Simultaneous use of FDG-18 and ^{68}Ga-citrate PET/CT for the differential diagnosis of sarcoidosis and malignant disease

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Abstract

A 67-year-old male presented with cutaneous rash, lassitude and fatigue of three weeks. Personal history included psoriasis and sarcoidosis. Physical examination revealed macular rash on the anterior chest wall. Laboratory results were within normal limits. Chest X-ray showed normal findings. Pulmonary function tests demonstrated a mild obstructive pattern and a mild decrease in DLCO/VA. Thorax CT revealed two nodules in the right upper and middle lobe. ^{68}Ga-citrate PET/CT did not demonstrate any active inflammatory reaction associated with sarcoidosis while ^{18}F-FDG PET/CT revealed increased FDG uptake in the right middle lobe, upper division bronchus and in the left lower abdominal quadrant. Histopathologic examination of the colon biopsy was compatible with adenocarcinoma and bronchoscopic biopsy of the lung lesions revealed nonspecific granulomatous inflammation. BAL cytology was normal while BAL culture did not grow any pathologic organisms.

Simultaneous use of ^{18}F-FDG and ^{68}Ga-citrate PET/CT was the hallmark for the final diagnosis in our patient. While FDG/PET has detected the pulmonary and colonic malignant foci in our patient, ^{68}Ga-citrate PET/CT excluded the presence of active granulomatous inflammation of sarcoidosis. Simultaneous utility of these two imaging modalities in patients with sarcoidosis is of great importance in terms of guiding the clinician towards the accurate diagnostic pathway which is the hallmark for final diagnosis, especially in the presence of concomitant malignant disease.

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Introduction

Several diagnostic imaging modalities are used for the clinical evaluation of sarcoidosis, but all have their own limitations relevant to disease identification or activity. The frequently used ^{18}F-FDG PET/CT [Positron emission tomography with 2-deoxy-2-[fluorine-18]fluoro- D-glucose integrated with computed tomography (^{18}F-FDG PET/CT)] may not reveal the optimal results in sarcoidosis patients. Novel radiopharmaceuticals aimed at other disease targets may be conducive, particularly in cardiac sarcoidosis as ^{18}F-FDG PET/CT has a low diagnostic accuracy. ^{68}Ga-labeled somatostatin based receptor hybrid imaging appears to be a potential alternative to ^{18}F-FDG PET/CT for sarcoidosis [1-3]. Consequently, this imaging modality has emerged as a useful diagnostic screening tool to assess the disease activity and treatment response in patients with pulmonary sarcoidosis revealing a sensitivity and a specificity of 92.5% and 83.3%, respectively [4-6].

Simultaneous application of ^{18}F-FDG and ^{68}Ga-citrate PET/CT [^{68}Ga-citrate positron emission tomography-computed tomography (^{68}Ga-citrate PET/CT)] for the suspicion of a newly developing asymptomatic colon adenocarcinoma in a patient with a previous history of sarcoidosis led the clinician in the right pathway for the final diagnosis. Concurrent use of these two imaging modalities appears to be an indispensable approach for a definitive diagnosis when sarcoidosis occurs concomitantly with malignant disease.

Case Report

A 67-year-old male was admitted for the evaluation of dry cough, lassitude, fatigue and maculopapular rash on the anterior

chest wall of three weeks. The patient was a non-smoker. Past medical history included a diagnosis psoriasis for 35 years and persistant chronic sarcoidosis for 30 years. Physical examination was completely normal other than the maculopapular rash on the anterior chest wall. Laboratory results including blood count, serum biochemistry, ACE [angiotensin-converting-enzyme (ACE)] serum and urinary calcium were within normal levels. ECG demonstrated regular sinus rythm of 84/min and a normal QRS axis. Chest X-ray showed normal parenchymal and mediastinal findings. Thorax CT [Computed tomography (CT)] revealed a nodule in the the left upper division bronchus orifice (Figure 1a) and two nodules in the lateral segments of both lower lobes (Figure 1b). ^{18}F-FDG PET/CT demonstrated moderate FDG uptake in the left upper division and in the left lower lobe laterobasal segment nodules (Figure 2 a,b) with SUVmax of 2.9, without any significant FDG uptakes in right upper lobe anterior and middle lobe lateral segments nodules, significant and diffuse FDG uptake in the major vessels with an incidental left lower abdominal quadrant lesion of 18 mm with a SUVmax of 18.2 (Figure 3 a,b). An additional ^{68}Ga-citrate PET/CT revealed normal findings (Figure 4 a,b) and did not indicate any active granulomatous inflammation relevant to sarcoidosis in the lung, in the mediastinum and in any other organ. Dermatology consultation concluded that the maculopapular rash on the anterior chest wall was associated with psoriasis exacerbation. The high FDG uptake in the major vessels was evaluated as vasculitic changes due to psoriasis. Histopathologic examination of the colon biopsy revealed low grade

