Positron Emission Tomography/Computed Tomography (PET/CT) During the Coronavirus Disease of 2019 (COVID-19) Pandemic: a Case Series

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ABSTRACT

Introduction: A number of nuclear medicine procedures significantly dropped worldwide during the COVID-19 pandemic. Every nuclear medicine department has faced changed working environment in terms of the type of requested procedures, number of requests and personal protection issues. Also, some specificities emerged that affect standard operating procedures. Aim: The aim here is to present different clinical scenarios related to RT PCR molecular testing and COVID-19-associated pulmonary findings on PET/CT in oncologic patients. Methods: A case series of four patients imaged on oncologic PET/CT is presented. Short clinical history followed by description of significant PET/CT findings and their importance from the perspective of COVID-19 pandemic and interpretation of PET/CT findings is presented. Conclusion: PET/CT imaging remains of paramount importance for oncologic patients during the pandemic. Under the unprecedented circumstances, interpretation of PET/CT findings has become more complex having some specificities that must be kept in mind.

Keywords: PET/CT, COVID-19, pneumonia, RT PCR, SARS-CoV-2.

1. INTRODUCTION

A number of both diagnostic and therapeutic nuclear medicine procedures significantly dropped throughout the departments worldwide during the COVID-19 pandemic. Over that time, all health systems have been forced to shift to SARS-CoV-2-related clinical and epidemiological issues and urgent procedures, mostly leaving diagnostic imaging to be available only for such purposes, at least in the beginning.

According to the survey performed by the International Atomic Energy Agency (IAEA) in 72 countries, the total number of diagnostic procedures in nuclear medicine decreased 54%. Out of all nuclear diagnostic procedures, PET/CT was the least affected and displayed a decrease of 36% (1).

This can be attributed to the fact that most of PET/CT studies are oncologic, and the diagnostics and treatment of oncologic patients remain of paramount importance.

2. METHODS

We present a case series of four oncologic patients referred to 18F-FDG PET/CT imaging for evaluation of the primary oncologic disease, follow-up or evaluation of treatment response. For each oncologic patient, a different and unexpected clinical scenario is presented.

All patients were imaged in accordance with the institutional protocol upon the application of 370 MBq of 18F-fluorodeoxyglucose (18F-FDG) intravenously. Low-dose whole body PET/CT acquisition was performed with a 16-slice CT scanner without IV contrast. The results were interpreted visually and semi-quantitatively by a nuclear medicine physician and a radiologist together.

Three patients got RT PCR SARS-CoV-2 tested and proved negative within 48 hours prior to the imaging. The fourth patient was not tested within 48 hours before the imaging, and also never had any symptoms suggestive of SARS-CoV-2 infection. Molecular
RT PCR SARS-CoV-2 testing was performed at our Institution. Clinical signs suggestive of COVID-19 disease were also observed during history taking.

3. CASE SERIES

CASE 1
A fifty-six-year-old male with Mantle cell lymphoma was referred to a follow-up PET/CT exam due to a suspected relapse of disease. The patient was diagnosed with Mantle cell lymphoma four years ago after the neck lymph node biopsy. He was treated with chemotherapy until two years ago. In a follow-up he noticed neck lymph node enlargement. Patient also has hepatitis B under treatment. The patient was asymptomatic and RT-PCR negative within 48 hours from the imaging. PET/CT images demonstrated peripheral lung consolidation in both lungs. All lesions accumulated 18F- FDG with high intensity, SUVmax 7,8 (Figure 1a,b,c). Described lung lesions were very highly suggestive of the COVID-19 disease, and the patient was isolated and referred for retesting immediately. PET/CT also demonstrated extensive 18F-FDG-positive lymphadenopathy (neck, axillary, mediastinal, hilar, retroperitoneal, abdominal and pelvic lymph nodes involvement) confirming the relapse of Mantle cell lymphoma. In order to rule out COVID-19 disease, repeated RT PCR testing was performed only hours from PET/CT imaging. It was negative, and the patient proceeded to chemotherapy. In this case, in RT PCR negative patient, PET/CT detected 18F-FDG positive lung consolidations that were very suspicious of active COVID-19 pneumonia in the absence of respiratory symptoms and fever. After repeatedly negative RT PCR SARS-CoV-2 test and X-rays confirming the presence of pulmonary opacities, described lung consolidations were concluded to be lymphoma-related. Five months later the patient became symptomatic and tested RT PCR positive with a quick resolution of fever and cough. Follow-up PET/CT is planned.

