PET/CT Scan as a Surrogate for Treatment Outcomes in Pulmonary Sarcoidosis

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Research article

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Abstract

Background: One of the challenges in treating sarcoidosis is that there is currently no reliable modality to measure disease activity and prognosis. This study was conducted to determine if PET/CT scans could be used to evaluate clinical response to sarcoidosis treatment.

Methods: In a retrospective cohort study, subjects with symptomatic pulmonary sarcoidosis followed by the University of Miami Sarcoidosis program from 2015 through 2018 were assessed. Inclusion criteria were subjects ≥18 years who had histologically-confirmed pulmonary sarcoidosis for ≥2 years. Subjects that had PET/CT scans completed prior to starting treatment and approximately one year later were enrolled. Demographics, circulatory blood biomarkers, subjective symptoms, and medications were recorded at baseline (T0) and a year later (T1).

Results: Ten subjects with symptomatic pulmonary sarcoidosis were enrolled. All subjects had at least one organ affected by sarcoidosis and a highest of five organs involved (mean 2.75, SD 1.21). Mean serum angiotensin-converting enzyme (ACE) level was 56.0 U/L (SD 43.08), mean lysozyme was 7.78 µg/mL (SD 3.78), and mean C-reactive protein (CRP) was 0.73 mg/dL (SD 0.85) at T0. Further, mean number of positive lesions was 4.27 (SD 2.65) and mean highest SUV was 5.59 (SD 3.59), with a highest of 14.5 at T0. After one year of therapy, a significant improvement in measured outcomes was noted. Dyspnea was absent in all subjects at T1 and only 1 (10%) reported cough at T1. The mean ACE was 42.17 U/L (SD 20.24), mean lysozyme was 6.24 µg/mL (SD 0.80), and mean CRP was 1.67 mg/dL (SD 1.60) at T1. Furthermore, five (50%) subjects were receiving a reduced dose of their respective medication at T1. In terms of PET/CT findings, the mean number of positive lesions decreased at T1 to 1.73 (SD 2.87) and the mean highest SUV decreased to 2.18 (SD 3.3).

Conclusion: PET/CT scans can be used as a surrogate modality to help guide treatments in those subjects affected by sarcoidosis, as shown by significant reductions in the involvement of multiple organs. Further studies with larger sample sizes are necessary to explore the potential PET/CT scans have to influence treatment outcomes in sarcoidosis.

Background

Sarcoidosis is a multi-organ disease of unknown etiology, characterized by the formation of non-necrotizing epithelioid granulomas which can affect any organ, but has a predilection for lung involvement (1, 2). Epidemiologically, sarcoidosis affects approximately 10 out of every 100,000 subjects per year in the United States, is present in all ethnic groups, and has a peak onset in adults between 20 and 40 years of age (3–5). Sarcoidosis has an unpredictable clinical presentation, ranging from incidentally discovered radiographic abnormalities in an asymptomatic patient to chronic progressive illness affecting multiple organ systems (6).

The initial evaluation of patients with suspected sarcoidosis involves a battery of tests, including blood cell counts, serum chemistry, urinalysis, and biomarkers (7, 8). In those with pulmonary symptoms,

pulmonary function tests (PFTs) and chest images are usually obtained. However, one of the difficulties in treating this condition is that there is currently no single test to monitor the response to therapy or monitor disease activity.

Positron emission tomography (PET)/computed tomography (CT) scans are widely used in the assessment of subjects with suspected or confirmed malignancies. There are limited small series and case reports addressing the use of PET/CT scans with a glucose analogue of 18F-fluorodeoxyglucose (18-FDG) for the assessment of inflammatory diseases (9–11). The advantage of PET/CT scans is that it visualizes FDG accumulation in activated inflammatory cells and provides whole-body images, allowing clinicians to assess the activity of sarcoidosis throughout the body. However, little is known regarding the role of PET/CT scans in the evaluation of the response to sarcoidosis treatment. The aim of this study was to understand whether PET/CT scans can be used to monitor disease outcomes and treatment responses.

Methods

This is a retrospective case series which included ten subjects with symptomatic pulmonary sarcoidosis that were followed by the University of Miami (UM) Sarcoidosis Program from 2015 to 2018. Subjects were ≥ 18 years and had histologically-confirmed pulmonary sarcoidosis for ≥ 2 years. Our sarcoidosis program has an active patient registry that has been approved by the Institutional Review Board (IRB) of the university and all participants have provided written consent. Subjects that had PET/CT scans completed prior to starting treatment and approximately one year later were enrolled. Patients who were unwilling to consent to the IRB-approved protocol were excluded. In addition, patients without evidence of pulmonary sarcoidosis, patients with a history of cancer, or patients who had PET/CT scans done > 1 year apart were excluded.

