A Comprehensive work up of Sarcoidosis

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AGENDA

1) Our patient of sarcoidosis and the course in the hospital
2) Sarcoidosis- Explanation, Organs involved
3) Systemic as well as Pulmonary manifestations
4) Signs to look out for on imaging for Pulmonary sarcoidosis
5) Silzbach Stages of Pulmonary Sarcoidosis on Xray
6) Sarcoid on CT
7) Extra Pulmonary Manifestations
8) Further evaluation and management
Our Patient

- Mrs X, a 59 yr old female with a history of breast cancer, s/p resection 1999 comes to the Emergency Department with
  - 2 weeks progressive parathesia of chest wall, more on left than on right
  - Feeling constriction of lungs and pain with deep inspiration.
  - Denied dyspnoea, cough, hemoptysis, activity intolerance, fever, chills
Plan

- After this presentation the plan was:
  1. CT Scan – to
  - Rule out Pulmonary embolism
  - Evaluate for other causes
  2. ECG-which came back normal and negative for pericarditis
For further evaluation, a CT scan was ordered.

FINDINGS
Enlarged Hilar and mediastinal lymph nodes.
Imaging

Enlarged Bilateral Hilar and mediastinal lymph nodes
Imaging

Enlarged Bilateral Hilar and mediastinal lymphadenopathy
Differential Diagnosis

After the CT-Scan the diagnosis under consideration were:

• Lymphoma,
• Sarcoidosis
• Metastatic disease
Further Evaluation

1. Flexible bronchoscopy.
2. Endobronchial ultrasound with transbronchial needle aspiration

Final Diagnosis: Presence of granulomas and absence of metastatic disease which is consistent with Sarcoidosis.
Follow Up - Most Recent Presentation

- Upper lobe predominant nodular and reticular opacities
- Scarring also visible
Follow Up-Most Recent Presentation

- Reticular opacities
- Fibrosis

The diagnosis was confirmed to be Stage IV sarcoidosis
Follow Up-Most Recent Presentation

- Widespread fibrosis and scarring visible
- Supports the Diagnosis of Stage IV sarcoidosis
What Is Sarcoidosis?

- Sarcoidosis is an inflammatory granulomatous disease that can affect any organ.

- Either infectious agents or non-infectious particles can cause sarcoidosis.

- Infectious agents, such as fungi and mycobacteria, and noninfectious particles, such as certain dusts can induce the response.

- Activated T cells and macrophages accumulate at site of inflammation.

- It is characterised by accumulation and persistence of non-caseating granulomatous inflammation within an organ which can lead to dysfunction and cause scarring.
## Organs Involved commonly

<table>
<thead>
<tr>
<th>Organ involvement</th>
<th>Number*</th>
<th>Percent</th>
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<tbody>
<tr>
<td>Lungs</td>
<td>699</td>
<td>95.0</td>
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<tr>
<td>Skin•</td>
<td>117</td>
<td>15.9</td>
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<tr>
<td>Lymph node</td>
<td>112</td>
<td>15.2</td>
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<tr>
<td>Eye</td>
<td>97</td>
<td>11.8</td>
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<tr>
<td>Liver</td>
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<td>Erythema nodosum</td>
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<td>Spleen</td>
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<tr>
<td>Neurologic</td>
<td>34</td>
<td>4.6</td>
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<tr>
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<td>3.9</td>
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<tr>
<td>Bone marrow</td>
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<td>3.9</td>
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<tr>
<td>Calcinosis</td>
<td>27</td>
<td>3.7</td>
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<tr>
<td>ENT</td>
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</tr>
<tr>
<td>Cardiac</td>
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<td>2.3</td>
</tr>
<tr>
<td>Renal</td>
<td>5</td>
<td>0.7</td>
</tr>
<tr>
<td>Bone/joint</td>
<td>4</td>
<td>0.5</td>
</tr>
<tr>
<td>Muscle</td>
<td>3</td>
<td>0.4</td>
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</tbody>
</table>

*Table taken from Uptodate*

**ENT**: ear, nose, and throat.

*Total n=736.

* Excluding erythema nodosum.

