Eosinophilic lung diseases

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The eyes do not see what the mind does not know

Not very common

A high index of suspicion is required
Introduction

• Increased eosinophils in one or more compartments of the lung – airway, pleural, parenchyma.

• Lung involvement + peripheral eosinophilia = Eosinophilic lung disease?

• Eosinophilic lung diseases may not always have peripheral eosinophilia.

• Not all patients with peripheral eosinophilia has eosinophilic lung disease.
The obligatory classification slide

• Eosinophilic (Eos) lung disease of undetermined cause
  • Lung limited: acute eos pneumonia, chronic eos pneumonia
  • Systemic: Eos granulomatosis with polyangiitis (formerly Churg-Strauss syndrome), hypereosinophilic syndrome

• Eosinophilic lung disease of determined cause (secondary causes)
  • Parasites
  • Allergic bronchopulmonary aspergillosis (ABPA)
  • Drugs and toxins
  • Others: malignancy, asthma, idiopathic interstitial pneumonia (IPF, chronic HP, Cryptogenic organizing pneumonia)
Hence history should include

• Symptoms: Acute/subacute/chronic
• Occupation/environmental exposures
• Drugs
• Travel history
• Infectious symptoms
• History of asthma
• Systemic symptoms
Investigations

• Directed by history

• May include, but not limited to:
  • Lung function tests
  • ANCA
  • Serum IgE levels
  • Stool for ova cyst parasites
  • Bronchoscopy and bronchoalveolar lavage

• May need ID, hematology or rheumatology consult
My approach
Peripheral eosinophilia

1. If it is persistently elevated, evaluate for the causes of eosinophilia – long list of causes
2. Is there pulmonary involvement?
3. Are lungs the only organ involved? Or part of a systemic disease?
4. Evaluate for secondary causes of pulmonary eosinophilia
5. Primary causes – diagnosis of exclusion
Other causes of peripheral eosinophilia

- Allergies – food, drug, environment
- Worms and other infectious disease
- Malignancy especially hematological malignancy
- Other organ involvement can also cause peripheral eosinophilia eg GI, renal, dermatology etc.
Case 1
Case 1

- 45 year old Indian male
- Cough x 3/52 with fever for 1/52
- Symptoms not better after a course of clarithromycin
- Recently returned from India
- Referred from ED to TBCU for possible PTB
Progress

• Following tests were ordered:
  • Sputum AFB smears
  • Mantoux test
• Another course of antibiotics
• Review in 1/52

• Then we received a call from Dr Cynthia Chee
How come you did not see the eosinophil counts done in ED?

<table>
<thead>
<tr>
<th>Full Blood Count</th>
<th></th>
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<tbody>
<tr>
<td>White Blood Cell</td>
<td>12.2</td>
<td>H</td>
<td>x10 9/L</td>
</tr>
<tr>
<td>Red Blood Cells</td>
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<td>Haemoglobin</td>
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<td>g/dL</td>
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<tr>
<td>MCV</td>
<td>86</td>
<td>N</td>
<td>fl</td>
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<td>MCH</td>
<td>30</td>
<td>N</td>
<td>pg</td>
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<tr>
<td>MCHC</td>
<td>35</td>
<td>H</td>
<td>g/dL</td>
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<td>Haematocrit</td>
<td>41.1</td>
<td>N</td>
<td>%</td>
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<tr>
<td>Platelets</td>
<td>293</td>
<td>N</td>
<td>x10 9/L</td>
</tr>
<tr>
<td>MPV</td>
<td>8.6</td>
<td>N</td>
<td>fl</td>
</tr>
<tr>
<td>RDW</td>
<td>13.1</td>
<td>N</td>
<td>%</td>
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<tr>
<td>Differential Counts</td>
<td></td>
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<tr>
<td>Neutrophils %</td>
<td>50.5</td>
<td>%</td>
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<td>Neutrophils</td>
<td>6.16</td>
<td>H</td>
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<td>Lymphocytes %</td>
<td>17.4</td>
<td>%</td>
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<td>Lymphocytes</td>
<td>2.13</td>
<td>N</td>
<td>x10 9/L</td>
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<tr>
<td>Monocytes %</td>
<td>8.2</td>
<td>%</td>
<td></td>
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<tr>
<td>Monocytes</td>
<td>1.09</td>
<td>H</td>
<td>x10 9/L</td>
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<tr>
<td><strong>Eosinophils %</strong></td>
<td><strong>23.7</strong></td>
<td>%</td>
<td></td>
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<tr>
<td><strong>Eosinophils</strong></td>
<td><strong>2.89</strong></td>
<td>H</td>
<td>x10 9/L</td>
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<tr>
<td>Basophils %</td>
<td>0.2</td>
<td>%</td>
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</tr>
<tr>
<td>Basophils</td>
<td>0.02</td>
<td>N</td>
<td>x10 9/L</td>
</tr>
</tbody>
</table>
Progress

