Eosinophilic Granulomatosis with Polyangiitis (Churg-Strauss syndrome)

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EGPA (Churg-Strauss)

- An inflammatory disease affecting multiple organ systems and characterized by:
  - **Vasculitis** of small vessels
  - **Eosinophils** in blood and inflamed tissues
  - Almost all patients also have **asthma**, which is a disease in which eosinophilic inflammation in the airways in common
White Blood Cells in Vasculitis

- Macrophage
- Eosinophil
- Neutrophil
- T cell
- B cell
- Immune Complexes
White Blood Cells in EGPA

- Neutrophil
- Eosinophil
- T cell
- B cell

- IL-5
- ANCA
- 40%

6/30/17
The Two Sides of EGPA

- Eosinophilic:
  - Nose / sinus
  - Heart
  - Lung (no DAH)

- Vasculitic:
  - Kidney
  - Lung (DAH)
  - GI
  - Skin
  - Nerve
# Organ Systems in GPA, MPA, EGPA

<table>
<thead>
<tr>
<th></th>
<th>GPA</th>
<th>MPA</th>
<th>EGPA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ENT</strong></td>
<td>83-99</td>
<td>1-20</td>
<td>48-77</td>
</tr>
<tr>
<td>Joint/Muscle</td>
<td>59-77</td>
<td>14-54+</td>
<td>30-39+</td>
</tr>
<tr>
<td><strong>Kidney</strong></td>
<td>66-77</td>
<td>69-100</td>
<td>22-27</td>
</tr>
<tr>
<td><strong>Lung</strong></td>
<td>66-85</td>
<td>25-55</td>
<td>51-58</td>
</tr>
<tr>
<td><strong>Eye</strong></td>
<td>34-61</td>
<td>1-15</td>
<td>7</td>
</tr>
<tr>
<td><strong>Heart</strong></td>
<td>8-25</td>
<td>3-24</td>
<td>16-27</td>
</tr>
<tr>
<td><strong>Skin</strong></td>
<td>33-46</td>
<td>11-62</td>
<td>40-57</td>
</tr>
<tr>
<td><strong>Nerve</strong></td>
<td>15-40</td>
<td>13-60</td>
<td>51-76</td>
</tr>
<tr>
<td><strong>CNS</strong></td>
<td>8-11</td>
<td>5-12</td>
<td>5-14</td>
</tr>
<tr>
<td><strong>GI</strong></td>
<td>6-13</td>
<td>3-31</td>
<td>22-31</td>
</tr>
<tr>
<td>Constitutional</td>
<td>58+</td>
<td>67-84</td>
<td>49-68</td>
</tr>
</tbody>
</table>
Organ systems in EGPA - 1

• **ENT**
  – Eosinophilic infiltrate, non-destructive
    • Nasal polyps, chronic sinusitis

• **Eye**
  – Rare
Organ systems in AAV - 2

• Lung
  – Transient “infiltrates” on X-ray or CT
    • Eosinophilic pneumonia
  – Everyone has asthma also (by definition, has no infiltrate)
  – Hemorrhage rare

• Kidney
  – Much less common in EGPA than MPA or GPA
    • Almost exclusively in ANCA-positive patients
Organ systems in AAV - 3

• **Skin**
  - “Leukocytoclastic vasculitis”, or
    • Necrotizing nodules with prominent eosinophils on biopsy

• **Peripheral nerve**
  - EGPA > MPA, GPA
    • Sensory neuropathy with or without motor neuropathy
    • Numbness, tingling, pain, with or without weakness
    • More common in ANCA-positive patients, but more common in EGPA than MPA: maybe an additional toxicity from eosinophils?
GPA or EGPA: 
“Churg-Strauss granuloma”
Organ systems in AAV - 4

• **Heart**
  - Eosinophilic myocarditis >> vasculitis

• **GI**
  - Eosinophilic infiltrative GI disease > vasculitis

• **CNS**
  - Uncommon, pathology unclear, probably vasculitis rather than eosinophilic infiltration
Organ systems in AAV - 5

• **Musculoskeletal**
  – “Arthralgia” > objective arthritis, in GPA, MPA, EGPA
    • One, a few, or many joints
  – Myalgia = muscle pain
    • Vasculitis of muscle in unknown percentage of cases

• **Constitutional**
  – Fatigue / malaise very common
  – Fever less common
Diagnosing EGPA

• **Distinguishing EGPA from “asthma+sinonasal”**
  – Degree of eosinophilia (>800, often much higher)
  – Eosinophilic inflammation in lung, heart, GI, other organs (biopsy)
  – Doesn’t distinguish EGPA from hypereosinophilic syndromes (HES)

• **Distinguishing EGPA from HES**
  – Vasculitis
    • Biopsy proven vasculitis - anywhere
    • Correlates of vasculitis: neuropathy, digit ischemia (blue finger/toe)
  – ANCA-positive (usually MPO)
  – Arthritis, myalgia, or prior history of asthma favors EGPA
White Blood Cells in Vasculitis: implications for treatment
White Blood Cells in EGPA: implications for treatment

Eosinophil
- ANCA

Neutrophil
- 40%

IL-5

Mepolizumab

Rituximab

T cell

B cell
Treatment – remission induction

• **Severe disease**
  – Heart, kidney, alveolar hemorrhage, and possibly GI or neuropathy
  – High-dose corticosteroids plus cyclophosphamide