CASE 2
A twenty-three-year-old female patient with a newly diagnosed Hodgkin lymphoma was referred to PET/CT for staging purposes. History and clinical examination revealed neck lymphadenopathy with no signs of respiratory distress. Diagnostic CT of the thorax revealed extensive neck and mediastinal lymphadenopathy with no signs of lobar or interstitial pneumonia.

PET/CT confirmed the presence of the lymphoma-related active disease in the neck and mediastinal lymph nodes as well as diffuse hypermetabolism of the bone marrow (Figure 2a, 2c). Lung analysis revealed only mild atelectasis in the left lung that was considered clinically non-significant (Figure 2b, 2c).

A day later and upon the hematologist’s referral, the patient was re-tested and confirmed RT PCR positive. She still had no symptoms and was followed-up by a hematologist. In this case, the patient tested RT PCR positive one day after PET/CT imaging. In the course of her disease, the patient had always been symptom-free. PET/CT was also negative for COVID-19 disease. Noteworthy is the absence of B symptoms including fever that might be lymphoma-related but also might be caused by an infection. The patient was isolated at home, retested in a couple of weeks time and then proceeded to treatment. Normal PET/CT not suggestive of COVID-19 pneumonia in a RT PCR positive patient may be a result of the timing of imaging that was performed early in the course of disease without lung lesions developed yet. Another reason might be unaffected lungs in general in the course of COVID-19. Mild atelectasis detected on PET/CT, however, might be attributed to earlier COVID-19 pneumonia, especially given the patient’s young age.

CASE 3
A fifty-year-old patient with the history of breast cancer was referred to a follow-up PET/CT in order to evaluate treatment response. Radical mastectomy was performed five years earlier revealing HER-2 positive invasive ductal cancer. She was treated with chemotherapy, hormonal therapy and radiotherapy. A year ago a metastatic disease was diagnosed in the liver when the combined immune targeted therapy was initiated. On imaging, the patient was asymptomatic. CT (Figure 3b) and PET/CT (Figure 3c) images demonstrated in both lungs multiple ground glass opacities (GGO) located peripherally in the lung parenchyma. All lung lesions accumulated 18F-FDG with low intensity, SUVmax 3,8 as depicted on PET (Figure 3a) and fused PET/CT images (Figure 3c). Detected lung lesions were very highly suggestive of the COVID-19 disease, and the patient was isolated and referred for retesting immediately. PET/CT also demonstrated multiple 18F-FDG positive lesions in the liver, bones and the local and distant lymph nodes consistent with the metastatic disease.

Repeated RT PCR SARS-CoV-2 testing performed hours from PET/CT imaging was positive. Continued isolation was recommended and the oncology visit was postponed. In this case, PET/CT demonstrated typical findings for COVID-19 pneumonia in the otherwise asymptomatic patient who tested RT PCR negative within 48 hours before the imaging. When she was contacted, the patient was at work and referred only to a mild cold that had spontaneously resolved before the imaging. In this case, PET/CT helped in identifying and isolating a potential source of the spread of disease in the community. The patient’s RT PCR false negative test might be attributed to the time elapsed from the infection to testing, which was insufficient for the required viral load to be formed. Another cause might be an inherent sensitivity of the test itself.