Systemic Manifestation of Sarcoidosis

• Most Frequent: Fatigue, Malaise, Fever, and Weight loss

• Systemic inflammation may contribute to muscle weakness and exercise intolerance

• Visual changes with dry eyes or mouth

• Parotid swelling

• Palpitations

• Syncope

• Joint pain or swelling, or muscle weakness.
Pulmonary Sarcoidosis

1) Diffuse interstitial lung disease is the classic type of lung involvement;

2) Common presenting respiratory symptoms include cough, dyspnea, and chest pain.

3) Digital clubbing is rare and typically associated with advanced pulmonary fibrosis.

4) Other Patterns of presentation of a patient with sarcoidosis
   - Pneumothorax
   - Pleural thickening
   - Chylothorax
   - Pulmonary hypertension
Diagnostic Approach to sarcoidosis

- Compatible clinical and radiographic manifestations

Exclusion of other diseases that may present similarly
- Infection (tuberculosis, fungal infection, Mycobacterium avium intercellulare)
- Hypersensitivity pneumonitis
- Lymphomas
- Metastasis

- Histopathologic detection of noncaseating granulomas
  - Flexible bronchoscopy with bronchoalveolar lavage (BAL)
  - Endobronchial biopsy
  - Transbronchial biopsy
Radiological Diagnosis Of Pulmonary Sarcoidosis
Radiological Options Available

• Chest Radiograph
• High resolution Computed Tomography.
• Other imaging tests (in special conditions)
  1. FDG-PET
  2. Gallium-67
  3. Thallium-201
  4. Technetium sestamibi (MIBI-Tc)
  5. Single photon emission computed tomography (SPECT)
Special Signs to look out for that give a clue to the diagnosis
1-2-3 Sign or Garland's triad

- This is a lymph node enlargement pattern comprising of:
  1) Right paratracheal nodes
  2) Right hilar nodes
  3) Left hilar nodes
- Hilar lymphadenopathy is symmetrical and usually massive, so called ‘Potato nodes’

Galaxy Sign

- Represents a mass-like region composed of numerous smaller granulomas.
- The appearance of a central core with peripheral nodules is reminiscent of a globular cluster galaxy.
- Central cavitation does occur and the lesions may be surrounded by ground-glass opacity.
- Differential includes Sarcoidosis and Tuberculosis.

Image: http://radiopaedia.org/articles/galaxy-sign
Galaxy Sign

Confluent nodule with multiple small peripheral nodules emanating from the margins of the central nodule

Differential diagnosis

- Sarcoidosis
- Active Tuberculosis
- Malignancy (less likely)
- Progressive Massive Fibrosis (less likely)
Panda Sign and Lambda Sign

- **Panda Sign**
  1) on gallium-67 scan
  2) bilaeral involvement of parotid and lacrimal glands in sarcoidosis, superimposed on the normal uptake in the nasopharyngeal mucosa

- The panda sign is not specific for sarcoidosis

- **Lambda Sign**
  1. on gallium-67 scan in thoracic sarcoidosis
  2. Bilateral hilar and right paratracheal lymph-nodes are typically involved

Image: [http://www.ijem.in/article.asp?issn=2230-8210;year=2013;volume=17;issue=2;spage=332;epage=335;aulast=Yanamandra](http://www.ijem.in/article.asp?issn=2230-8210;year=2013;volume=17;issue=2;spage=332;epage=335;aulast=Yanamandra)
Egg Shell Calcification

• Not a very specific marker.
• Just denotes shell-like calcifications up to 2 mm thick is present in the peripheral zone.

