Renal Vasculitis
Definition & Introduction:

- Kidney has a large number & variety of renal vessels.
- Kidneys are targets of a variety of systemic vasculitides especially of small vessels.
- Vasculitides are classified into:
  - Large-vessel vasculitis
  - Medium-sized vessel vasculitis
  - Large-vessel vasculitis
Clinical manifestations depend on the type of renal vessel affected

1. Small vessel vasculitis:
   • Affects vessels smaller than arteries (capillaries, venules & arterioles)
   • Most common target is the glomeruli ---- GN

2. Medium-vessel vasculitis:
   • Mostly affecting interlobar & arcuate arteries --- Renal infarction or hge

3. Large-vessel vasculitis:
   • Mostly affecting aorta (renal ostia) & its major branches (main renal artery) ---- RVH
Small-Vessel Pauci-Immune Vasculitis

Definition:

- Absence or paucity of immune complexe deposits in vessel walls
- Affects capillaries, venules, arterioles & small arteries:
  - Glomerular capillaries ---- GN
  - Pulmonary alveolar capillaries ---- Alveolar he
  - Dermal venules ---- Purpura
• They include:

1. Microscopic polyangiitis

2. *Granulomatosis with polyangiitis* (Wegener) (GPA) :
   Small-vessel vasculitis + necrotizing granulomatous inflammation (Respiratory tract)

3. *Eosinophilic granulomatosis with polyangiitis* (Churg-Strauss) (EGPA) :
   Small-vessel vasculitis + necrotizing granulomatous inflammation (Respiratory tract)
   Asthma & eosinophilia

4. Renal-limited vasculitis or idiopathic RPGN

• All of them can produce pauci-immune crescentic GN
Pathogenesis:
- Epidemiology:
- 5th, 6th & 7th decades
- Male ≥ Female
- Caucasions > African Americans
- Europe:
  - Microscopic polyangiitis: 2.5/100,000
  - GPA: 2.5/100,000
  - EGPA: 1/100,000
Clinical Manifestations

2. Renal (MP & GPA):
   - Proteinuria, haematuria, renal failure (RPGN).
   - May be subacute or chronic renal failure.

3. Cutaneous:
   - Purpura:
     - Lower extremities in recurrent crops
     - May be accompanied by small areas of ulceration

4. Cardiac (EGPA):
   - Transient heart block & ventricular hypokinesia
   - Infarction & life threatening myocarditis.
5. Respiratory tract (GPA& EGPA):
A. Upper (GPA):
   Subglottic stenosis, rhinitis, sinusitis, OM, ocular inflammation, septal perforation & saddle nose deformity.
B. Lower:
   • Alveolar hge
   • Nodular or cavitary lesions (GPA & EGPA)

6. Neurological (EGPA):
   • Peripheral neuropathy: mononeuritis multiplex

7. GIT:
   Abdominal pain, blood in stool, mesenteric ischemia & rarely intestinal perforation.
<table>
<thead>
<tr>
<th>Organ System</th>
<th>Microscopic Polyangiitis</th>
<th>GPA (Wegener)</th>
<th>EGPA (Churg-Strauss)</th>
<th>IgA Vasculitis (HSP)</th>
<th>Cryoglobulinemic Vasculitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney</td>
<td>90</td>
<td>80</td>
<td>45</td>
<td>50</td>
<td>55</td>
</tr>
<tr>
<td>Skin/cutaneous</td>
<td>40</td>
<td>40</td>
<td>50</td>
<td>90</td>
<td>90</td>
</tr>
<tr>
<td>Lungs</td>
<td>50</td>
<td>90</td>
<td>90</td>
<td>&lt;5</td>
<td>&lt;5</td>
</tr>
<tr>
<td>Ear, nose, throat</td>
<td>35</td>
<td>90</td>
<td>50</td>
<td>&lt;5</td>
<td>&lt;5</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>60</td>
<td>60</td>
<td>50</td>
<td>75</td>
<td>70</td>
</tr>
<tr>
<td>Neurologic</td>
<td>30</td>
<td>50</td>
<td>60</td>
<td>10</td>
<td>40</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>50</td>
<td>50</td>
<td>70</td>
<td>60</td>
<td>30</td>
</tr>
</tbody>
</table>
Antineutrophil Cytoplasmic Autoantibodies (ANCA)