CASE 4
A fifty-nine-year-old female patient with metastatic ovarian cancer was referred to PET/CT exam for restaging of disease. The patient was diagnosed with ovarian cystadenocarcinoma after hysterectomy and adnexectomy in 2016. In 2019, she underwent surgery because of suspected local recurrence when metastatic disease in the colon and paraurethral region was diagnosed and chemotherapy was initiated. One month before PET/CT imaging, the patient had asymptomatic RT PCR SARS-CoV-2- positive infection. CT (Figure 4b) and PET/CT (Figure 4c) images demonstrated bilateral
ground glass opacities (GGO) in the superior pulmonary lobes that were located peripherally. There was no 18F-FDG accumulation in those lesions (Figure 4a, 4c). Also, 18F-FDG positive metastatic lymph node in the pelvis was noted.

This is the case in which PET/CT findings were in accordance with both clinical stage of COVID-19 disease and RT PCR molecular testing result. Described eumetabolic pulmonary opacities are characteristic of COVID-19 pulmonary infection which is not in the active phase.

4. DISCUSSION

COVID-19 seems to be a versatile disease with different clinical presentations and severity of symptoms, if any. To establish a diagnosis of COVID-19 disease, molecular and serological testings for viral RNA or antibodies, clinical findings and diagnostic imaging results are correlated.

RT PCR tests are considered the gold standard for detecting COVID-19 disease. In the UK, RT PCR tests have sensitivity and specificity of more than 95%. Reports in systematic review hold false negative rates of tests between 2% and 33% in repeat sample testing. Both false-negative and false-positive tests impose burden on health systems, and that for different reasons. False-negative tests cause unimpeded spread of disease, especially by asymptomatic and mildly symptomatic patients. False-positive results are mostly caused by contamination and cross-reactions with other viruses or genetic material. They affect the healthcare system through the unnecessary workload on its workers and financial burdens. That is why any diagnostic test should be interpreted in the context of pretest probability of disease which is an estimate, before testing, of the person’s symptoms and chance of being infected (2-5, 11).

Radiological modalities chest radiography and chest CT remain the mainstay of COVID-19 imaging. Typical radiological presentations most commonly include ground-glass opacities (GGO), coarse horizontal linear opacities and consolidations of the lung parenchyma. They are most likely to be found on the lung periphery and in the lower zones, most often bilaterally (6).

A hybrid diagnostic modality PET/CT is not indicated in making a diagnosis or follow-up of COVID-19 disease. Also, it is not recommended in the emergency setting (7). However, different clinical scenarios position PET/CT in the diagnostic algorithm of COVID-19. Described in our case series are only some scenarios that might be encountered in a PET/CT office. In the oncologic clinical setting, PET/CT remains one of the most commonly in-
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Positron Emission Tomography/Computed Tomography (PET/CT) is a dedicated diagnostic procedure for staging, restaging and evaluation of therapeutic response purpose. Estimates are that about 80% of PET/CT is oncologic.

When performed and interpreted in the COVID-19 pandemic, necessary is for PET/CT interpreting physicians to be aware of two issues. First, the clinical presentation of SARS-CoV-2 infection varies from asymptomatic to multi-organ involvement and failure of organs and systems in severe forms of disease. Secondly, but no less important, laboratory, clinical and diagnostic findings are different in different stages of COVID-19.

18F-FDG PET/CT is considered a sensitive but not specific imaging method given the fact that apart from the tumors, infection and inflammation sites also accumulate 18F-FDG due to their cellular metabolism (8, 9). For this reason, active sites of viral pneumonitis caused by SARS-CoV-2 present as 18F-FDG positive on PET and fused PET/CT images, increasing the specificity of the study. Besides, other types of pneumonitis also present as 18F-FDG positive when in active phase.

PET/CT findings may also be helpful in diagnosing the stage of COVID-19 pneumonia using semi-quantification of metabolism of 18F-FDG, and differing active vs. non-active or earlier disease. Our cases indicate different values of SUVmax, which reflect different stages of COVID-19 pneumonia.

