Decision to treat sarcoidosis

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It's all about the granuloma...
The 2 big questions regarding treatment...

- When?
- How?

When?

- When do we need to treat.
- What is natural course of disease.
- What influences the decision for the need to start treatment?
How?

• How do we treat?
  – What’s our armamentarium?
  – Algorithm for treatment.
  – How do we follow and see response of treatment?

Why is decision to treat so complex?

• Natural course of disease.
• Clinical presentation varies and so is the outcome.
Natural course of disease

• Normally 2/3rd of sarcoidosis resolve within 2 years of diagnosis.
• Scadding staging system 1 – 90% resolve in 2 years
• Scadding staging 3 – 10 to 30% resolve in 2 years

Course of disease

• Spontaneous regression
• Persistence of lesion
• Improvement with treatment
• Relapse/Recurrence
• Progression of disease
Course of Pulmonary disease

Factors associated with worse prognosis

- Age > 40 at onset of disease
- African American race
- Requirement of steroid
- Extra Pulmonary Involvement
  - Cardiac
  - Nervous system except Cranial nerve palsy
  - Lupus pernio
  - Hypercalcemia
  - Osseous disease
- Pulmonary Involvement
  - Stage 3-4 disease
  - Pulmonary hypertension
  - Significant lung function impairment
  - Moderate to severe dyspnea on presentation
  - Bronchoalveolar lavage showing neutrophilia
Decision to treat

• Influenced by
  – Natural course of disease
  – Symptoms of disease? (Mild vs Severe)
  – Duration of disease? (Acute vs Chronic)
  – Organs involved?
    • Isolated Pulmonary vs Pulmonary + Extra Pulmonary
  – Factors associated with worse prognosis at diagnosis?
  – Risks of therapy?

How?

• How do we treat?
  – What’s our armamentarium
  – Algorithm for treatment
  – How do we follow and see response of treatment
## Level of evidence for treatment

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level A</td>
<td>At least one double-blind, placebo-controlled trial with positive results and one or more case series supporting the results.</td>
<td>At least one double-blind, placebo-controlled trial with positive results and one or more case series supporting the results.</td>
</tr>
<tr>
<td>Level B</td>
<td>Majority of the case series showing positive results.</td>
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</tr>
<tr>
<td>Level C</td>
<td>Case series with mixed reports or effectiveness for only a small number of case reports.</td>
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</tr>
</tbody>
</table>

- **1A**
- **1B**
- **1C**
- **2A**
- **2B**
- **2C**

Adapted from Guyatt G. Grading strength of recommendations and quality of evidence in clinical guidelines: report from an American college of chest physicians task force. 2006.

### Table: Medications and Indications

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indications/Level of evidence</th>
<th>Dosage</th>
<th>Common Side Effects</th>
<th>Serious Side Effects</th>
<th>Specific Monitoring</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Celecoxib</td>
<td>Chronic/IA, Refractory/IA</td>
<td>400mg/7A</td>
<td>Weight gain, Diarrhea, Headache</td>
<td>Nephrotoxicity</td>
<td>Blood pressure</td>
<td>More than 6 months of use should be added to reduce risk of cardiovascular events.</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Chronic/IA, Refractory/IA</td>
<td>5-15mg weekly</td>
<td>Nausea, Diarrhea, Fatigue</td>
<td>Leukopenia, Hepatitis, Myelosuppression</td>
<td>CBC, LFT</td>
<td>More than 6 months of use should be added to reduce risk of cardiovascular events.</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>Chronic/IA, Refractory/IA</td>
<td>10-20mg/day</td>
<td>Fatigue, Diarrhea, Ocular changes</td>
<td>Hepatitis, Neurotoxicity</td>
<td>CBC, LFT, LFT at baseline every 2-3 months and every 8-12 weeks</td>
<td>Higher incidence of liver toxicity when combined with methotrexate. Can give Cholestyramine washout to reduce toxicity.</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>Chronic/ID, Refractory/B</td>
<td>2-4mg/kg</td>
<td>Nausea, Diarrhea, Myelosuppression</td>
<td>Leukopenia, Myelosuppression, Hepatic veno-occlusive disease</td>
<td>CBC, LFT</td>
<td>LFT (every 1-3 months)</td>
</tr>
<tr>
<td>Mycophenolate</td>
<td>Chronic/IN, Refractory/IC</td>
<td>5-1000mg/daily</td>
<td>Nausea, Diarrhea</td>
<td>Leukopenia, Infections</td>
<td>CBC, LFT</td>
<td>Frequency less before starting. Double contraceptive.</td>
</tr>
<tr>
<td>Infliximab</td>
<td>Chronic/IA, Refractory/A</td>
<td>3mg/kg, every 2 weeks for 4 weeks then every 8-12 weeks</td>
<td>Anorexia, Vomiting</td>
<td>Lymphopenia, Infections</td>
<td>CBC, LFT</td>
<td>Frequency less before starting. Double contraceptive.</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>Chronic/IN, Refractory/AC</td>
<td>150mg loading, 80 mg/week</td>
<td>Anorexia, Vomiting</td>
<td>Lymphopenia</td>
<td>CBC, LFT</td>
<td>Frequency less before starting. Double contraceptive.</td>
</tr>
</tbody>
</table>
Treat the Penumbra...

Algorithmic approach for treatment
Factors associated with improved response to Anti TNF therapy

- Lower vital capacity
- Shortness of breath
- Longer duration of disease
- Refractory extra pulmonary disease
  - Lupus pernio
  - Neuro sarcoidosis
- Higher CRP
Follow up of treatment...

- Clinical symptoms
- Radiology– Chest X–ray, CT scan
- Lung Function

Reasons for Failing Therapy

- Non compliance
- Advanced disease at presentation
- Extra Pulmonary Involvement
  - Cardiac
  - Nervous system
- Infection
- Pulmonary hypertension
Organ specific treatment

- Cardiac Sarcoidosis: Pacemaker, Anti-arrhythmic drug, Heart failure drugs
- Advanced Pulmonary disease
  - Respiratory failure: Oxygen therapy, Pulmonary rehabilitation
  - Pulmonary HTN: Anti-PAH drugs
  - Lung transplantation