Nuclear Imaging: Diagnosis of Sarcoidosis

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Outline

- Background
- Criteria for diagnosis
- Guiding therapy
- Conclusions
History

- 61y/o with increased SOB, chest discomfort, lightheadedness in 4/13.
- Prior to this he had been well, active (played hockey, rides horses).
- Denies significant cough, no vision changes, has rash on nasal bridge but otherwise minimal problems.
- Found to have third degree heart block - admitted to cardiology who noted conduction system disease and decreased EF (39%).
Echo
CMR
Coronary Angiogram
F-18 FDG PET/CT
Biventricular ICD
F-18 FDG PET/CT

- Overall, the spectrum of findings involving the right breast, lungs, mediastinal and right supraclavicular lymph nodes, and bones is compatible with sarcoid; however, this needs to be proven with biopsy.
- The right retroareolar lesion could be biopsied percutaneously.
Mammography-Male Breast
Pathology

- Invasive ductal carcinoma and metastatic carcinoma to lymph nodes
- OTHER FINDINGS: Core biopsy site Non-necrotizing granulomatous inflammation, consistent with patients' known sarcoidosis
- Prior pathology report: Basal cell cancer of a skin lesion
Treatment

- Methotrexate (HEM-ONC.) 15 MG (2.5 MG TABLET Take 6) PO QWEEK
- Prednisone 30 MG (20 MG TABLET Take 1.5) PO TAPER, Take 1 and 1/2 20mg tablets PO QD for 1 month then take 1 20mg tablet PO QD for 1 month then take 1/2 of a 20mg tablet PO QD for 1 month x 120 days
- Carvedilol, Furosemide, Atorvastatin, Amiodarone,
- Clonazepam, Rivaroxaban, Sertraline, Tamoxifen, Tamsulosin
Follow-up (2 years later)

Baseline

2 years later

SUV\textsubscript{max} 5.16;
Volume of inflamed myocardium
60.21 cc

SUV\textsubscript{max} 3.01
Volume of inflamed myocardium
0.5 cc
Significant improvement

Baseline

2 years later
LVEF: Before and after
$^{18}$F-FDG PET to identify recurrent cardiac sarcoid post transplant

~2 years post transplant
Cardiac Sarcoidosis

- Cardiac sarcoid frequently underdiagnosed
  - Clinically seen in 5%, autopsy diagnosis in 25-79%
- Location
  - LV free wall > septum, conduction system
- Clinical presentation
  - Cardiomyopathy, tachyarrhythmias and bradyarrhythmias, palpitations, syncope, and death
- Endomyocardial biopsy has a low diagnostic yield (<20%)
  - Cardiac involvement patchy
  - Endomyocardial biopsies usually in the right ventricle
  - Granulomas are more likely in the left ventricle and basal ventricular septum
Disease Course

- 2/3 rd have a remission within a decade after diagnosis
- 1/3 rd of patients have ongoing disease significant organ impairment
- <5% of patients die from sarcoidosis
  - pulmonary fibrosis
  - cardiac or
  - neurologic involvement

Disease course

• Sudden death may be the first sign of cardiac sarcoidosis
  • EP studies, Pacemaker, and AICD – VT/ VFIB, or very low EF
• Early intervention with steroids may improve prognosis
• Early diagnosis essential
Scar without significant inflammation

Granuloma and chronic inflammation

Interstitial fibrosis with granulomas/inflammation
Outline

- Background
- Criteria for diagnosis of cardiac sarcoid
## Japanese Ministry criteria for the diagnosis of cardiac sarcoidosis

1. Histologic diagnosis group: Histological analysis of operative or endomyocardial biopsy specimens demonstrate epitheloid granuloma without caseation

2. Clinical diagnosis group

   extracardiac sarcoidosis is diagnosed histologically or clinically and satisfies the following conditions

