“Dilemma of Thoracic Tuberculosis Vs. Sarcoidosis in TB Endemic Areas: An Imaging Approach”

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FINANCIAL DISCLOSURES

- A. S. Bhalla - Nothing to disclose
- A. Das - Nothing to disclose
- A. GOYAL - Nothing to disclose
- P. NARANJE - Nothing to disclose
- R. GULERIA - Nothing to disclose
- G. C. KHILNANI - Nothing to disclose
LEARNING OBJECTIVES

1. To review the definitive and indeterminate imaging features of thoracic sarcoidosis.

2. To summarize the differentiating and overlapping imaging features of thoracic sarcoidosis and tuberculosis (TB).

3. To propose an imaging algorithm for evaluation of patients with non-specific/overlapping clinical features of sarcoidosis and tuberculosis in TB endemic areas.
INTRODUCTION

• Sarcoidosis is a multi-system chronic granulomatous disease of unknown etiology
• Hypothesized to be an immune-mediated inflammatory disease
• Characterized by non-caseating granulomas with variable surrounding collagen deposition on histopathology
• Progressive fibrosis leads to architectural distortion and irreversible damage to organs involved
INTRODUCTION

- Tuberculosis is an infectious disease caused by organism *Mycobacterium tuberculosis*
- Characterized by caseating granulomas on histology
- The disease closely mimics sarcoidosis in its clinical manifestations and histopathological features.
CLINICAL PRESENTATION

• Both diseases share common nonspecific systemic symptoms such as
  - Chronic fever
  - Fatigue
  - Night sweats
  - Malaise
  - Weight loss
  - Anorexia

• Both diseases share common nonspecific respiratory symptoms as well
  - Cough with or without sputum production
  - Respiratory distress
  - Chest pain
  - Hemoptysis
Chest radiograph (CXR)-PA view showing classical bilateral hilar and right paratracheal lymph nodes.

- ? Sarcoidosis
- ? TB
THE DILEMMA

• The diagnostic guidelines developed in western literature for clinico-radiological diagnosis of sarcoidosis cannot be replicated for use in tuberculosis-endemic areas such as India.

• The overlapping clinical and imaging manifestations of tuberculosis and sarcoidosis - pose a diagnostic challenge to the clinicians.

• Implications of this problem
  
  • Entirely different treatment regimens for the two diseases
  
  • Sarcoidosis responds well to corticosteroids, the administration of the latter in a patient with tuberculosis may flare up the disease.
Few characteristic clinical features which help in distinguishing the two diseases

<table>
<thead>
<tr>
<th>Clinical feature</th>
<th>Tuberculosis</th>
<th>Sarcoidosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Constitutional symptoms</strong></td>
<td>Fever, chills, malaise, Weight loss</td>
<td>Fatigue, myalgia, mild fever</td>
</tr>
<tr>
<td><strong>Respiratory symptoms</strong></td>
<td>Cough with frank sputum Hemoptysis</td>
<td>Dry cough, dyspnea Chest tightness/pain</td>
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<tr>
<td><strong>Extrathoracic symptoms</strong></td>
<td>Cervical lymphadenopathy (more common)</td>
<td>Cervical lymphadenopathy (less common)</td>
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<tr>
<td></td>
<td>Lymph nodal swellings with sinus formations</td>
<td>Arrhythmias</td>
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<tr>
<td></td>
<td>Pain and swelling of joints</td>
<td>Lupus pernio</td>
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<tr>
<td></td>
<td></td>
<td>Bell’s palsy</td>
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<td></td>
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<td>Parotid enlargement</td>
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</table>
Role of laboratory investigations

- Constellation of some of the laboratory investigations are helpful in distinguishing sarcoidosis from tuberculosis.

<table>
<thead>
<tr>
<th>Laboratory investigations</th>
<th>Tuberculosis</th>
<th>Sarcoidosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biopsy (Diagnostic)</td>
<td>AFB, necrotizing granuloma</td>
<td>Non-necrotizing granuloma</td>
</tr>
<tr>
<td>Acid-fast bacilli (AFB) positive and/or culture-positive</td>
<td>Diagnostic</td>
<td>Rare, May be seen in coexistent cases</td>
</tr>
<tr>
<td>Tuberculin sensitivity Test (TST)</td>
<td>Specificity of &gt;85 percent</td>
<td>Rare</td>
</tr>
<tr>
<td>IGRA using QuantiFERON-TB-Gold In Tube assay (QFT) in blood</td>
<td>Higher sensitivity and specificity for MTB detection, positive in upto 60%</td>
<td>Positive in upto 34%</td>
</tr>
<tr>
<td>Serum ACE</td>
<td>Variable</td>
<td>&gt;2 times elevation in 60 to 80% cases</td>
</tr>
<tr>
<td>Hypercalcemia</td>
<td>Not seen</td>
<td>Fairly characteristic</td>
</tr>
<tr>
<td>Hypercalciuria</td>
<td>Not seen</td>
<td>Fairly characteristic</td>
</tr>
<tr>
<td>Neutrophil/lymphocyte ratio in blood</td>
<td>&gt;2.55</td>
<td>&lt;2.55</td>
</tr>
</tbody>
</table>
# ROLE OF IMAGING