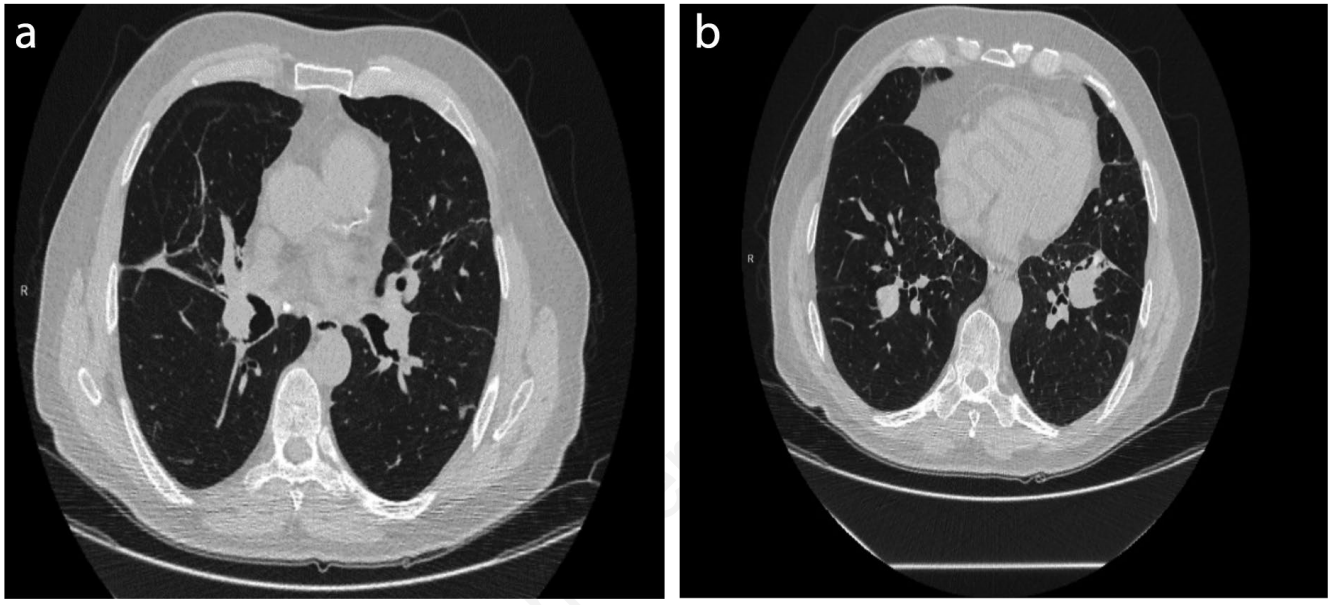

Figure 1. Thorax CT revealing narrowing of the upper division bronchus (a) and two nodules in the lateral segments of both lower lobes (b).

