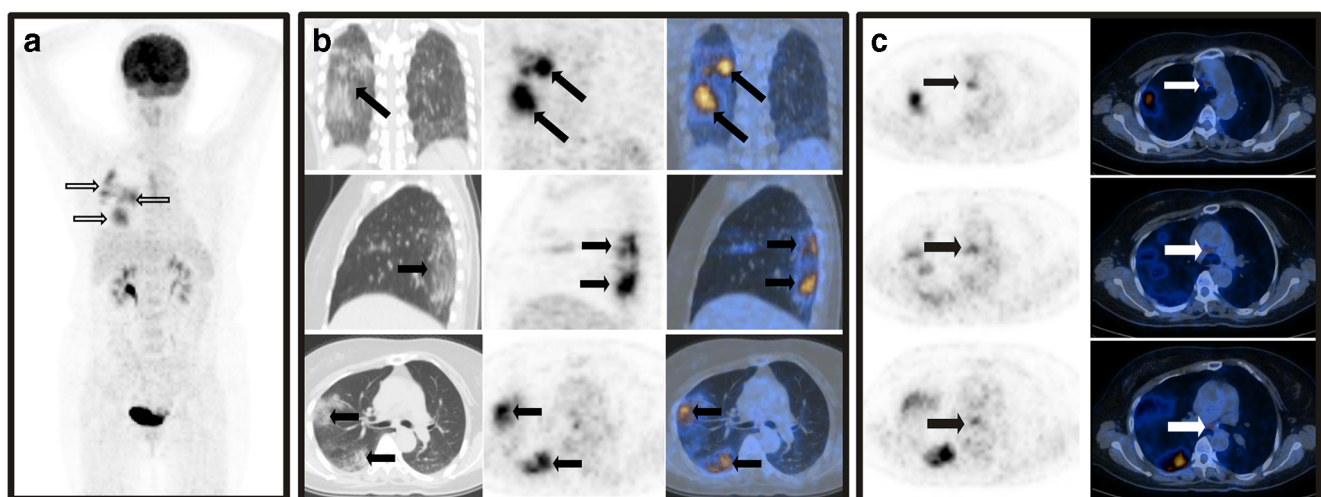


Fig. 3 Multiple peripheral FDG-avid GGOs in the right lung and multiple FDG-positive nodes in the mediastinum and the right subclavian region