<table>
<thead>
<tr>
<th>Frontal chest radiograph (CXR)</th>
<th>Computed tomography (CT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial diagnosis and assessment of extent of involvement</td>
<td>Baseline imaging (contrast enhanced CT)</td>
</tr>
<tr>
<td>Can depict findings highly suggestive (HS) for TB, HS for Sarcoidosis or non-specific (NS).</td>
<td>Comprehensive assessment of mediastinal and hilar LN</td>
</tr>
<tr>
<td>Follow up imaging for assessing the stability or progression of the disease</td>
<td>Can depict findings HS for TB, HS for Sarcoidosis or NS</td>
</tr>
<tr>
<td><strong>Magnetic Resonance Imaging (MRI)</strong></td>
<td><strong>HRCT chest without contrast can suffice for follow up of stage 3 and 4 patients</strong></td>
</tr>
<tr>
<td>Greater sensitivity to detect necrosis within the nodes.</td>
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<tr>
<td>Can help detecting activity /fibrosis within nodes and lung parenchymal lesion</td>
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<tr>
<td>Radiation free modality for serial imaging follow-up</td>
<td></td>
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<tr>
<td><strong>PET CT</strong></td>
<td></td>
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<tr>
<td>Does not feature in the routine diagnostic algorithm for evaluation of sarcoidosis or tuberculosis and does not help in their differentiation.</td>
<td></td>
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<tr>
<td>Disease activity assessment</td>
<td></td>
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<tr>
<td>Assessment of site of biopsy</td>
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Objective 1
To review the definitive and indeterminate imaging features of thoracic sarcoidosis.
Siltzbach Stage 1. Plain radiograph showing enlarged bilaterally symmetric hilar and right paratracheal lymphadenopathy (arrow) (most typical pattern of sarcoidosis)

Stage 2. Plain radiograph showing hilar lymphadenopathy (red arrow) and pulmonary parenchymal nodules (blue arrow)
Typical radiographic staging patterns of sarcoidosis

Stage 3. CT topogram showing multiple nodules (arrow) in bilateral lung fields without significant hilar lymphadenopathy

Stage 4. CT topogram showing bilateral upper zones fibrotic changes (arrows)
Typical distribution and pattern of lymphadenopathy in sarcoidosis:
“Homogenous, non-necrotic, enlarged nodes”

- Bilateral hilar nodes
- Right paratracheal nodes
- Bronchopulmonary nodes
- Amorphous/“Icing sugar” pattern of calcification in nodes
Typical lung involvement in sarcoidosis
“Discrete, sharply defined, rounded micronodules”

Red arrow - Along peribronchovascular interstitium
Blue arrow - Subpleural nodules

Red arrow - Along interlobular septa
Blue arrow - Along fissures
Typical lung involvement in sarcoidosis
“Bilateral perihilar opacities”

Bilateral symmetric parahilar conglomerate masses representing peribronchovascular fibrous tissue
Atypical nodal involvement in sarcoidosis “Unilateral, isolated, anterior or posterior mediastinal”

Isolated subcarinal lymph node

Unilateral left hilar lymph nodes
Atypical lung involvement in sarcoidosis

Cluster sign - Micronodules in focal, rounded clusters

Multiple bilateral irregular macronodules representing coalescence of granulomas (arrow).
Atypical lung involvement in sarcoidosis

Miliary nodules: Innumerable tiny micronodules in a random distribution
Atypical lung involvement in sarcoidosis

Sarcoid galaxy sign.

Asymmetric parahilar mass

Alveolar sarcoid pattern
Atypical lung involvement in sarcoidosis

- Ground glass opacities
- Interlobular septal thickening
- Aspergilloma in fibrotic region
Airway and pleural involvement - Atypical in sarcoidosis

Airway involvement:
- Endobronchial nodules

Pleural involvement:
- Thickening and effusion
Imaging features which suggest definite TB

- Conglomerated necrotic lymph nodes
- Centrilobular nodules in tree-in-bud pattern (red arrow)
- Cavitatory lesion in upper lobe (blue arrow)
- Empyema
Indeterminate imaging features

- Lymph nodes in AP Window, prevascular locations.
- Centrally hypodense lymph nodes
- Centrilobular nodules
- Peripheral consolidation in background of perilymphatic nodules
A 24-year-old female presented with non-specific fever and breathlessness. CECT chest (A,B) showed discrete homogeneous mediastinal lymph nodes in characteristic right paratracheal and hilar location, no parenchymal abnormality—radiologically consistent with sarcoidosis and was started on steroids.