- Useful diagnostic procedure for pauci-immune small-vessel vasculitis & pauci-immune crescentic GN + clinical features

Testing should include:
- Indirect immunofluorescence microscopy assay (IFA):
  - Cytoplasmic (c-ANCA)
  - Perinuclear (p-ANCA)
- Enzyme immunoassay (EIA):
  - PR3-ANCA
  - MPO-ANCA
• Good sensitive (80-90%)
• Specificity ??????
• Changes of ANCA titer correlate with disease activity
• 10 – 20% ANCA negative

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Proteinase 3 (PR3, usually c-ANCA)</th>
<th>Myeloperoxidase (MPO, usually p-ANCA)</th>
<th>Frequency (%)</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Granulomatosis with polyangiitis (Wegener)</td>
<td>70</td>
<td>25</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Microscopic polyangiitis</td>
<td>40</td>
<td>50</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Eosinophilic granulomatosis with polyangiitis (Churg-Strauss)</td>
<td>5</td>
<td>40</td>
<td>55</td>
<td></td>
</tr>
<tr>
<td>Renal-limited pauci-immune crescentic GN</td>
<td>20</td>
<td>70</td>
<td>10</td>
<td></td>
</tr>
</tbody>
</table>
• False positive results:
  ▪ SLE: IFA 25%
    EIA 5%
  ▪ Anti-GBM disease: 25 – 33%
  ▪ Idiopathic immune complex crescentic GN: 25%
  ▪ IBD
  ▪ Rheumatoid disease
  ▪ Bacterial endocarditis
  ▪ Inflammatory liver disease
  ▪ Cystic fibrosis
## Histopathological classification

<table>
<thead>
<tr>
<th>Class</th>
<th>Description</th>
<th>5 year renal survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sclerotic</td>
<td>≥50% globally sclerotic glomeruli</td>
<td>50%</td>
</tr>
<tr>
<td>Mixed</td>
<td>none of these features predominated</td>
<td>61%</td>
</tr>
<tr>
<td>Crescentic</td>
<td>≥50% of glomeruli with cellular crescents</td>
<td>76%</td>
</tr>
<tr>
<td>Focal</td>
<td>≥50% normal glomeruli</td>
<td>93%</td>
</tr>
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</table>
## Differential Diagnosis

<table>
<thead>
<tr>
<th>Features</th>
<th>Microscopic Polyangiitis</th>
<th>GPA (Wegener)</th>
<th>EGPA (Churg-Strauss)</th>
<th>IgA Vasculitis (HSP)</th>
<th>Cryoglobulinemic Vasculitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vasculitic signs and symptoms*</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>IgA-dominant immune deposits</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Cryoglobulins in blood and vessels</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>ANCA in blood</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Necrotizing granulomas</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Asthma and eosinophilia</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>
Natural History

• 5-year renal & patient survival: 65 – 75% with adequate immunosuppression

• Poor prognostic factors:
  ▪ Older age
  ▪ Pulmonary hge (↑ relapse)
  ▪ Dialysis dependent renal failure
  ▪ PR3 (c-ANCA) (↑ relapse)
  ▪ Advanced glomerulosclerosis, tubular atrophy & interstitial fibrosis
Treatment

Induction therapy

- No life-threatening or organ-threatening disease
  - Rituximab with prednisone 6 mo or cyclophosphamide IV Q mo × 3 mo, prednisone × 16 wk
    - Remission following rituximab
      - Follow patient closely to detect disease early relapse
        - Relapse
          - Rituximab ± prednisone if relapse caught early or cyclophosphamide IV monthly with prednisone for life/organ-threatening disease
    - Remission following cyclophosphamide

- Life-threatening or organ-threatening disease
  - Methylprednisolone and/or plasma exchange, cyclophosphamide IV Q mo × 3–6 mo, prednisone × 16 wk
    - Remission maintenance with azathioprine
      - Remission
        - Following 12–18 mo in remission, maintenance immunosuppression may be discontinued with close follow-up
    - Treatment resistance
      - Rituximab or oral cyclophosphamide
        - Relapse
Polyarteritis Nodosa (PAN)

- **Definition:**
  - Systemic necrotizing arteritis affecting main visceral arteries & their intraparenchymal branches
  - Only arteritis
  - GN excludes diagnosis of PAN
  - May be associated with HBV infection

