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Case Report

Value of PET/CT and MATLAB in Detection of COVID-19 in an Oncology Patient - Case Report

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Abstract: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes the infectious disease COVID-19, was declared a global pandemic in March 2020. The SARS-CoV-2 infection has polymorphic clinical presentations. The real time PCR is the reference diagnostic test; however, it can only detect the presence of virus for a specific window of time and its sensitivity has been reported as low as 60–70%. Case: We report a clinical case for a 28-year-old male patient. His clinical history included known NHL (large B-cell lymphoma) that treated with chemotherapy and autologous bone marrow transplant in 2017. He initially presented with fewer, URTI (upper respiratory infection) and weight loss to have a PET/CT scan for restaging. The follow up PET/CT scan, suggested no worrisome FDG metabolic activity elsewhere to suggest disease recurrence, though, hypermetabolic mediastinal lymph nodes, which were kept with active infectious process and bilateral FDG-avid ground glass attenuation in between the consolidation patches were noted. The follow up RT-PCR post PET/CT scan was proved to be positive. A developed pixelated quantitative map of CT part of the lung using MATLAB showed clearly severity of the lung disease that strongly suggested COVID-19 lung in association with the positive RT-PCR. FDG PET/CT has the potential to add value to the challenges of diagnosing complications caused by viruses such as COVID-19.

Keywords: PET/CT, MATLAB, COVID-19, Oncology Patient

1. Introduction

Coronavirus disease 2019 (COVID-19) [1], caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [2], has become an increasingly prevalent worldwide, declared a pandemic on March 11, 2020 by WHO [3]. Several recent publications have described CT imaging features of COVID-19, the evolution of these features over time, and the performance of radiologists in distinguishing COVID-19 from other viral infections [4-8]. These studies have shown that COVID-19 often produces a CT pattern resembling organizing pneumonia, notably peripheral ground-glass opacities (GGO) and nodular or mass-like GGO that are often bilateral and multilobar [9].

CT findings of COVID-19 pneumonia have been widely reported [10-12]. As for the FDG PET/CT imaging results after COVID-19 infection, Qin et al. [13] found lung lesions characterized by increased FDG uptake and evidence of lymph node involvement. In fact, as a non-invasive imaging method, FDG PET/CT plays an important role in evaluating inflammatory and infectious pulmonary diseases, monitoring disease progression and treatment effect, and improving patient management [14]. When the virus infects the body, the cascade of reactions activates inflammatory cells such as neutrophils, monocytes, and effector T cells by releasing local chemokines. In acute inflammation or chest infection, activated neutrophils are heavily dependent on anaerobic glycolysis, requiring increased glucose and resulting in the high FDG uptake [15].

The radiological sequelae of COVID-19 may persist for a long time regardless of the clinical course or whether the patient is infective. Such post-inflammatory change may cause diagnostic challenge and during this period of uncertainty patients may require 18FDG-PET/CT scans as part of their active management. Italian researchers reported that several patients who entered their facility asymptomatic for the novel coronavirus later showed signs of pneumonia on CT and FDG avidity on PET, which made them suspicious for COVID-19. By acting upon the incidental detection of COVID-19 pneumonia in its early stages, subsequent preemptive steps could help to prevent the spread of the virus. While nuclear medicine procedures are unlikely to play a role in the primary diagnosis of COVID-19, there may be incidental detection in asymptomatic but infected cases undergoing scans for other indications, which may have relevant implications for further management [16].

We are presenting our local experience by an incidental detection of COVID-19 in a routine oncology, molecular imaging, highlighting the spectrum of imaging findings. A first case reported in Kuwait.

2. Materials and Methods

An asymptomatic 24-year-old male with known NHL (large B-cell lymphoma) which was treated with chemotherapy and autologous bone marrow transplant in 2017 was referred to the Nuclear Medicine Section in Adan Hospital, Kuwait as an outpatient to have a PET/CT scan for restaging. He initially presented with fewer, URTI (upper respiratory infection) and weight loss. Hematology test lab indicated low WBC (4x10*4/L0, normal Lymphocyte (1.65x 10*9/L) and D-Dimer (144 ng/mL). No prior PET/CT images were available for comparison at the time.