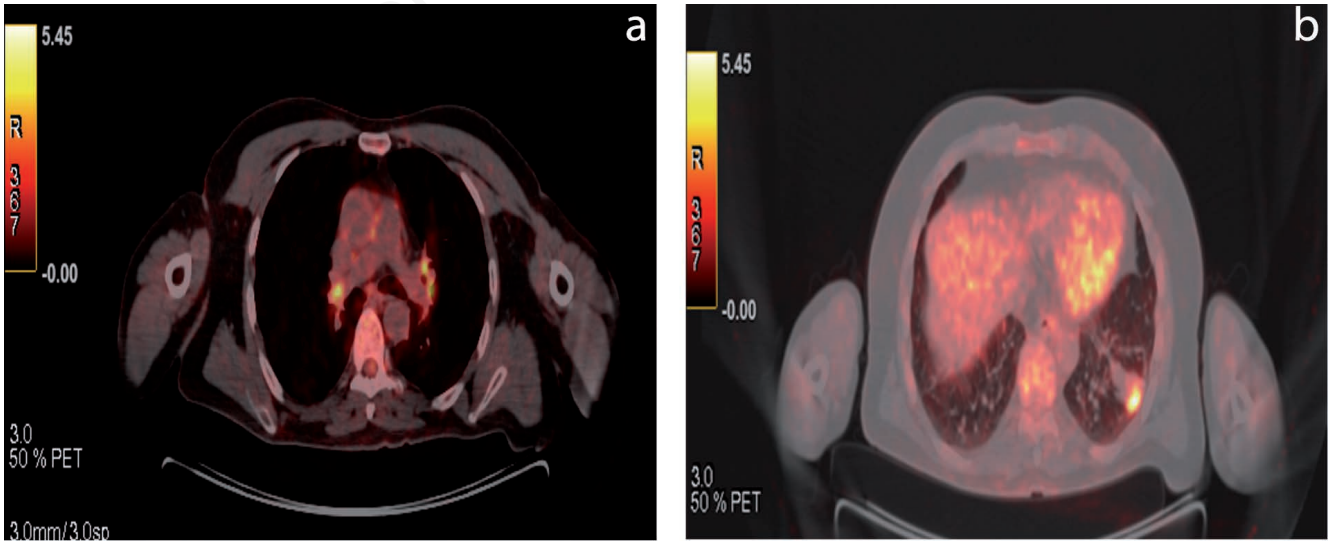

Figure 2. Axial (a) and coronal (b) ^{18}F-FDG PET/CT fusion image revealing high FDG uptake in the left upper division bronchus and in the left lower lobe laterobasal segment nodules.

colonic adenocarcinoma. Bronchoscopy demonstrated funnel-shaped narrowing of the left upper division and two submucosal nodules at the orifice of right middle lobe. Pathologic examination of the bronchoscopic biopsy of the left upper division bronchus and the right middle was not diagnostic revealing nonspecific granulomatous inflammation. BAL cell count and differential cytology were within normal limits. Histopathology of the EBUS samples from 4R and 11L lymp nodes revealed anthracosis. Culture of BAL did not grow any pathologic organisms including bacteria, fungus or mycobacteria. Final diagnosis was low grade colonic adenocarcinoma with bronchial anthracosis in the right middle and left upper division lobe bronchus with stenosis. The patient was referred to the surgery department for further treatment of the colon adenocarcinoma.

Discussion

Sarcoidosis is a chronic granulomatous disease of unknown origin commonly affecting the lungs and the mediastinal lymph nodes but also the extrapulmonary organs with varying frequency [7]. Several imaging modalities are available for the identification and the evaluation of the treatment response of sarcoidosis but unfortunately these may not provide compatible consequences with the current clinical profile in all patients leading to a diagnostic challenge for the clinician. ^{18}F-FDG PET/CT has emerged as a useful adjunct for identifying pulmonary or extrapulmonary sarcoidosis disease activity including targets for tissue diagnosis

