Sarcoidosis Mimicking a Malignancy and Sarcoid Reactions in the Chest: Collaborative Interpretation of CT and F18 FDG PET/CT

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Introduction

- Sarcoidosis is a multi-systemic disease characterized by cellular immunity activity with formation of non-caseating granulomas in various organ systems.

- The diagnosis of sarcoidosis is based on clinical, radiological, biochemical and histological finding. The clinical course of sarcoidosis is extremely variable.

- Sarcoidosis most commonly affects patients between 20 and 40 years of age. There is a slight female predominance (M:F = 1:3), particularly among African-Americans.
Lungs are the most common site of disease involvement. Classic imaging findings and patterns of sarcoidosis involving the chest are quite well known.

However, uncommon radiographic findings and marked FDG avidity may complicate matters which may lead to false-positive results of malignancy.

It can also occur after chemotherapy in oncologic patients (sarcoid reaction) while being associated with other disease entities such as lymphoma.
Learning Objectives

- Describe common and uncommon findings of sarcoidosis on radiography and CT
- Identify PET/CT features of sarcoidosis and its added value on other imaging modalities as well as pitfalls in diagnosis of disease and management of patients
- Recognize sarcoid reactions seen in oncologic patients following chemotherapy and sarcoidosis-lymphoma syndrome
- Describe the importance of collaborative interpretation of CT and F18 FDG PET/CT
Sarcoidosis

- Approximately 50% of patients are asymptomatic, 50% develop respiratory or skin (erythema nodosum) disease.
- The subacute form diagnosed in most patients under the age of 30 affects mainly intrathoracic organs and lasts generally less than two years.
- The chronic form begins more often over the age of 40 and might involve extrathoracic organs.
- ACE elevated in 70%, hypercalcemia + hypercalciuria occurs.
- Staging at presentation on chest radiography:
  - 0 normal CXR 5%
  - I LAP only 50%
  - II LAP + parenchymal 30%
  - III parenchymal only 10%
  - IV pulmonary fibrosis 5% (up to 25% during the courses of disease)
Sarcoidosis

Stage I

Stage II

Stage III

Stage IV
Pulmonary Sarcoidosis

- Lymphadenopathy:
  - bilateral hilar/right paratracheal
  - commonly decreases as parenchymal disease gets worse
  - eggshell calcification
- Upper/mid-zone predominance
- Perilymphatic nodules
- Alveolar/acinar sarcoidosis
- Progressive fibrosis with upper lobe retraction and bullae
- Associated with Tuberculosis in ~13%
- Complicated by Aspergilloma in apical bulla (in >50% of stage IV)
CT Findings of Pulmonary Sarcoidosis

- Small sharply defined nodules
  - Typical of active lung disease
  - Perilymphatic distribution
    - parahilar and peribronchovascular
    - adjacent to fissures, subpleural
    - interlobular septal nodules in some
    - centrilobular nodules in some
  - Upper lobe predominance in most
  - Calcification may occur
CT Findings of Pulmonary Sarcoidosis

- Large nodules and masses
  - 15%-25% of patients
  - Due to confluence of small granulomas
  - With or without air bronchograms
  - Parahilar/peribronchovascular
  - Associated with satellite nodules (the “galaxy sign”)

![Image of CT scan showing large nodules and masses associated with sarcoidosis](image)
CT Findings of Pulmonary Sarcoidosis

- **Ground-glass opacity**
  - Uncommon
  - Due to numerous very small granulomas
  - Small nodules may be associated

- **Reticular opacities and fibrosis**
  - Develops in 15% of patients
  - Peribronchovascular fibrosis with traction bronchiectasis
  - Upper lobe volume loss
  - Air-filled cysts
  - Honeycombing in some
  - Mycetoma may develop
Bronchial/bronchiolar abnormalities
  • Endobronchial granulomas
  • Atelectasis in some
  • Mosaic perfusion and air trapping
F18 FDG PET/CT

- F18 is the commonly used PET radiotracer because of its availability, the relatively long half-life (110 minutes) and its high uptake in malignant lesions and inflammatory/infectious disorders.