Demographics, symptoms, biomarkers, medications and imaging were recorded at baseline (T_0) and approximately one year after starting therapy (T_1). Positive pulmonary lesions were defined as either involving the parenchyma, mediastinal lymph nodes, or both. The study outcomes were symptom resolution, radiological (PET/CT) improvement, and reduction in the total dose of medication.

Results

The baseline characteristics of the study population were as follows: 3 (30%) subjects were female, 4 (40%) were African-Americans, 5 (50%) were European-American, and 1 (10%) was Latino. Mean age (standard deviation, SD) was 58.36 years (10.05). All subjects had at least one organ involved and a highest of five organs involved (mean 2.75, SD 1.21). Six subjects (60%) had dyspnea, 3 (30%) had fatigue, and 5 (50%) had cough at T_0. The upper limit of normal for angiotensin-converting enzyme (ACE), lysozyme, and C-reactive protein (CRP) were 82 U/L, 12.8 µg/mL, and 0.5 mg/dL, respectively. Mean serum ACE level was 56.0 U/L (SD 43.08), mean lysozyme was 7.78 µg/mL (SD 3.78), and mean CRP was 0.73 mg/dL (SD 0.85). At T_0, 9 (90%) subjects were receiving steroids, 1 (10%) was receiving

methotrexate (MTX), and 1 (10%) was receiving azathioprine (AZA). All 10 (100%) subjects had positive pulmonary lesions on PET/CT scans. Mean number of positive lesions was 4.27 (SD 2.65). Mean highest SUV was 5.59 (SD 3.59), with a highest of 14.5 and lowest 2.7 at T_0.

After one year of therapy, a significant improvement in measured outcomes was noted. Dyspnea was absent in all subjects at T_1 compared to 6 (60%) at T_0, 1 (10%) had cough at T_1 compared to 5 (50%) at T_0, and the same number of subjects reported fatigue at T_1 as they did at T_0. Furthermore, 5 (50%) subjects were receiving a reduced dose of their respective medication at T_1. The mean ACE was 42.17 U/L (SD 20.24), mean lysozyme was 6.24 µg/mL (SD 0.80), and mean CRP was 1.67 mg/dL (SD 1.60) at T_1. Regarding the PET/CT findings, the mean number of positive lesions decreased to 1.73 (SD 2.87) and the mean highest SUV decreased to 2.18 (SD 3.3). Figure 1 shows a representative PET/CT scan imaging at baseline T_0 and after one-year T_1. Given the small sample size of this case series, we cannot correlate biomarker activity or changes in pulmonary function with PET/CT scans.

Conclusions

The current study suggests PET/CT scans can be used as a surrogate modality to help guide treatments in those subjects affected by sarcoidosis, as shown by significant reductions in the involvement of multiple organs. Larger longitudinal studies are necessary to explore the potential of PET/CT scans to influence sarcoidosis treatment protocols.

Abbreviations

PFTs: Pulmonary function tests

PET: Positron emission tomography

CT: Computed tomography

UM: University of Miami

IRB: Institutional Review Board

ACE: Angiotensin-converting enzyme

CRP: C-reactive protein

MTX: Methotrexate

AZA: Azathioprine

Declarations

Ethics Approval and Consent to Participate

The sarcoidosis program at the University of Miami has an active patient registry that has been approved by the Institutional Review Board (IRB) of the University of Miami (IRB: 20150612) and all participants have provided written consent.

Consent for Publication

Consent for publication has been obtained.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing Interests

The authors declare that they have no competing interests.

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Authors' Contributions

NSK and IJS conducted literature review, reviewed the charts, collected data, and helped in manuscript preparation. MM conducted literature review, visited the patients, and helped manuscript preparation.