Another diagnostic dilemma appears when a primary disease which may affect the lungs, such as lymphoma causes pulmonary changes that raise suspicion of COVID-19 pneumonia. In such cases, additional testing, therapeutic regimes and a follow-up imaging yield a necessary resolution. In every clinical setting, signs and symptoms of disease are to be closely monitored and relied upon (10).

In asymptomatic patients, whole-body or total-body acquisitions on PET/CT may detect COVID-19 incidentally. Such incidental findings are to be reported and immediately addressed to the referring physicians in order to adjust or change the treatment plans and carry out personal protection measures.

In COVID-19 pandemic, nuclear medicine departments are obliged to follow personal protection measures and protect their staff. Such measures are to combine with radiation safety measures already in place without contradicting any. Nuclear medicine staff must be aware that there is a possibility of the spread of disease in PET/CT units, which is facilitated by the procedure guidelines and the workflow in the unit (11). When performing PET/CT, nuclear medicine staff must be aware of the laboratory, clinical and diagnostic variations related to COVID-19. Although at present PET/CT does not play an established part in making a diagnosis of COVID-19 or fol-

Figure 3. RT PCR negative breast cancer patient was detected with positive pulmonary lesions on axial PET (a) (arrow). Axial CT (b) demonstrates peripheral ground-glass opacities (GGO) in both lungs (arrow), typical of COVID-19 pneumonia. Fused PET/CT image (c) confirms moderate 18F-FDG positivity of GGO, SUVmax 3.8 consistent with active COVID-19 pneumonia. Patient was retested and at that time proved RT PCR positive.

Figure 4. Patient with ovarian cancer and COVID-19 resolved a month before the imaging. Both axial CT (b) and fused PET/CT (c) demonstrate multiple peripheral GGO (arrow) bilaterally. Lack of 18F-FDG accumulation on PET (a) indicates non-active disease consistent with COVID-19 pneumonia sequelae.

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low-up of the disease, in some cases it aids both of them.

The advances in medical technology have been rapidly brought into healthcare, and more and more sophisticated medical devices have been introduced into clinical practice and experiences are described in a lot of scientific publications, including some of them by authors from Bosnia and Herzegovina during corona time (12–21).

At present, a very large proportion of state-of-the-art healthcare is technology-based (22). Implementation of new technologies and information systems attached to them has been given a tremendous rise, but it is still limited by financial requirements and uneven distribution of resources. One of the latest improvements in PET/CT technology is digital PET/CT vs. analog PET/CT, which is considered specific as it maintains the quality of images, but reduces time of scanning substantially.

In digital PET/CT, image quality is improved and lesion detectability is increased (23). The world of imaging is changing very rapidly, with healthcare becoming a very dynamic field. In their recent work, Beyer et al. (24) suggested that we treat diagnostic images as „data”, and then analyze them using machine learning techniques via analysis platforms. The authors are of the opinion that „the scans we will be reading in 10 years from now will likely be composed of highly diverse multi-dimensional data from multiple sources”.

In parallel with development of technology, the patient setting has been subject to constant changes, too. The population gets older in general, incidence of age-related diseases such as neurodegenerative ones and cancer is increasing, and focussed healthcare responses on a global scale. Necessary is to adjust the existing technologies to the requirements of ongoing trends.

Coleandra et al. suggest that the new strategies must be designed to effectively handle a viral disease such as COVID-19 and the cancer, including, among other things, a „careful surveillance of the appearance of SARS-CoV-2 symptoms, earlier diagnoses and correct allocation of resources” (25).

From this perspective, the role of PET/CT in COVID-19 still needs to be validated. One of the directions for further research might be establishing of 18F-FDG PET/CT imaging features of COVID-19 at different stages of disease, and their potential predictive role in the course of disease (26).

5. CONCLUSION

PET/CT imaging remains of paramount importance for oncologic patients during the pandemic. Under the unprecedented circumstances, interpretation of PET/CT findings has become more complex having some specificities that must be kept in mind.

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