   1≥ 2 major criteria

   2. 1 major criteria and ≥ 2 minor criteria

<table>
<thead>
<tr>
<th>Major criteria</th>
<th>Minor criteria</th>
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<tbody>
<tr>
<td>a. Advanced atrioventricular block.</td>
<td>a. Abnormal ECG findings: ventricular arrhythmias (ventricular tachycardia, multifocal or frequent PVCs), CRBBB, axis deviation or abnormal Q-wave.</td>
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<tr>
<td>b. Basal thinning of the interventricular septum.</td>
<td>b. Abnormal echocardiography: regional abnormal wall motion or morphological abnormality (ventricular aneurysm, wall thickening).</td>
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<tr>
<td><strong>c. Positive $^{67}$gallium uptake in the heart.</strong></td>
<td><strong>c. Nuclear medicine: perfusion defect detected by $^{201}$thallium or $^{99m}$technetium myocardial scintigraphy.</strong></td>
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<tr>
<td>d. Depressed ejection fraction of the left ventricle (&lt;50%).</td>
<td>d. Gadolinium-enhanced CMR imaging: delayed enhancement of myocardium.</td>
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<td>f. Endomyocardial biopsy: interstitial fibrosis or monocyte infiltration over moderate grade.</td>
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Tahara et al J Am Coll Cardiol Img 2010; 1219-1228
Heart Rhythm Society Consensus Recommendation

**Expert Consensus Recommendations on Criteria for the Diagnosis of CS**

There are 2 pathways to a diagnosis of Cardiac Sarcoidosis:

1. **Histological Diagnosis from Myocardial Tissue**
   - CS is diagnosed in the presence of non-caseating granuloma on histological examination of myocardial tissue with no alternative cause identified (including negative organismal stains if applicable).

2. **Clinical Diagnosis from Invasive and Non-Invasive Studies**:
   - It is probable* that there is CS if:
     a) There is a histological diagnosis of extra-cardiac sarcoidosis
     and
     b) One or more of following is present
        - Steroid +/- immunosuppressant responsive cardiomyopathy or heart block
        - Unexplained reduced LVEF (<40%)
        - Unexplained sustained (spontaneous or induced) VT
        - Mobitz type II 2nd degree heart block or 3rd degree heart block
        - **Patchy uptake on dedicated cardiac PET (in a pattern consistent with CS)**
        - **Late Gadolinium Enhancement on CMR (in a pattern consistent with CS)**
        - **Positive gallium uptake (in a pattern consistent with CS)**

     and
     c) Other causes for the cardiac manifestation(s) have been reasonably excluded

*In general, ‘probable involvement’ is considered adequate to establish a clinical diagnosis of CS.*

Birnie DH et al. HeartRhythm2014;11:1304–1323
Outline

- Background
- Criteria for diagnosis
- Imaging techniques
Perfusion imaging

- SPECT
  - Thallium-201
  - Tc-99m
- PET
  - Rubidium-82
  - N-13 ammonia
# Imaging of Inflammation

<table>
<thead>
<tr>
<th>Radiopharmaceutical</th>
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<tr>
<td>F18-FDG</td>
<td></td>
</tr>
<tr>
<td>Tc-99m/ In 111 labeled</td>
<td></td>
</tr>
<tr>
<td>WBC’s</td>
<td></td>
</tr>
<tr>
<td>Tc-99m bisphonates</td>
<td></td>
</tr>
<tr>
<td>Ga-67 citrate</td>
<td></td>
</tr>
<tr>
<td>Tc-99m nanocolloids</td>
<td></td>
</tr>
<tr>
<td>Tc-99m / In 111 labeled proteins (IgG, albumin)</td>
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Gallium-87 imaging:

**F18-FDG PET is Superior Quality**

![Image with Gallium-87 SPECT, F-18 FDG PET/CT, Non-contrast CT scan, and Fused F-18 FDG PET/CT images in transverse, coronal, and sagittal views.]
18F-FDG PET Imaging to Phenotype Cardiac Sarcoid Activity

Structure

Post-Rx

+ Immuno-suppression

Met. activity +

Immuno-suppression

- Immuno-suppression
FDG PET: Highly accurate to diagnose cardiac sarcoidosis

FDG-PET Protocol

10 mCi F-18 FDG

IV Heparin-UFH

Diet Instructions: 12 hours prior

Rest Perfusion study

Uptake period 90 minutes

F-18 FDG study
Diffuse FDG Uptake: a Limitation

Repeat FDG scan
Patterns of cardiac sarcoid

<table>
<thead>
<tr>
<th>STAGES</th>
<th>PET Patterns</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Perfusion Defect</td>
</tr>
<tr>
<td>Normal</td>
<td>None</td>
</tr>
<tr>
<td>Early</td>
<td>None</td>
</tr>
<tr>
<td>Progressive</td>
<td>Mild</td>
</tr>
<tr>
<td>Peak active stage</td>
<td>Moderate</td>
</tr>
<tr>
<td>Progressive myo.impairment</td>
<td>Severe</td>
</tr>
<tr>
<td>Fibrosis</td>
<td>Severe</td>
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Response to therapy