DIFFERENTIALS INCLUDE
1) Sarcoidosis - calcification occurs late in the disease
2) Silicosis
3) Treated lymphoma: (postirradiation Hodgkin Disease) usually 1-9 years following treatment
4) Coal Workers Pneumoconiosis - 1% patients
5) Scleroderma
6) Amyloidosis - rare
PULMONARY SARCOIDOSIS
Silzbach’s Stages of Pulmonary Sarcoidosis as seen on Radiograph

STAGE 0: • Normal chest radiograph

STAGE I: • Hilar or mediastinal nodal enlargement only

STAGE II: • Nodal enlargement and parenchymal disease

STAGE III: • Parenchymal Disease only

STAGE IV: • End Stage Disease (Pulmonary Fibrosis)
Chest Radiograph-Stage I

1) In Stage I-Only lymphadenopathy present
2) This is called the 1-2-3 sign or Garland's triad
3) Differential also includes Lymphoma but that can be excluded as the “potato nodes” do not abut the cardiac border
Chest Radiograph-Stage II

Lymphadenopathy present along with parenchymal involvement

Case courtesy of Dr Mohammed Alshammari, Radiopaedia.org. From the case Sarcoïdosis.
Chest Radiograph-Stage III

Diffuse parenchymal disease only

Case courtesy of Dr Frank Gaillard, <a href="http://radiopaedia.org/">Radiopaedia.org</a>. From the case <a href="http://radiopaedia.org/cases/sarcoidosis-2">Sarcoidosis</a>
Chest Radiograph - Stage IV

- End Stage Disease
- As evidenced by Pulmonary Fibrosis
- Reticular opacities seen too.
HRCT findings in Sarcoidosis

• **Common findings:**
  - Upper and middle zone predominance.
  - Small nodules in a perilymphatic distribution (along subpleural surface and fissures, along interlobular septa and the peribronchovascular bundle).
  - 1-2-3 sign: Often with calcifications.

• **Differential for Perilymphatic Nodules:**
  - Sarcoidosis
  - Lymphangitis carcinomatosis (often asymmetrical and lower lobe).
  - Silicosis
  - Coal workers pneumoconiosis
  - Rare causes include amyloidosis and Lymphocytic Interstitial Pneumonitis
HRCT findings in Sarcoidosis. (Contd)

- Uncommon findings:
  - Honeycombing pattern: In end stage disease (Fibrosis)
  - Larger nodules > 1cm in diameter, in Grouped nodules or coalescent nodules surrounded by multiple satellite nodules (Galaxy sign)
  - Nodules so small and dense that they appear as ground glass or even as consolidations (alveolar sarcoidosis)
Some patterns visible on CT

- A: Ground glass opacity
- B: Micronodule
- C: Nodule
- D: Consolidation
CT showing Beading of Major fissure

- Sarcoidosis with multiple nodules, 1 to 2 mm in diameter, in peribronchiolar location.
- Beading of the major fissures is characteristic of lymphatic involvement.
- There is also prominent bilateral hilar lymph node enlargement.
Progressive fibrosis in sarcoidosis may lead to peribronchovascular (perihilar) conglomerate masses of fibrous tissue.

The typical location is posteriorly in the upper lobes, leading to volume loss of the upper lobes with displacement of the interlobar fissure.
Extra Pulmonary Sarcoidosis
Brain complications
Eye problems (burning, itching, tearing, or pain)
Salivary glands
Enlarged lymph nodes in neck and chest
Heart complications
Granulomas (inflamed lumps) in lungs
Liver enlargement
Spleen enlargement

Lupus pernio (painful skin sores on face) and skin lesions on back, arms, neck, face, and scalp

Enlarged lymph nodes in chest near windpipe and lungs
Scarring and granulomas in lung

Erythema nodosum (itchy and painful rashes) on the lower legs and ankles

Closeup view of lung cross-section
Sarcoidosis on Skull

- **Lytic lesions** visible
- **CT** is not as sensitive or specific as **MRI**, with up to 60% of patients with subsequently proven neurosarcoidosis having negative CT scans

Case courtesy of Dr Angela Byrne. <a href="http://radiopaedia.org/">Radiopaedia.org</a>. From the case <a href="http://radiopaedia.org/cases/sarcoidosis-skull">Sarcoidosis - skull</a>
Role of MRI in Neurosarcoidosis

- MRI with contrast is the modality of choice for investigating suspected neurosarcoidosis.
- Parenchymal and leptomeningeal involvement is most common.
- **T1**: iso- or hypointense with respect to adjacent grey matter
- **T2**
  - most are hyperintense
  - some lesions can be iso or hypointense
MRI Sarcoidosis

- MRI is a proven better modality for neurosarcoid imaging.
- The MRI of leptomeninges, in this patient here, shows “tongues of fire” sign.