• **Limited / mild disease**
  – Lung, nose/sinus, lung nodules, skin, musculoskeletal, constitutional
  – Moderate / high corticosteroids but may taper more quickly
  – With or without azathioprine or methotrexate
Treatment – remission maintenance

• **Relapse risk**
  – < 50% for vasculitis or severe eosinophilic disease
  – Very high for asthma and nasal/sinus

• **Steroid-sparing in patients who require treatment for chronic inflammation**
  – Very common for asthma / sinonasal symptoms in patients with EGPA
  – Methotrexate, azathioprine, mycophenolate, leflunomide...
  – Mepolizumab (Nucala) may be a new option
  – Rituximab may be an option especially for ANCA-positive patients
Common approaches to a first episode of EGPA

Severe

- Prednisone
- Cyclophosphamide
- Azathioprine or Methotrexate

Non-severe

- Prednisone
- Azathioprine or Methotrexate
- Azathioprine or Methotrexate (if needed for steroid sparing)
Corticosteroid Dosing

• **Severe disease**
  – 1000 mg IV methylprednisolone (Solumedrol) x 1-3
  – Prednisone start 60 mg or 1 mg/kg and reduce every 2 weeks
    • E.g. 60, 50, 40, 30, 20, 15, 10, 7.5, 5, 2.5, off if possible
      (my own regimen, but consistent with regimens used in trials)

• **Limited / mild disease**
  – Consider starting at 30-40 mg prednisone, then taper every 2 weeks

• **Maintenance**
  – Reasonable to reduce based on symptoms
  – Usually not adjusted just based on eosinophil count, unless count is very high and patient has had heart involvement
  – Most patients remain on a low dose of prednisone to control asthma or nasal/sinus symptoms
Monitoring

• **Patient education** is most important
  – Recurrent or new symptoms
  – Infection risk if immune-suppressed
• Be compulsive about **urinalysis** if ANCA-positive!
  – You can buy urine dipsticks on-line
• **Eosinophil counts?**
  – Not very useful once treatment is started
• **ANCA levels?**
  – Rise predicts relapse – but only modestly
  – Most data are on PR3 (Wegener’s) rather than MPO
Prognosis

• Treatment is highly successful!
  – > 90% remission or very good control of disease

• Treatment has risk of infection
  – Dose dependent, highest risk early

• Long-term problems are mostly due to irreversible damage and treatment toxicity
  – Congestive heart failure
  – Neuropathic pain
  – Side effects of prednisone
Prophylaxis

- **Pneumocystis pneumonia**
  - Bactrim (unless sulfa-allergic) if on high-dose prednisone and a second immune-suppressive drug

- **Osteoporosis**
  - Calcium and vitamin D
  - Low threshold for bisphosphonate (alendronate, etc)

- **Vaccination**
  - Usually cannot delay treatment...
  - Avoid live vaccines in highly immune-suppressed
  - No increase in risk of relapse after vaccination
  - Vaccines may not work as well – but give them anyway
Nociceptive vs. Neuropathic pain: why it matters

<table>
<thead>
<tr>
<th></th>
<th>Nociceptive (NC) component</th>
<th>Neuropathic (NP) component</th>
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<tbody>
<tr>
<td>Non-opioids (NSAIDs)</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Weak Opioids</td>
<td>+</td>
<td>O</td>
</tr>
<tr>
<td>Strong Opioids</td>
<td>+</td>
<td>O</td>
</tr>
<tr>
<td>Co-analgesics</td>
<td>O</td>
<td>+</td>
</tr>
</tbody>
</table>

+ Effective          
O Partially efficient
- No NP-mechanism-related action

Modified from Davis et al. 2007 [1]
Approaches to Pain Management

• **Pharmacologic (Medications)**
  – FDA-approved
  – Experimental, anecdotal, “alternative”

• **Non-pharmacologic**
  – Physical
  – Psychological

• “Multi-modal” or “multi-disciplinary” approach is currently recommended
Combining approaches

• Multi-modal therapy works better than single approaches...

• ... but not a lot better, no synergy

• The key message is that different approaches work (or don’t) for different people – try something and then move on if necessary
Thanks
Medications for Pain Relief
(supported by scientific evidence)

• Acetaminophen (Tylenol)
• Non-steroidal anti-inflammatory drugs (NSAIDs)
  – Ibuprofen (Motrin, Advil), naproxen (Aleve), many others
• Weak opioids
  – Tramadol
• Strong opioids
  – Oxycodone (Percocet), hydrocodone (Vicodin), morphine, hydromorphone (Dilaudid), others
• Anti-depressants and anti-convulsants
  – Gabapentin (Neurontin), pregabalin (Lyrica), duloxetine (Cymbalta), amitriptyline, nortriptyline
Anti-depressants and anti-convulsants

• Drugs of choice for neuropathic pain
• Drugs of choice for fibromyalgia
• Not helpful for nociceptive pain unless there is a central/neuropathic component due to development of chronic pain
• Still only modestly effective for most patients
• Safe, but wide range of side effects, because these drugs act in the brain....
Surveys in Painful Conditions

= FDA-approved drug for pain relief
Non-pharmacologic approaches for treating chronic pain

• Physical
  – TENS
  – Physical therapy, Chiropractic
  – Acupuncture
  – Tai chi, Yoga, Aquatic therapy, other exercise... or rest
  – Diet change

• Psychological
  – Mindfulness / meditation
  – Cognitive-behavioral therapy
  – Group therapy

• When tested scientifically, these perform about the same as medications for chronic pain
Surveys in Painful Conditions

- Non-pharmacologic approach to pain relief