Three months later, she developed large parenchymal consolidation in right upper lobe with air bronchogram and cavitation. Sputum *acid fast bacilli* was now positive. Subsequently, anti-tubercular therapy was started.
Tuberculosis or Sarcoidosis or concurrent Tuberculosis and Sarcoidosis ??

41 yr old man with nonspecific cough and chest pain. CECT demonstrates homogenous mediatsinal lymph nodes (A) and perbronchovascular thickening and nodules (C). In addition, right sided pleural effusion and thickening of visceral and parietal pleura suggesting empyema is noted (b), raising a suspicion of concurrent tuberculosis.

Multiple times pleural biopsy revealed non-necrotising epitheloid cell granulomas - suggesting pleural involvement by sarcoidosis.
Objective 2
Summarizing the differentiating and overlapping imaging features of thoracic sarcoidosis and tuberculosis.
## Differentiating and overlapping CT features of thoracic sarcoidosis and TB

<table>
<thead>
<tr>
<th>Highly suggestive for active TB</th>
<th>Highly suggestive for active sarcoidosis</th>
<th>Nonspecific/overlapping features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air-space nodules/centrilobular nodules (especially tree-in-bud nodules)/clustered nodules especially in bilateral upper lobes, right middle lobe, lingula, superior segment any lower lobe</td>
<td>Perilymphatic distribution of micronodules (in subpleural/peribronchovascular / along interlobular septa) in bilateral upper, right middle and lingular lobes</td>
<td>Consolidation/centrilobular nodules in other non-specific lung segments.</td>
</tr>
<tr>
<td>Consolidation in above mentioned regions with ipsilateral LN enlargement</td>
<td>Peribronchovascular ill-defined consolidation in upper and middle lobes bilaterally</td>
<td>Ground glass opacities</td>
</tr>
<tr>
<td>Miliary nodules</td>
<td>Multiple and bilateral coalescent interstitial nodules</td>
<td>Septal thickening/ linear opacities</td>
</tr>
<tr>
<td>Highly suggestive for active TB</td>
<td>Highly suggestive for active sarcoidosis</td>
<td>Nonspecific/overlapping features</td>
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<tr>
<td>Thick-walled cavity</td>
<td>-</td>
<td>Bilateral upper lobe fibrotic opacities with cavitation</td>
</tr>
<tr>
<td>Cavity with surrounding consolidation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enlarged mediastinal lymph nodes showing peripheral rim enhancement (due to central necrosis) or heterogeneous enhancement</td>
<td>Enlarged bilateral hilar and right paratracheal lymph nodes. Well-defined, discrete, homogenous, non-coalescent lymph nodes.</td>
<td>Borderline enlarged discrete lymph nodes with homogeneous enhancement or preserved perinodal fat. Involvement of left paratracheal, subcarinal, aortopulmonary window and prevascular region lymph nodes.</td>
</tr>
<tr>
<td>Conglomeration of lymph nodes or obscuration of perinodal fat</td>
<td>Enlarged bilateral hilar and right paratracheal lymph nodes. Well-defined, discrete, homogenous, non-coalescent lymph nodes.</td>
<td>Borderline enlarged discrete lymph nodes with homogeneous enhancement or preserved perinodal fat. Involvement of left paratracheal, subcarinal, aortopulmonary window and prevascular region lymph nodes.</td>
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<tr>
<td>Effusion/empyema with split pleura sign</td>
<td>Enlarged bilateral hilar and right paratracheal lymph nodes. Well-defined, discrete, homogenous, non-coalescent lymph nodes.</td>
<td>Borderline enlarged discrete lymph nodes with homogeneous enhancement or preserved perinodal fat. Involvement of left paratracheal, subcarinal, aortopulmonary window and prevascular region lymph nodes.</td>
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Differentiating and overlapping CT features of thoracic sarcoidosis and TB, contd..
Objective 3
Propose an imaging algorithm for evaluation of patients with non-specific/overlapping clinical features of sarcoidosis and tuberculosis in TB endemic areas
Suggested algorithm for suspected case of sarcoidosis in TB endemic areas

Clinically Suspected case of sarcoidosis (in tuberculosis endemic areas)

CXR- PA

HS for active TB

* Sputum positive

Sputum negative

HS for active Sarcoïdosis

NS

Alternate diagnosis

Workup accordingly

CECT chest

HS for active TB

Supportive lab parameters:
- Elevated serum ACE
- Hypercalcemia
- Hypercalciuria

# Supportive laboratory parameters:
- TST negative

Overlapping CT features

Alternate diagnosis

Sputum/TST positive

Suspect concurrent TB + Sarcoïdosis

Histopathologic confirmation of noncaseating granulomas
Suggested readings


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