• Treated as tropical pulmonary eosinophilia
• Diethylcarbamazine x 2/52

• Not surprisingly AFB cultures were negative
Tropical pulmonary eosinophilia

- Associated with mosquito-borne filarial parasites Wuchereria bancrofti and Brugia malayi.
- Endemic in Indian subcontinent, SEA, S America, Africa, S Pacific islands.
- Immune hyper-responsiveness to microfilariae trapped in the lungs.
- Midnight blood film to “catch” the microfilariae in blood.
- Serologies
- Treatment: Diethylcarbamazine for 2 to 3 weeks
- 20% may relapse
Simple pulmonary eosinophilia (Löffler syndrome)

- Usually more acute
- Transient, mild self limited hypersensitivity response to parasites migrating through the lungs.
- Migratory pulmonary infiltrates
- Ascaris lumbricoides, Strongyloides stercoralis etc
- Treatment: Mebendazole
Case 2
Case 2

• 54 year old Indian male
• Previous history of PTB in 2003 complicated by bronchiectasis
• Worsening cough, greenish sputum, dyspnoea over 6 months
• On and off fever
Differential diagnosis of “fleeting” or “migratory” pulmonary infiltrates on CXR

- Aspiration pneumonia
- Drug induced lung injury
- Cryptogenic organizing pneumonia
- Simple pulmonary eosinophilia
- Chronic eosinophilic pneumonia
- Allergic bronchopulmonary aspergillosis
<table>
<thead>
<tr>
<th>Test Name</th>
<th>UoM</th>
<th>16-Dec-2009 13:19</th>
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</thead>
<tbody>
<tr>
<td>Eosinophils (EOS)</td>
<td>x10 9/L</td>
<td>1.2</td>
</tr>
<tr>
<td>Eosinophils % (EOSP)</td>
<td>%</td>
<td>20.5</td>
</tr>
<tr>
<td>Haemoglobin (HB)</td>
<td>g/dL</td>
<td>14.6</td>
</tr>
<tr>
<td>Platelets (PLT)</td>
<td>x10 9/L</td>
<td>196</td>
</tr>
<tr>
<td>White Blood Cell (WBC)</td>
<td>x10 9/L</td>
<td>5.9</td>
</tr>
</tbody>
</table>
Proximal bronchiectasis
Mucus plugging
Tree in bud opacities
Peribronchial thickening
Progress

• Broncho-alveolar lavage
  • Bacterial, AFB cultures NEG
  • Fungal culture: Aspergillus flavus

• Total IgE > 1000
• Aspergillus antibody NEG
Started on Prednisolone and Itraconazole

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</thead>
<tbody>
<tr>
<td>Eosinophils (EOS)</td>
<td>x10 9/L</td>
<td>1.2</td>
<td>1.06</td>
<td>0.9</td>
<td>0.28</td>
<td>0.36</td>
<td>0.21</td>
<td>0.17</td>
<td>0.15</td>
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<tr>
<td>Eosinophils % (EOSP)</td>
<td>%</td>
<td>20.5</td>
<td>12.7</td>
<td>11.6</td>
<td>3.1</td>
<td>4.3</td>
<td>2.4</td>
<td>2.8</td>
<td>2.7</td>
</tr>
<tr>
<td>Haemoglobin (HB)</td>
<td>g/dL</td>
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<td>14.7</td>
<td>14.2</td>
<td>14.2</td>
<td>13.2</td>
<td>15</td>
<td>13.6</td>
<td>14.1</td>
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<tr>
<td>Platelets (PLT)</td>
<td>x10 9/L</td>
<td>196</td>
<td>202</td>
<td>221</td>
<td>199</td>
<td>218</td>
<td>241</td>
<td>160</td>
<td>168</td>
</tr>
<tr>
<td>White Blood Cell (WBC)</td>
<td>x10 9/L</td>
<td>5.9</td>
<td>8.4</td>
<td>7.8</td>
<td>9</td>
<td>8.5</td>
<td>8.6</td>
<td>6</td>
<td>5.7</td>
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</table>
Allergic bronchopulmonary aspergillosis (ABPA)

**International Society for Human and Animal Mycology (ISHAM) working group diagnostic criteria for allergic bronchopulmonary aspergillosis**