- **Epidemiology:**
  - 3/100,000
  - 40 – 60 years
  - Male = Female
Clinical Manifestations

1. Constitutional: fever, myalgia, arthralgia & weight loss
2. Peripheral neuropathy; mononeuritis multiplex
3. Renal infarction or hematuria
4. Abdominal pain & blood in stool
5. Red inflammatory cutaneous nodules, infarction, ulceration & livedo reticularis
6. Arterial aneurysm may be detected; but not completely
Pathology
# Differential Diagnosis

<table>
<thead>
<tr>
<th>Clinical Feature</th>
<th>Polyarteritis Nodosa</th>
<th>Microscopic Polyangiitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microaneurysms by angiography</td>
<td>Yes</td>
<td>No (rare)</td>
</tr>
<tr>
<td>Rapidly progressive nephritis</td>
<td>No</td>
<td>Yes (very common)</td>
</tr>
<tr>
<td>Pulmonary hemorrhage</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Renovascular hypertension</td>
<td>Yes (10%-33%)</td>
<td>No</td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td>Yes (50%-80%)</td>
<td>Yes (10%-20%)</td>
</tr>
<tr>
<td>Positive hepatitis B serology</td>
<td>Uncommon</td>
<td>No</td>
</tr>
<tr>
<td>Positive ANCA</td>
<td>Rare</td>
<td>Frequent</td>
</tr>
<tr>
<td>Relapses</td>
<td>Rare</td>
<td>Frequent</td>
</tr>
</tbody>
</table>
Natural History

• 10-year survival: 80% with appropriate management
• 15% with remission develop relapse
• Poor prognostic factors:
  ▪ Age > 50 years
  ▪ Cardiac involvement
  ▪ Gut involvement
  ▪ Renal involvement
Treatment

• No risk factors for poor outcome: Steroids only

• With risk factors for poor outcome: Steroids + cytotoxic drugs (cyclophosphamide)

• With HBV infection (EULAR recommendations):
  ▪ Initial ttt with high dose steroids tapered during 2 weeks
  ▪ followed by antiviral therpay
  ▪ ± Plasma exchange
Kawasaki Disease

- **Definition:**
  - Acute febrile illness
  - Usually in young children (< 1 year)
  - With MCLN syndrome
  - Clinically significant renal affection is very rare

- **Epidemiology:**
  - First described in Japan
  - Occur worldwide
  - Japan: 50/100,000 children < 5 years
Clinical features

1. Arteritis:
   - Most often manifest as cardiac disease
   - Most common cause of childhood MI

2. MCLN syndrome:
   - Fever (38 – 40)
   - Mucosal inflammation
   - Swollen red tongue (Strawberry tongue)
   - Polymorphous erythematous rash
   - Indurative edema of the extremeties
   - Erythema of palms & soles
   - Conjunctival injection
   - Enlarged LN
Natural history

• Self limited with ttt by IVIG
• 1% develop severe coronary complications

Treatment

• Aspirin + IVIG
• Steroids may increase coronary complications
Takayasu Arteritis & Giant Cell Arteritis

- Definition:
  - Affect aorta & its major branches
  - GCA affects commonly extracranial branches of carotid artery
  - GCA is associated with polymyalgia rheumatica
  - TA affects commonly major arteries supplying the extremeties

- Epidemiology:
  - GCA: Female : Male = 4:1 >50 years
  - TA: Female : Male = 9:1 10 – 20 years
Clinical features

A. Takayasu arteritis:
• Reduced peripheral pulse
• Vascular bruit
• Claudication
• Renovascular HTN

B. Giant cell arteritis:
• Headache (most common)
• Temporal artery tenderness, nodularity & reduced pulses (50%)
• Blindness, deafness, jaw claudication, tongue dysfunction.
• Polymyalgia rheumatica (> 50%): stiffness & aching in neck & proximal muscles of the shoulders & hips
Treatment

- Corticosteroids
- Cytotoxic drugs in resistant diseases
- Low dose aspirin in GCA
- Renovascular HTN (TA):
  - Medical therapy
  - Reconstructive bypass surgery or angioplasty during quiescent phase of the disease
## Vasculitis Categories and Definitions