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Table 1

Table 1: Demographic and radiographical findings of the included subjects with pulmonary sarcoidosis

Case	Age	Gender	Ethnicity	Highest SUV, T_0	Number of Positive Lesions, T_0	Highest SUV, T_1	Number of Positive Lesions, T_1
1	42	Male	European-American	4.6	4	2.6	3
2	47	Male	African-American	4.3	2	2.6	1
3	48	Male	European-American	9.1	3	0	1
4	52	Male	European-American	14.5	6	0	0
5	56	Female	African-American	2.7	2	1.5	2
6	63	Male	European-American	2.9	2	0	0
7	67	Male	African-American	7.5	8	11.3	10
8	70	Female	African-American	3	4	0	0
9	68	Male	European-American	3.5	10	3.1	2
10	70	Female	Latino	5.43	5	0	0

Figures

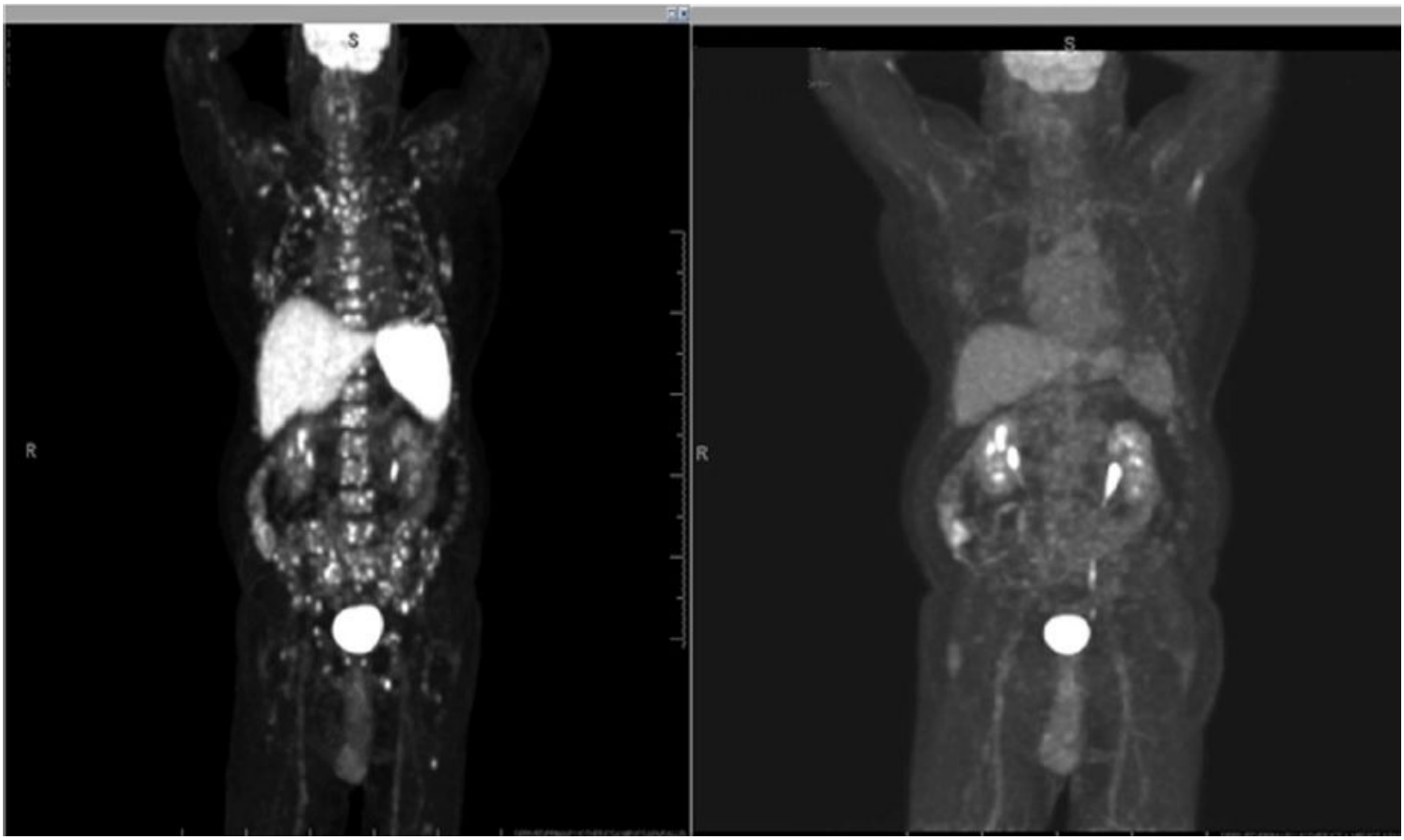

Figure 1

PET/CT scan imaging at baseline T0 (left) and after one year T1 (right). PET/CT imaging shows significant improvement after one year from the initial scan.