According to the local standard operating procedures, ^{18}F-FDG PET/CT was performed on a GE 710, 64-slice PET/CT scanner after >6 hours fasting. The patient blood glucose level was 79.2mm/dl (4.4 mmol/l). An activity of 2.9 MBq/kg was administered intravenously and imaging was acquired from the head to the mid-thigh (2 minutes per bed). A standard non-contrast free-breathing helical CT was obtained for morphological correlation and attenuation correction. The acquisition parameters were: 120kV, 128mA tube current, 64 slices×3. 75mm and 3.27mm intervals, spiral pitch 1.375. Body filter and Adoptive Statistical Iterative Reconstruction (ASiR) was used to achieve reductions in patient dose in CT scan while achieving image reconstruction speed similar to that of conventional analytical reconstruction using FBP. The PET WB images were reconstructed using VUE Point HDS, 3 iterations and 16 subsets. The whole body (WB) CT images were reconstructed using a 512×512 matrix, 3.75mm slice thickness, 3.27mm interval and window width was set to 1024 Hounsfield units (HU) and a 512 HU for window level.

In addition to PET SUV_{max} calculation, we developed a quantitative method to assess the severity of the lung disease based on CT axial images using MATLAB software to map HU numbers of the entire lung. The threshold for generating quantitative CT was set to window range of -750,100 HU and window width of 950. It has been reported that GGO is associated with modest increases in lung attenuation on lung window CT images, not obscuring the pulmonary vessels and consolidation, as high patch opacities, which inside air bronchogram (s) could be observed [17]. In terms of pattern, ground-glass opacity (GGO) was defined as a modest increase in lung attenuation on lung window CT images, not obscuring the pulmonary vessels.

3. Results and Discussion

Physiological uptake in the brain cortical and subcortical parenchyma as well as in the lymphoid and glandular tissue of the neck was noted. There were multiple hypermetabolic mediastinal lymph nodes at the AP window (SUV_{max} 3.5), subcarinal (SUV_{max} 4.4) and bilateral hilar with SUV_{max} 4.7 (right lobe) in the lung. We noted an increased FDG uptake at the basal lower lobe bilaterally (SUV_{max} 12.8) with the evidence of bilateral patchy areas of consolidations showing air bronchogram within, that is associated with area of ground glass attenuation in between the consolidation patches. No plural effusion or pneumothorax was observed. The heart is within normal limits and there was no pericardial thickening or effusion. The upper and middle lung lobes were clear.

There was homogenous physiological tracer localization within the liver and the spleen with no focal lesions seen and both adrenals appear unremarkable. The increased FDG uptake in the accessory respiratory muscle of neck, chest as well as the abdomen was keeping with the respiratory distress. The PET/CT scans demonstrated bilateral FDG- avid ground glass opacities with hypermetabolic mediastinal lymph nodes and no worrisome FDG metabolic activity elsewhere was noted to suggests disease recurrence, Figure 1.

We used MATLAB to present pixilated colour transaxial CT images of the lungs together with the related pixel density, Hounsfield Unit (UN), which clearly showed the variable pattern of density qualitatively and quantitatively with the modest elevated density, HU, in particular in the basal lower lung lobes. The non-subjective pixelated quantitative CT lung demonstrated severity of the infected area, Figure 2. According to the local rule, a follow up chest x-ray was taken that also showed, bilateral lower lobes patchy areas of consolidation and GGO, Figure 3. The patient was then admitted to the allocated COVID-19 ward for the follow up test and observation, as the Real Time PCR which was conducted on the same day post PET/CT scan reported to be positive.

Albano and colleagues found COVID-19 parenchymal change in asymptomatic patients undergoing ^{18}FDG-PET/CT in 9% of cases, based on retrospective review of asymptomatic patients [16]. Whilst not advocated by BNMS or European guidance, it may be beneficial to review localizing CT images of asymptomatic patients that include the chest for the presence of COVID-19 as soon as possible and/or before the next patient enters the imaging suite.