- FDG is transported into cells by glucose transporter (GLUT) and is metabolized to FDG-6-phosphate and trapped in the cells. The degree of the FDG uptake depends on the number of transporters and on the metabolic rate.

- PET/CT enables a more accurate localization and attenuation correction as well as simultaneous evaluation of morphological and metabolic features.
The Role of the PET Scan in Sarcoidosis

- PET is not useful for initial diagnosis as it could be misinterpreted as a malignancy.

- PET is a sensitive method to assess the inflammatory activity and the extent of disease in sarcoidosis which can be of great value to complement more routinely used techniques.

- PET appears especially helpful in patients with unexplained persistent disabling symptoms in the absence of serological signs of inflammatory activity, in patients with radiologic signs of fibrosis and in the detection of active cardiac sarcoidosis.
The Role of the PET Scan in Sarcoidosis

- The use of PET to assess the extent of disease can uncover a suitable location for biopsy to obtain histological evidence for the diagnosis or to explain the (mainly extrathoracic) symptoms. Furthermore, the detection of extrathoracic involvement can offer prognostic value.

- PET may assess response to anti-inflammatory therapy in sarcoidosis as well as guide the duration of treatment to increase the cost-effectiveness and avoid long-term side-effects.
CASES
56 yo female with history of SLE, presented with persistent mild dyspnea

- Numerous conglomerate nodules predominantly along the bronchovascular bundles (blue arrows)
- Some subpleural nodules (red arrows)

MIP image of F18 FDG PET/CT

- Extensive and marked FDG uptake in the bilateral lungs corresponding to multiple pulmonary nodules (blue arrows)
- Differentiating features from metastasis/infection
  - Upper lobe predominance
  - peri-bronchovascular distribution
- Biopsy proved sarcoidosis.

SUV max 9.9
62 yo asymptomatic female with abnormal chest radiography findings

- CT: multiple ill-defined masses in the right lung, predominantly upper and lower lobe superior segment, are located supleurally and along the bronchovascular bundles. One of these shows air-bronchogram (blue arrow). Lymphoma or metastasis was considered. Biopsy proved sarcoidosis.
- PET: markedly increased FDG uptake is seen in the masses and right hilar and mediastinal lymph nodes (red arrows).
- There are multiple enlarged, markedly hypermetabolic intra-abdominal lymph nodes (circle).
Disseminated Sarcoidosis

35 yo male with generalized bone pain

- Extensive bone and hepatosplenic involvement of disease
- Lymph node and lung involvement to a lesser degree in this case
- Scattered foci of intense uptake in the biventricular myocardium (arrows)
- Frequently indistinguishable from other advanced neoplasms/metastases, so histologic proof is typically necessary

PET provides more comprehensive image of sarcoidosis activity related to clinical findings.
Sarcoidosis Involving Clivus and Lymph nodes

46 yo male with headache

- CT: A lytic lesion in the left aspect of clivus (arrow)
- MR: The lesion shows hyperintensity on T2 and avid enhancement (arrow).
- PET: marked FDG uptake (SUV max 8) in clivus (blue arrow). There are hypermetabolic (SUV max 8) bilateral hilar and mediastinal lymphadenopathy (red arrows). Biopsy of clival lesion proved sarcoidosis.
Chemotherapy Induced Sarcoidosis

- Sarcoidosis must be considered in the differential diagnosis of oncologic patients who have developed hypermetabolic lesions during follow-up.
- All cancer types can be observed.
- Sarcoidosis appears usually within 3 years after cancer in the hila and mediastinum, may have atypical location but not serious complications.
- Possible hypothesis:
  - ? Sarcoidosis has been triggered by immunological disturbance induced by chemotherapy or associated with the lymphoma
  - ? Triggered by an infectious agent resulting in granuloma formation
  - ? Antineoplastic therapy might have reduced suppressor T cells leading to lymphocyte activation seen in sarcoidosis
Chemotherapy Induced Sarcoidosis

- This association could be considered as a protective factor against cancer relapse because of the very low rate of cancer relapse reported in these patients.
- Consequently, biopsy is mandatory to avoid unjustified treatment of cancer relapse.
Chemotherapy Induced Sarcoidosis

h/o orbital melanoma, treated with chemotherapy

At the time of completion of chemotherapy

1 year

1.5 years

• Chemotherapy induced sarcoid reaction can uncommonly occur in oncologic patients with variable durations and with variable antineoplastic therapy.