Case courtesy of Dr Frank Gaillard, <a href="http://radiopaedia.org/">Radiopaedia.org</a>. From the case <a href="http://radiopaedia.org/cases/neurosarcoidosis-and-chiari-i">Neurosarcoidosis and Chiari I</a>
Sarcoidosis Hands

- sclerotic bone lesions
- remodelling of the cortex of phalanges, in which the concave shaft is converted into a tubular structure

Abdominal Sarcoidosis on CT

- Hypodense lesions visible on liver here.
- Multiple Hypodense lesions on spleen here.
- Always look out for enlarged lymph nodes, which are usually found in the following areas:
  1) Porta hepatis
  2) Para-aortic region
  3) Coeliac axis
  4) Superior mesenteric artery
  5) Gastrohepatic ligament
  6) Retrocrural region

Further Evaluation Of a Patient with Sarcoidosis

- **Complete blood count** - Anemia of chronic disease
- **ESR and CRP** – non specific markers of inflammation
- **Pulmonary function testing**:
  - Reveal a restrictive pattern (reduced vital capacity and total lung capacity) associated with a reduction in the DLCO.
  - The six minute walk test distance is reduced in the majority of patients with sarcoidosis
- **Serum ACE** - Elevated as Non Caseating Granulomas are supposed to secrete ACE. Poor sensitivity and insufficient specificity.
Further Evaluation In a case of Sarcoidosis

- **Kveim test** - It is essentially a research tool due to limited availability of the reagent. Presence of non caseating granulomas confirm the diagnosis.

- **Testing for tuberculosis** - Mantoux is classically negative in sarcoidosis

- **Ocular Testing** - Anterior uveitis leading to glaucoma and vision loss is a common complication
Further Evaluation In a case of Sarcoidosis

- **Broncho-alveolar lavage**: reduced CD8 and elevated CD4 to CD8 ratio

- **Endobronchial and transbronchial lung biopsy** - A definitive diagnosis requires a biopsy of non-caseating granulomas

- **Transbronchial needle aspiration** — usually performed along with the biopsy

- **Gallium 67 scan** - localises an inflammatory foci.

- **FDG-PET scan** - Differentiates from lung cancer
Treatment Algorithm for Pulmonary Sarcoidosis
Pulmonary Sarcoidosis

Asymptomatic
- Follow with PFTs

Minimal symptoms e.g. cough
- Inhaled corticosteroids
  - No response, consider oral steroids

Moderate disease
- Chest x-ray stage II or higher PFTs below normal

Dyspnea
- Only one present
  - Consider steroids
  - Follow at least 3 months
- Two or more present
  - Begin prednisone\(^*\)
    - 20-40mg daily
  - Taper dose over next 3-6 months

Severe disease
- Evaluate for pulmonary hypertension
- Begin prednisone\(^*\)
  - 20-40mg daily

\(^*\)Where prednisone is indicated, an equivalent dose of corticosteroids (i.e. methylprednisolone) could also be used.

\(^\dagger\)Cytotoxic drugs include: methotrexate, azathioprine, mycophenolate and leflunomide.

\(^{++}\)Anti-TNF therapy includes infliximab and adalimumab.
Monitoring of Sarcoidosis

- Follow-up is generally at 3- to 6-month intervals, although more frequent monitoring is needed in the first 2 years of diagnosis and in higher radiographic stages of disease.

- Monitoring includes:
  1) Clinical signs of disease activity
  2) FBC
  3) LFTs to assess cytotoxic medications.

- Bone density screening every 2 years is recommended by the National Osteoporosis Foundation for patients with conditions or for those taking medicines that are associated with bone loss.

From: BMJ
Summary

Take Home Points

• Introduction to sarcoidosis, organs involved
• Pulmonary and extra pulmonary manifestations
• Key Signs to look out for on Radiograph
• Classification of Sarcoidosis on Radiograph
• Extra Pulmonary manifestations of Sarcoidosis
• Evaluation and treatment algorithm of Pulmonary Sarcoidosis
References

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- http://radiopaedia.org/articles/sarcoidosis-1
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