The added value of ^{18}FDG-PET/ CT as a functional imaging

modality relies on its ability to identify metabolically active disease in the early stages, predating structural change appreciated on conventional techniques. By detecting the active phase of an infectious or inflammatory condition, it may be theoretically possible to diagnose and monitor disease progression [18]. Deng and colleagues supported the possible utility of ^{18}FDG-PET/CT as a sensitive tool to detect and monitor inflammatory diseases such as viral pneumonia, although no feasibility study currently exists in COVID-19 [19]. It must be remembered that the cohort of patients predominantly imaged with ^{18}FDG-PET/CT are cancer patients and/or immunosuppressed, therefore particularly vulnerable to COVID-19. Benign GGOs demonstrate significantly higher ^{18}FDG uptake on PET/CT than malignant GGOs/GGNs [19-20]. Similarly, earlier case series by Qin et al and Setti et al suggest that COVID-19 pulmonary abnormalities display moderate to high ^{18}FDG uptake (GGO SUV_{max} range 4.6–12.2 and GGO SUV_{max} range 4.3–11.3 respectively) [21-22]. Correspondingly, our case study demonstrated marked GGO uptake (SUV_{max} 12).

A limitation of ^{18}FDG-PET/CT when assessing lungs is that routinely the CT component is low dose (120-kV tube voltage) and not performed on a breath-hold. Reducing the tube voltage improves image contrast to aid accurate localisation but in turn can mask GGO. Conversely, motion artefact generated on a free-breathing CT thorax can artificially create GGO, particularly in the lower lobes. Overall ^{18}FDG-PET/CT has a lower detection rate for smaller GGO and exhibits no clear advantage for the detection of pure GGO that are not metabolically active [20]. In inflammatory aetiologies such as active COVID-19, we can expect elevated glucose metabolism, however the sensitivity of ^{18}FDG-PET/CT in detecting post-infective GGO that is no longer hypermetabolic is potentially limited.