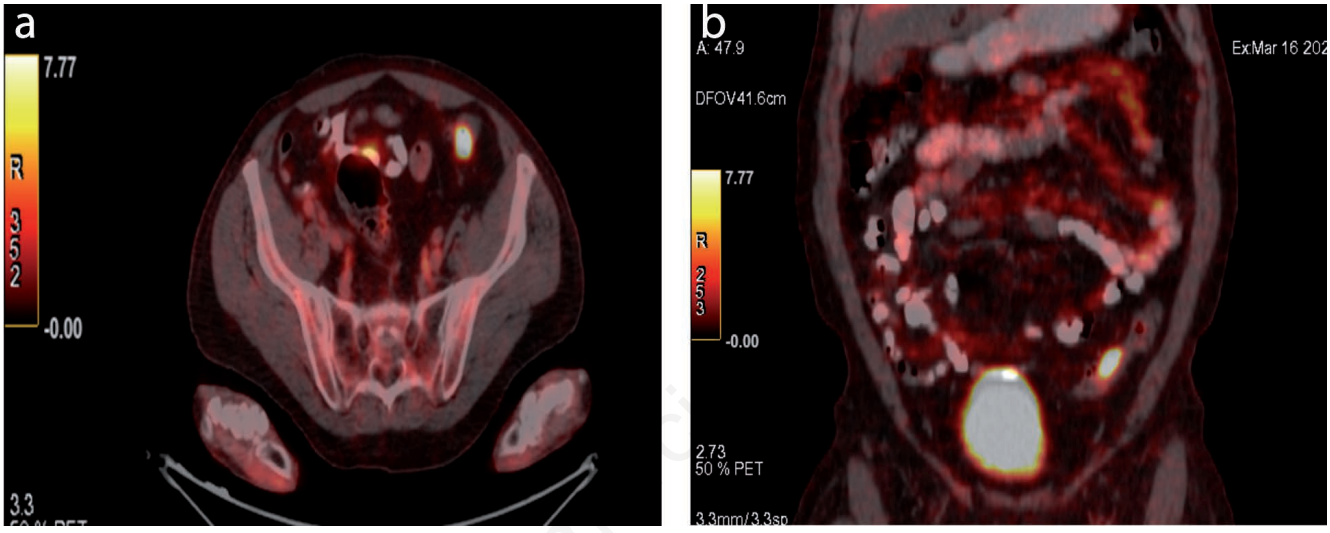

Figure 3. Axial (a) and coronal (b) ^{18}F-FDG PET/CT fusion image revealing high FDG uptake in the left lower quadrant.

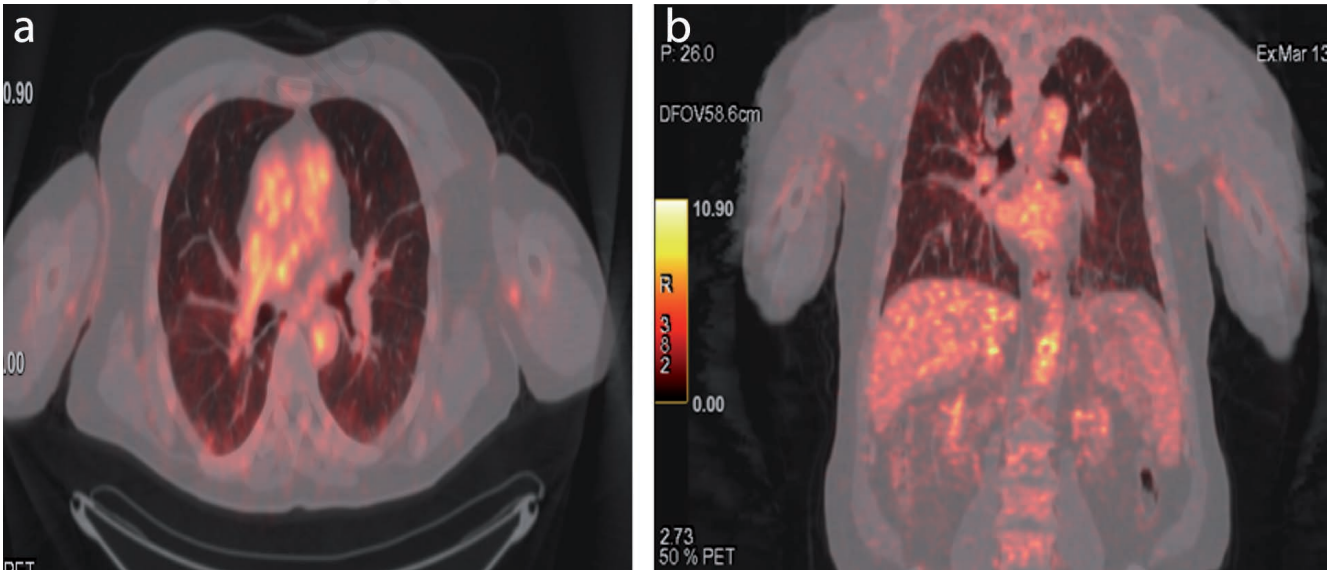

Figure 4. Axial (a) and coronal (b) ^{68}Ga-citrate PET/CT) fusion image showing no active inflammation associated with sarcoidosis disease in the lung and mediastinum.

that has been reported to exhibit variable sensitivity and specificity [6,8-10].