<table>
<thead>
<tr>
<th>Predisposing conditions (one must be present):</th>
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<tbody>
<tr>
<td>Asthma</td>
</tr>
<tr>
<td>Cystic fibrosis</td>
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</table>

<table>
<thead>
<tr>
<th>Obligatory criteria (both must be present):</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Aspergillus</em> skin test positivity or elevated IgE levels against <em>Aspergillus fumigatus</em></td>
</tr>
<tr>
<td>Elevated total IgE concentration (typically &gt;1000 IU/mL, but if the patient meets all other criteria, an IgE value &lt;1000 IU/mL may be acceptable)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other criteria (at least two must be present):</th>
</tr>
</thead>
<tbody>
<tr>
<td>Precipitating serum antibodies to <em>A. fumigatus</em> or elevated serum <em>Aspergillus</em> IgG by immunoassay</td>
</tr>
<tr>
<td>Radiographic pulmonary opacities consistent with ABPA</td>
</tr>
<tr>
<td>Total eosinophil count &gt;500 cells/μL in glucocorticoid-naive patients (may be historical)</td>
</tr>
</tbody>
</table>
ABPA

- Not very common:
  - Only complicates 1-2% of asthmatics and 2-15% with cystic fibrosis (CF)
  - Rarely it can happen in patients without asthma or CF
- Abnormal host response to fungus
- Consider in poorly controlled asthma
- Treatment: steroids ± itraconazole
Case 3
Case 3

• 72 year old Chinese man
• Admitted for non-resolving pneumonia – persistent lung infiltrates despite multiple courses of antibiotics
• Ex smoker
• Had been taking TCM
• Rhonchi heard on physical exam
Investigations

• CRP 19.4
• Sputum AFB smear x 2 NEG
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</thead>
<tbody>
<tr>
<td>Eosinophils (EOS)</td>
<td>x10 9/L</td>
<td>2.18</td>
<td>1.48</td>
<td>1.07</td>
<td>2.21</td>
<td>2.18</td>
<td>1.48</td>
<td>1.44</td>
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<tr>
<td>Eosinophils % (EOSP)</td>
<td>%</td>
<td>25.0</td>
<td>19.2</td>
<td>10.4</td>
<td>25.5</td>
<td>26.9</td>
<td>9.3</td>
<td>10.2</td>
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<tr>
<td>Haemoglobin (HB)</td>
<td>g/dL</td>
<td>12.0</td>
<td>13.5</td>
<td>12.2</td>
<td>12.8</td>
<td>13.1</td>
<td>13.3</td>
<td>13.3</td>
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<tr>
<td>Platelets (PLT)</td>
<td>x10 9/L</td>
<td>212</td>
<td>244</td>
<td>194</td>
<td>195</td>
<td>201</td>
<td>229</td>
<td>221</td>
</tr>
<tr>
<td>White Blood Cell (WBC)</td>
<td>x10 9/L</td>
<td>8.7</td>
<td>7.7</td>
<td>10.3</td>
<td>8.6</td>
<td>8.1</td>
<td>15.9</td>
<td>14.1</td>
</tr>
</tbody>
</table>
Previously noted infective/inflammatory changes of both lungs shows interval improvement. New ground-glass opacities in both lung apices, right middle lobe and left lingular segment.
Further investigations

- Stool ova cyst parasites: NEG
- ANCA NEG
- BAL ova cyst parasites NEG
Diagnosis:
Chronic eosinophilic pneumonia
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<td>2.21</td>
<td>2.18</td>
<td>1.48</td>
<td>1.44</td>
<td>0.08</td>
<td>0.14</td>
<td>0.00</td>
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<tr>
<td>Eosinophils % (EOSP)</td>
<td>%</td>
<td>10.4</td>
<td>25.5</td>
<td>26.9</td>
<td>9.3</td>
<td>10.2</td>
<td>0.9</td>
<td>3.1</td>
<td>0.0</td>
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<tr>
<td>Haemoglobin (HB)</td>
<td>g/dL</td>
<td>12.2</td>
<td>12.8</td>
<td>13.1</td>
<td>13.3</td>
<td>13.3</td>
<td>12.1</td>
<td>12.0</td>
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<td>194</td>
<td>195</td>
<td>201</td>
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<td>208</td>
<td>212</td>
<td>232</td>
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<tr>
<td>White Blood Cell (WBC)</td>
<td>x10 9/L</td>
<td>10.3</td>
<td>8.6</td>
<td>8.1</td>
<td>15.9</td>
<td>14.1</td>
<td>8.7</td>
<td>4.4</td>
<td>8.4</td>
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</tbody>
</table>
Chronic eosinophilic pneumonia