• Must be considered in the differential diagnosis when assessing patients with persistent or enlarging lymphadenopathy after chemotherapy (arrows).

• Difficult to differentiate from tumor recurrence/metastasis.

• A tissue biopsy is necessary.
Sarcoidosis as a Mimic of Malignancy

- The most common radiologic finding in sarcoidosis is intrathoracic lymphadenopathy seen in up to 85% of patients. Abdominal lymphadenopathy is seen 30%, with massive lymphadenopathy (lymph nodes > 2 cm) seen in 10%.

- One of the more common differential considerations in these patients is lymphoma.

- Musculoskeletal involvement in sarcoidosis can manifest as increased focal FDG uptake throughout the skeleton, which can mimic diffuse metastatic disease.

- A known association exists between sarcoidosis and lymphoma (both Hodgkin’s and non-Hodgkin’s lymphoma), described in 1986 by Brinker and called “sarcoidosis–lymphoma syndrome”.
By Brinker, et al. about 1.5 times higher incidence of cancer was seen in sarcoidosis patients. Lung cancer occurred 3 times and malignant lymphoma 11.5 times more frequently than in the control population.

Sarcoidosis predisposes for lymphoid malignancies, more often with a chronic type sarcoidosis.

Lymphoproliferative disease (LD) has occurred with a median interval of 24 months after the diagnosis of sarcoidosis and developed 5.5 times more frequently than expected, which may suggest that the chronic active type of sarcoidosis is a predisposing factor for LD.

Hodgkin’s disease was diagnosed more frequently than other types of lymphomas.

Mechanisms:
- ? the changes in the number and the functions of immune cells in sarcoidosis, suggesting dysfunction in the immunoregulatory pathways
- ? abnormality in defective T suppressor cells regulation
- ? steroid treatment which compromises further the immune system
58 yo male patient who has history of sarcoidosis diagnosed with diffuse large B cell lymphoma

- Multiple retroperitoneal and mesenteric lymph nodes (circle) with marked FDG uptake (SUV~15.9)
- Splenic involvement (SUV~12) (yellow arrows)
- Few mildly hypermetabolic mediastinal nodes (red arrows)
- Example of Sarcoidosis lymphoma syndrome

- Complete response to chemotherapy with resolved lymphadenopathy
- New mild to moderate FDG uptake (SUV~5.9) in the hilar and mediastinal lymph nodes which are essentially unchanged in size and number (purple arrows). Chemotherapy induced sarcoidosis.
78 yo former smoker with history of sarcoidosis developed lung cancer (adenocarcinoma)

- 1.9 cm spiculated subsolid nodule (adenocarcinoma) in the right lower lobe with SUV max 14 (red arrows)
- Multiple hilar, mediastinal and abdominal lymphadenopathy with marked FDG uptake (SUV max ~11) consistent with known sarcoidosis (blue arrows). No malignant cells identified on biopsy. Marked splenic uptake (yellow →)
- Higher incidence of cancer in sarcoidosis patients: Lung cancer was reported to occur 3 times more frequently.
The imaging features of sarcoidosis are diverse and can be shown on a variety of imaging techniques. FDG uptake on PET/CT in patients with sarcoidosis is variable and can mimic malignancies such as lymphoma and diffuse metastatic disease.

FDG PET/CT could be used for monitoring the response to treatment because FDG uptake correlates with disease activity but is not useful for initial diagnosis as it could be misinterpreted as a malignancy.

It is important for radiologists to recognize the importance/value of collaborative interpretation of axial imaging and PET/CT to raise the possibility in the appropriate clinical setting as well as implement proper patient management.
References

4. Prabhakar, et al. Imaging Features of Sarcoidosis on MDCT, FDG PET, and PET/CT AJR:190, March 2008 S1-S6
Thank you for your attention.

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