FDG uptake high

Delayed enhancement abnormal
FDG PET Identifies Myocardial Inflammation in Areas of Delayed Enhancement

- **Active disease**
  - Rb-82
  - F18-FDG

- **Inactive disease**
  - Rb-82
  - F18-FDG
Mismatch: Perfusion and FDG

- Differential diagnosis
  - Hibernating myocardium
  - Sarcoidosis
- Knowledge of coronary angiogram to exclude epicardial CAD is essential
Cardiac MRI: Sarcoidosis

81 patients, cardiac MRI, 21+/-8 months for major adverse events (death, defibrillator shock, or pacemaker requirement). DE-CMR identified cardiac involvement in 21 patients (26%) and JMH criteria in 10 (12%, 8 overlapping) (P=0.005).

FDG Imaging Enhances Prognostic Assessments of Patients with Suspected Cardiac Sarcoid

125 patients, 61% abnormal cardiac PET, 38 (30%) cardiac adverse events including 10 (8%) deaths over 17 months follow up (median)

Survival free of death or VT

Blakstein et al. ACC 2012 Abstract
Monitoring changes in cardiac FDG uptake in sarcoidosis

- FDG PET is useful to monitor response
  - Cardiac
  - Systemic
- But, it is hot spot imaging
  - Cannot compare relative FDG imaging to assess changes
  - Decreased FDG uptake
    - Normal
    - Scar
    - Decreased inflammation
- May use ratio of uptake to blood pool or other organs
- Standardized uptake values may help
Pre-treatment
Posttreatment
Follow-up (2 years later)

Baseline

2 years later

SUVmax 5.16;
Volume of inflamed myocardium
60.21 cc

SUVmax 3.01
Volume of inflamed myocardium
0.5 cc
Significant improvement

Baseline

2 years later
### Methods to Quantify FDG PET

<table>
<thead>
<tr>
<th></th>
<th>SUV Max</th>
<th>SUV LVBP</th>
<th>SUV volume w/ 1.5 × SUV&lt;sub&gt;LVBP&lt;/sub&gt;</th>
<th>SUV volume w/ 2.7 SUV threshold (Ahmadian A et al)</th>
<th>SUV volume w/ 4.1 SUV threshold (Osborne MT et al)</th>
<th>Qualitative Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>6.74</td>
<td>1.76</td>
<td>90.97 cm&lt;sup&gt;3&lt;/sup&gt;</td>
<td>88.24 cm&lt;sup&gt;3&lt;/sup&gt;</td>
<td>9.84 cm&lt;sup&gt;3&lt;/sup&gt;</td>
<td>++</td>
</tr>
<tr>
<td>6 months after Baseline</td>
<td>4.37</td>
<td>1.70</td>
<td>29.68 cm&lt;sup&gt;3&lt;/sup&gt;</td>
<td>20.19 cm&lt;sup&gt;3&lt;/sup&gt;</td>
<td>0.22 cm&lt;sup&gt;3&lt;/sup&gt;</td>
<td>+++</td>
</tr>
<tr>
<td>% Change</td>
<td>↓ 35%</td>
<td>-</td>
<td>↓ 67%</td>
<td>↓ 77%</td>
<td>↓ 98%</td>
<td>↑</td>
</tr>
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Summary-1
Approach to diagnosis of sarcoidosis

Birnie DH et al. HeartRhythm2014;11:1304–1323
Cardiac sarcoidosis is significantly underdiagnosed

- FDG PET is widely used for diagnosis and monitoring response to therapy
- No randomized clinical trial data to support the use of specific immunosuppressive therapy or to monitor response to therapy in cardiac sarcoidosis
- Quantitative FDG metrics may be superior to visual assessment to assess response to therapy
Thank You