<table>
<thead>
<tr>
<th>Category/Name</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Large-Vessel Vasculitis</strong></td>
<td></td>
</tr>
<tr>
<td>Takayasu arteritis</td>
<td>Arteritis, often granulomatous, predominantly affecting aorta and/or its major branches. Onset usually in patients younger than 50.</td>
</tr>
<tr>
<td>Giant cell arteritis</td>
<td>Arteritis, often granulomatous, usually affecting aorta and/or its major branches, with predilection for branches of carotid and vertebral arteries; often involves temporal artery. Onset usually in patients older than 50 and often associated with polymyalgia rheumatica.</td>
</tr>
<tr>
<td><strong>Medium-Vessel Vasculitis</strong></td>
<td></td>
</tr>
<tr>
<td>Polyarteritis nodosa</td>
<td>Necrotizing arteritis of medium or small arteries without glomerulonephritis (GN) or vasculitis in arterioles, capillaries, or venules; and not associated with ANCA.</td>
</tr>
<tr>
<td>Kawasaki disease</td>
<td>Arteritis associated with mucocutaneous lymph node syndrome and predominantly affecting medium and small arteries; coronary arteries are often involved; aorta and large arteries may be involved. Usually occurs in infants and young children.</td>
</tr>
<tr>
<td><strong>Small-Vessel Vasculitis</strong></td>
<td></td>
</tr>
<tr>
<td>ANCA-Associated Small-Vessel Vasculitis</td>
<td></td>
</tr>
<tr>
<td>Microscopic polyangiitis (MPA)</td>
<td>Necrotizing vasculitis, with few or no immune deposits, predominantly affecting small vessels (capillaries, venules, arterioles, small arteries), associated with MPO-ANCA or PR3-ANCA. Not all patients have ANCA. Add prefix indicating ANCA reactivity, e.g., PR3-ANCA, MPO-ANCA, ANCA-negative.</td>
</tr>
<tr>
<td>Granulomatosis with polyangiitis (Wegener) (GPA)</td>
<td>Necrotizing granulomatous inflammation usually involving upper and lower respiratory tract, and necrotizing vasculitis affecting predominantly small to medium vessels (capillaries, venules, arterioles, arteries, veins). Necrotizing GN is common. Pulmonary capillaritis often occurs. Granulomatous inflammation is absent.</td>
</tr>
<tr>
<td>Eosinophilic granulomatosis with polyangiitis (Churg-Strauss) (EGPA)</td>
<td>Eosinophil-rich and necrotizing granulomatous inflammation often involving the respiratory tract, and necrotizing vasculitis predominantly affecting small to medium vessels, and associated with asthma and eosinophilia. ANCA is more common when GN is present.</td>
</tr>
<tr>
<td><strong>Immune Complex Small-Vessel Vasculitis</strong></td>
<td></td>
</tr>
<tr>
<td>Anti-glomerular basement membrane (anti-GBM) disease</td>
<td>Vasculitis affecting glomerular capillaries, pulmonary capillaries, or both, with basement membrane deposition of anti-basement membrane autoantibodies. Lung involvement causes pulmonary hemorrhage, and renal involvement causes GN with necrosis and crescents.</td>
</tr>
<tr>
<td>Cryoglobulinemic vasculitis</td>
<td>Vasculitis with cryoglobulin immune deposits affecting small vessels (predominantly capillaries, venules, or arterioles) and associated with cryoglobulins in serum. Skin, glomerul, and peripheral nerves are often involved.</td>
</tr>
<tr>
<td>IgA vasculitis (IgAV) (Henoch-Schönlein purpura)</td>
<td>Vasculitis, with IgA1-dominant immune deposits, affecting small vessels (predominantly capillaries, venules, or arterioles). Often involves skin and gastrointestinal tract and frequently causes arthritis. GN indistinguishable from IgA nephropathy may occur.</td>
</tr>
<tr>
<td>Hypocomplementemic urticarial vasculitis (anti-C1q vasculitis)</td>
<td>Vasculitis accompanied by urticaria and hypocomplementemia affecting small vessels (capillaries, venules, arterioles), and associated with anti-C1q antibodies. GN, arthritis, obstructive pulmonary disease, and ocular inflammation are common.</td>
</tr>
</tbody>
</table>
Thank You