The somatostatin receptor subtype two is highly expressed in sarcoid granulomas. This high expression is extremely useful for somatostatin receptor scintigraphy to be used in sarcoidosis. Consequently, ^{68}Ga-citrate PET/CT which is primarily performed for oncologic applications is now available as a diagnostic tool to assess the disease activity and treatment response in patients with sarcoidosis with thoracic involvement [1-6]. Our patient was admitted for the evaluation of symptoms that were primarily thought to be associated with his previous sarcoidosis disease while ^{68}Ga-citrate PET/CT revealed no active inflammation in the lungs, the lymph nodes or other extrapulmonary organs as confirmed by BAL cell count and other laboratory markers. High FDG- uptake in the major vessels was most likely relevant to the exacerbation of the pre-existing psoriasis disease as no clinical, laboratory and radiological findings indicating an activation of sarcoidosis were identified. On the other hand, ^{18}F-FDG PET/CT demonstrated a high FDG uptake pointing out to the presence of malignancy in the colon. A colon adenocarcinoma and bronchial anthracosis were diagnosed as a result of the histopathological examination of the biopsies performed from two the organs that revealed a high FDG uptake which were identified by the aforementioned imaging modality.

Gallium compounds have displayed anti-inflammatory and immunosuppressive activity in animal models of human disease. Radioactive gallium has been used as a diagnostic and therapuetic agent in clinical medicine for cancer, disorders of calcium and bone metabolism. Adverse effects such as diarrhea, renal toxicity and visual or auditory toxicities have been observed in 12.5% and 1% of the patients following high continous infusion gallium doses, respectively [11]. Single administration of ^{18}F-FDG or ^{68}Ga-citrate PET/CT does not lead to any crucial short or long-term significant side effects. There are no currently reported remarkable or serious toxic effects for double administration of ^{18}F-FDG and ^{68}Ga-citrate PET/CT when performed as an imaging modality [12-14]. Although simultaneous application of ^{18}F-FDG and ^{68}Ga-citrate PET/CT may lead to potential hazards due to the cumulative dose, there is no data concerning such detrimental radioactive adverse impacts. As far as the previously cited references suggested, the simultaneous application of these two methods does not carry any short-term potential toxicity while the long-term sequela of this integrated application is currently unknown.

This case is novel in regard to the clinical profile of the patient who presented with symptoms that were preemptively suspected to be related to his previous sarcoidosis disease while there were no clinical manifestations relevant to the primary malignant disease constituting the hallmark of our case. Inactive sarcoidosis inflammation was demonstrated by ^{68}Ga-citrate PET/CT together with the other laboratory findings while the malignant disease in the colon was identified by ^{18}F-FDG PET/CT imaging. Utility of two different PET imaging modalities simultanoeusly in the same patient led the clinician to the accurate clinical pathway thereby reaching the final diagnosis without any further delay which is extremely crucial in patients with malignancy, especially in the asymptomatic patients relevant to the tumor.

Conclusions

^{68}Ga-citrate PET/CT emerged as a useful imaging tool in our patient excluding an active inflammatory state of sarcoidosis in which the current clinical symptoms were primarily thought to be connected with his preexisting disease. On the other hand, ^{18}F-FDG PET/CT identified a high FDG-18 uptake in the colon thereby pointing out to the presence of malignant disease that presented with a completely asymptomatic clinical profile with a high degree of probability while ^{68}Ga-citrate PET/CT excluded an active sarcoidosis inflammation thereby leading the clinician in the accurate diagnostic pathway. Using these two imaging modalities together in sarcoidosis patients will provide great convenience and rapid diagnosis in terms of the final diagnosis for sarcoidosis patients in whom a concomittant malignancy is considered or appears to be a probability. Another hallmark of this case is the asymptomatic clinical patient profile due to colon adenocarcinoma that was identified by ^{18}F-FDG PET/CT imaging which otherwise could not be ascertained.

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