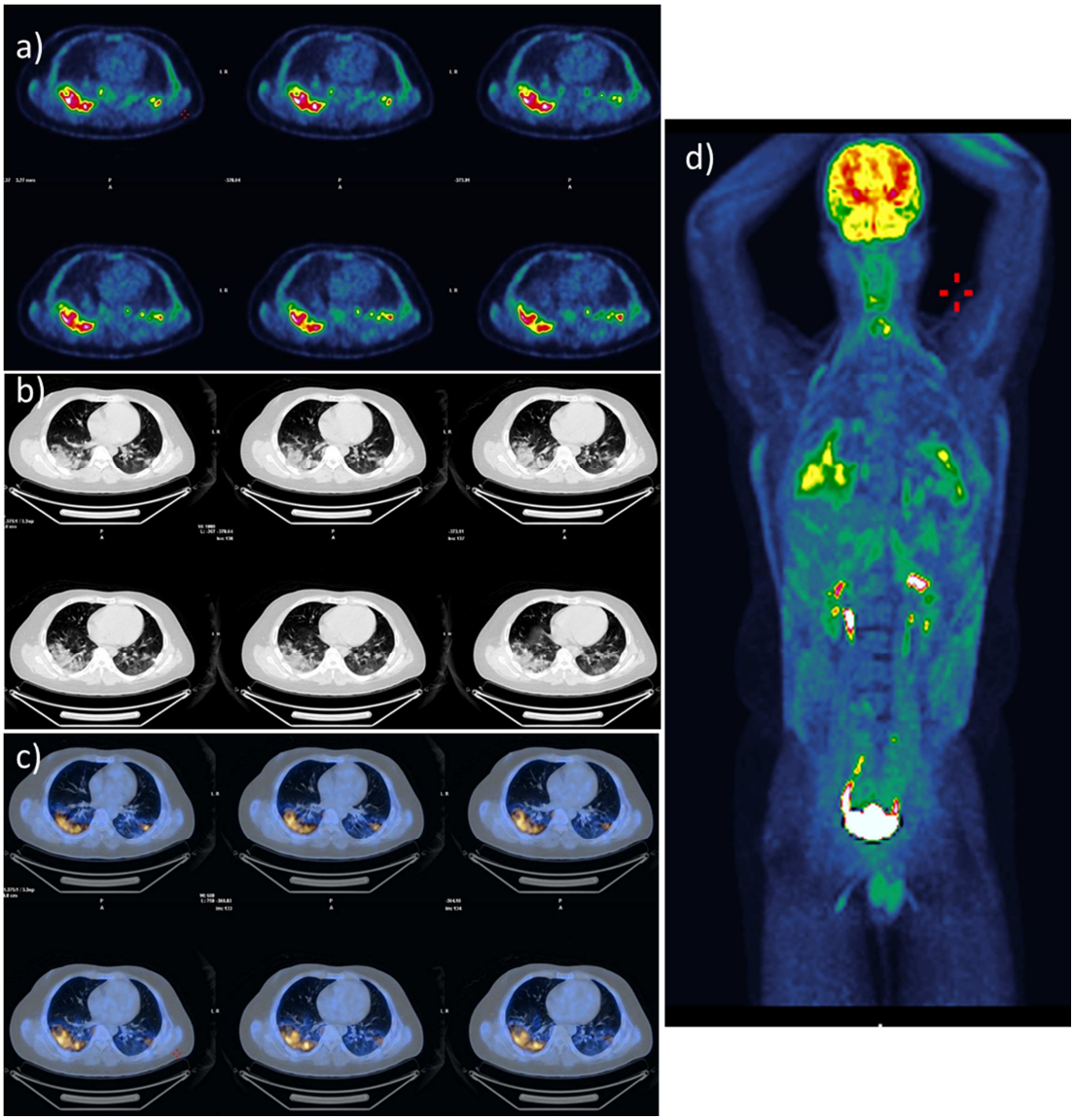

Figure 1. *Transaxial images; (a) ^{18}FDG-PET thorax, (b) Low-dose CT thorax, (C) fused 18FDG-PET/CT and (d) WB maximum intensity projection. The images demonstrate hypermetabolic mediastinal lymph node, bilateral hilar in the right lobe and increased FDG uptake at the basal lower lobe bilaterally with consolidation and ground glass opacity. 18FDG-PET=18-fludeoxyglucose-positron emission tomography; GGO=ground glass opacity.*