- Chronic onset dyspnoea, cough, wheeze
- < 10% has no peripheral eosinophilia
- BAL eosinophilia
- Treatment: Corticosteroids – taper over 6 to 12 months
- Relapse up to 50%
The classical photographic negative of pulmonary oedema

Only seen in <25% of the cases
Acute eosinophilic pneumonia

- Presentation similar to ARDS, severe community acquired pneumonia or acute interstitial pneumonia
- Smokers
- 2/3 need mechanical ventilation
- Peripheral blood eosinophilia not prominent
- BAL eosinophilia
- High dose steroids with rapid improvement
Case 4
Case 4

- 71 year old Chinese man
- Non smoker
- History of stiff person syndrome on long term prednisolone
- Cough for 2 weeks, fever, hemoptysis, hypotensive, hypoxic.
In this instance, there is no eosinophilia
DESpite IV PIP/TAZO + VANCOMYCIN
Progress

• Patient was deemed too sick for bronchoscopy and BAL (on 50% ventimask)
• Bacterial cultures, AFB smears, PCP from induced sputum were all negative

<table>
<thead>
<tr>
<th>Test Name</th>
<th>UoM</th>
<th>08-Dec</th>
<th>11-Dec</th>
<th>12-Dec</th>
<th>13-Dec</th>
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<th>15-Dec</th>
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<td>Albumin</td>
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<td>25</td>
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<td>29</td>
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<tr>
<td>AST</td>
<td>U/L</td>
<td>48</td>
<td>20</td>
<td></td>
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<td>Brain Natriuretic Pt</td>
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<td>C-Reactive Protein</td>
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<td>4.9</td>
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<td>Creatinine</td>
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<td>53</td>
<td>65</td>
<td>53</td>
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<td>0.01</td>
<td>0.01</td>
<td>0.18</td>
<td>0.10</td>
<td>0.07</td>
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<tr>
<td>Eosinophils %</td>
<td>%</td>
<td>2.5</td>
<td>0.2</td>
<td>0.1</td>
<td>2.3</td>
<td>1.3</td>
<td>0.8</td>
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<tr>
<td>Haemoglobin</td>
<td>g/dL</td>
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<td>10.4</td>
<td>9.9</td>
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<td>9.7</td>
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<td>163</td>
<td>162</td>
<td>156</td>
<td>165</td>
<td>179</td>
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<td>Procalcitonin</td>
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<td>0.11</td>
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<tr>
<td>White Blood Cell</td>
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<td>20.0</td>
<td>7.6</td>
<td>6.3</td>
<td>7.9</td>
<td>7.6</td>
<td>8.7</td>
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</table>
Then this happened

- An astute microbiology lab technician saw larvae on the sputum gram stain.

<table>
<thead>
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<th>MICROBIOLOGY</th>
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<tr>
<td>Ova, cyst parasite</td>
<td></td>
</tr>
<tr>
<td>Sample Origin</td>
<td>Sputum, Induced</td>
</tr>
<tr>
<td>Request status</td>
<td>Completed</td>
</tr>
<tr>
<td>Visual Aspect</td>
<td>.</td>
</tr>
<tr>
<td>S. stercoralis larva</td>
<td>seen</td>
</tr>
</tbody>
</table>
• Bronchoalveolar lavage done one week later when patient improved:
  • Cell counts – unable to perform
  • Strongyloides not seen in BAL
  • Bacterial cultures: **E Coli**
  • PCP NEG
  • AFB cultures NEG
  • Fungal cultures yeast 1+
Progress

- Covered with Ivermectin and albendazole
- Iv ceftriaxone for E Coli
CXR 6 months post discharge
Strongyloides hyperinfection

• Immunocompromised host
• Heavy hematogenous seeding to various organs including lungs, liver, heart, CNS.
• 30-45%: Gram negative septicemia from GI source
• High mortality
• Optimal treatment duration uncertain – determined by clinical response
None of the patients had peripheral eosinophilia.

Could be due to long term immunosuppression or gram negative septicemia

In summary

• Know the causes of peripheral eosinophilia

• Eosinophilic lung disease can occur with or without systemic involvement

• If there is eos + lung involvement: evaluate for secondary causes first

• Some cases of eosinophilic lung disease do not have peripheral eosinophilia:
  • Strongyloides hyperinfection
  • Acute eosinophilic pneumonia
  • Chronic eosinophilic pneumonia (<10% of patients)

• Don’t forget the other causes: malignancy, asthma, idiopathic interstitial pneumonia (IPF, chronic HP, Cryptogenic organizing pneumonia)
Thank you

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