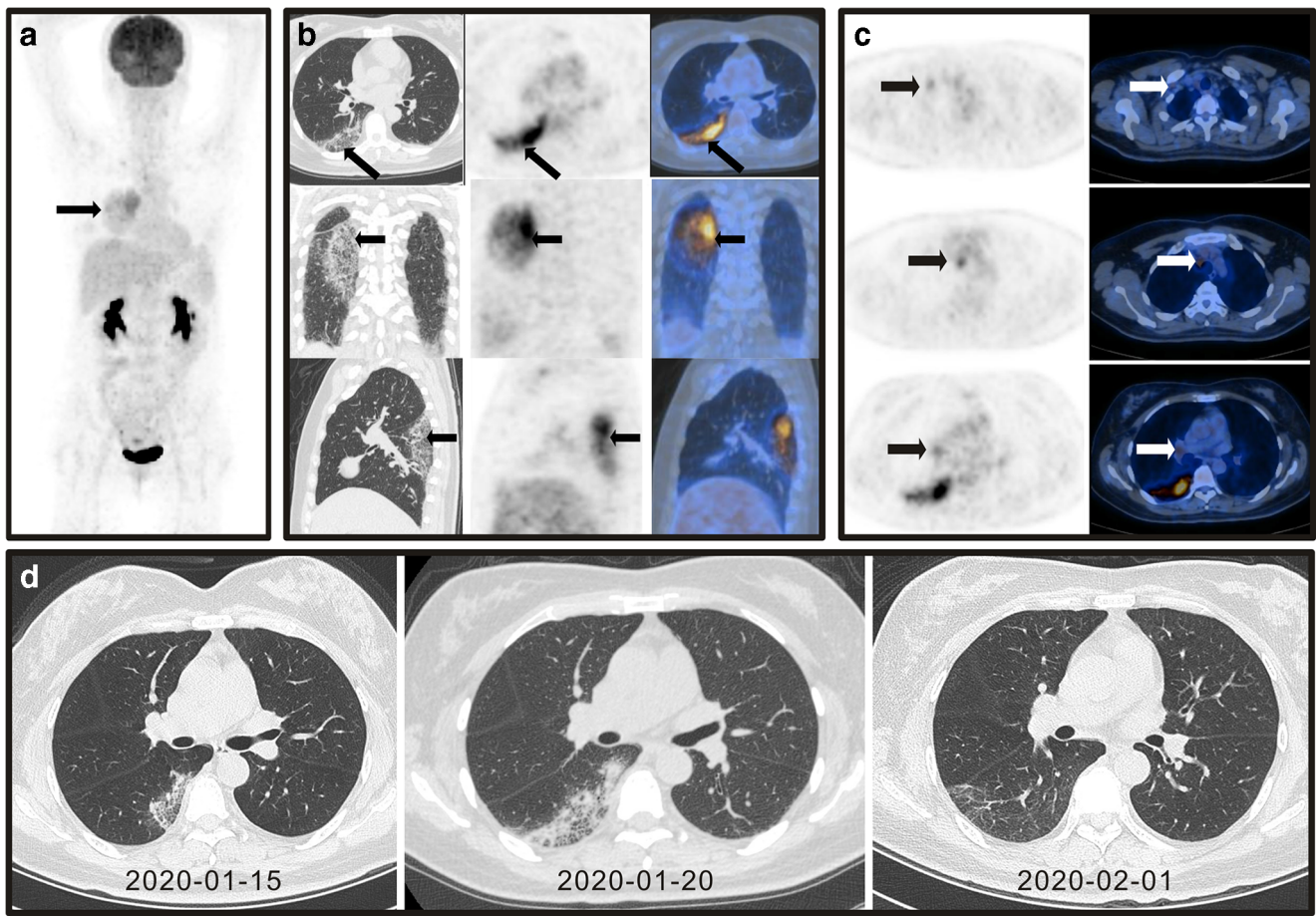


Fig. 4 Peripheral FDG-avid GGOs with interlobular septal thickening in both lungs and multiple FDG-positive lymph nodes in the mediastinum and right hilar region

data obtained from non-human primates exposed to MERS-CoV [9]. Another interesting finding is that no disseminated lesions were evident in our patients—suggesting that COVID-19 has pulmonary tropism.

Although ^{18}F -FDG PET/CT cannot be routinely used in an emergency setting and is generally not recommended for infectious diseases, our current findings demonstrate that this imaging modality may play a complementary diagnostic role in COVID-19—especially at early stages when clinical symptoms are not specific and differential diagnosis is challenging.

Our case series is limited by the small sample size and the lack of molecular confirmation of SARS-CoV-2 infection. However, only 30–50% of infected patients had positive test for SARS-CoV-2 nucleic acid on RT-PCR (Chinese Academy of Sciences; unpublished data). High rates of false-negative findings may be explained by several reasons, including (1) the lack of SOPs for SARS-CoV-2 nucleic acid detection, differences in sample handling, storage, and processing, (2) disease stages and different viral loads according to anatomical site (e.g., alveoli versus upper respiratory tract), (3) the lack of independent validation of current testing, and (4) the

potential high mutation rates of COVID-19. In light of these limitations, some cases of COVID-19 in China are currently diagnosed on clinical, laboratory, and imaging grounds, without resorting to molecular confirmation.

These caveats notwithstanding, we show for the first time that (1) lung lesions of patients with COVID-19 pneumonia are characterized by high ^{18}F -FDG uptake, (2) this condition is accompanied by nodal involvement detectable on ^{18}F -FDG PET/CT imaging, and (3) there is no evidence of disseminated disease, indicating that COVID-19 may have specific lung tropism.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Research involving human participants and/or animals This retrospective study of existing patient data and images was approved by the institutional review board of Union Hospital, Tongji Medical College, Huazhong University of Science and Technology. The requirement for informed consent was waived.

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