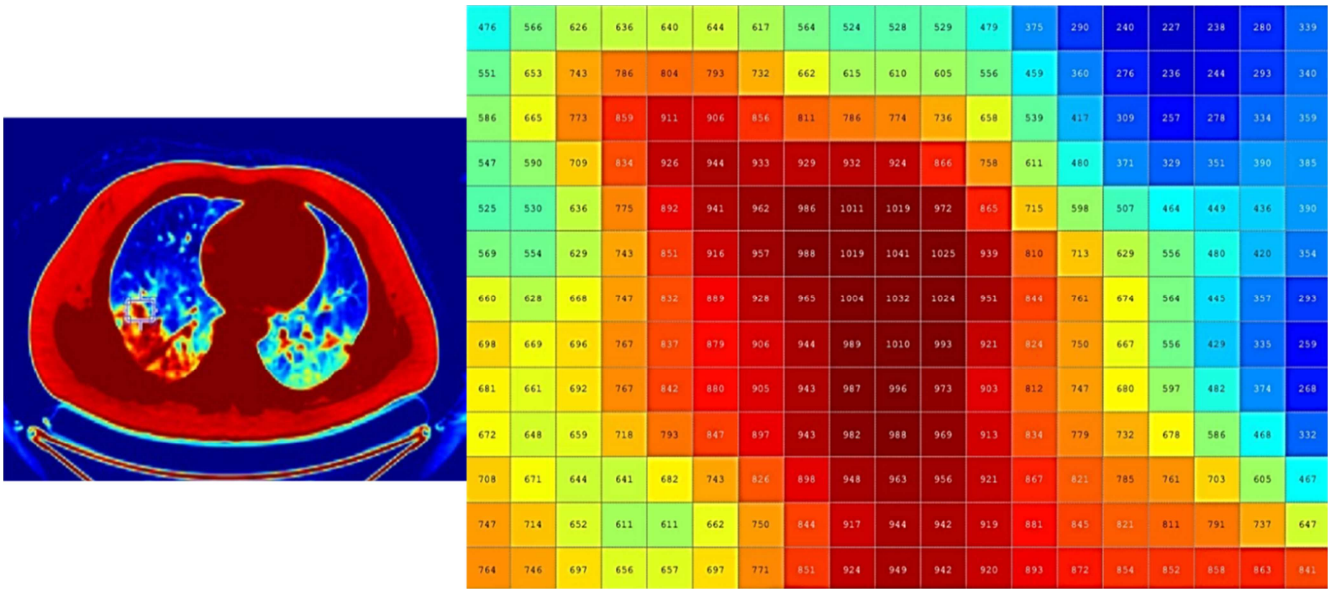

Figure 2. *A developed colour axial thoracic CT image of the 28 years old male patient and the related pixelated CT map (using MATLAB), which together with the various density levels of the infected lung demonstrates quantitatively severity of the disease.*

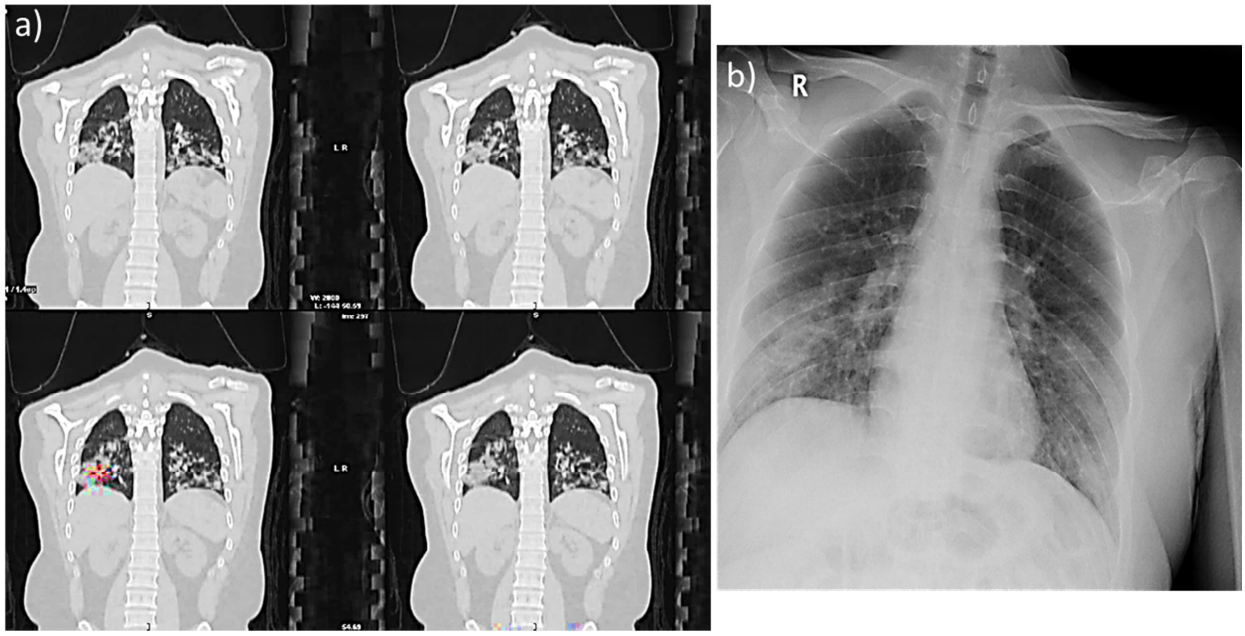

Figure 3. *(a) Coronal thoracic CT image and (b) the chest X-ray. The images demonstrate bilateral patchy areas of consolidations associated with areas of ground glass attenuation in between the consolidation patches. Normal cardiac size and configuration are seen on x-ray.*

4. Conclusion

FDG PET/CT has the potential to add value to the challenges of diagnosing complications caused by viruses such as COVID-19. It is anticipated that incidental findings on patients PET/CT obtained for unrelated reasons could be attributable to COVID-19 detection. COVID-19 positive patients may have a spectrum of findings on ^{18}FDG-PET/CT from a normal study to the classically described moderately FDG avid, peripheral GGOs in at least two lobes. NM physicians, should be aware of the thoracic appearances that can be seen in unsuspected COVID-19 infection in routine outpatient ^{18}FDG-PET/CT in order to flag to referring clinicians when necessary.

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