PAEDIATRIC VASCULITIS

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OUTLINE

• Introduction and Definition
• Recognition of possible vasculitis
• Classification
• Clinical manifestations
• Diagnosis and Management
• Complications
Introduction

Vasculitides are disorders associated with inflammation of blood vessels. This may lead to narrowing (stenosis) and dilation (aneurysms) of the blood vessels. IgA vasculitis (Henoch Shonlein Purpura) and Kawasaki disease are the most common. HSP incidence 10-20/100,000.
### Estimated burden of rheumatic disorders

<table>
<thead>
<tr>
<th></th>
<th>Estimated Incidence</th>
<th>SSA (numbers)</th>
<th>Kenya (Pop&lt;18=22M)</th>
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</thead>
<tbody>
<tr>
<td><strong>Global incidence</strong></td>
<td></td>
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<tr>
<td><strong>JIA</strong></td>
<td>1:1000</td>
<td>336-528,000</td>
<td>22,000</td>
</tr>
<tr>
<td><strong>SLE</strong></td>
<td>0.36-0.8/100,000</td>
<td>1,209-4,224</td>
<td>79-176</td>
</tr>
<tr>
<td><strong>JDM</strong></td>
<td>0.2-0.3/100,000</td>
<td>672-1,584</td>
<td>44-66</td>
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<tr>
<td><strong>Vasculitides</strong></td>
<td>22/100,000</td>
<td>73,920-116,160</td>
<td>4,840</td>
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<tr>
<td><strong>HSP</strong></td>
<td>10-20/100,000</td>
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<td>2,200-4,400</td>
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</table>

*Global incidence rates from Oxford specialist handbook of Paediatric Rheumatology*
Introduction 2: “Could this be Vasculitis?”

- **Systemic**
  - Fever, weight loss, fatigue

- **Vascular**
  - Hypertension
  - Absent/asymmetric pulse.
  - Palpable aneurysms
  - Tissue gangrene

- **Cutaneous**
  - Palpable purpura, painful nodules
  - Livedo reticularis, ulceration
Introduction: “Could this be Vasculitis?”

- Pulmonary infiltrates or hemorrhage
- Neurologic
  - Headache, focal CNS signs
- Musculoskeletal
  - Arthralgia, arthritis, myalgia, myositis
- Renal
  - Hematuria, hypertension, renal failure
- Laboratory: Abnormal urinalysis; ANCA.
Childhood Vasculitis classification

Large vessel
- Takayasu’s arteritis
- Giant Temporal Arteritis

Medium vessel
- PAN
- Kawasaki disease

Small vessel
- ANCA vasculitis
- Wegeners
- MPA
- Churg Strauss

Relatively common vasculitides
Immune Complex Small Vessel Vasculitis
Cryoglobulinemic Vasculitis
IgA Vasculitis (Henoch-Schönlein)
Hypocomplementemic Urticarial Vasculitis
(Anti-C1q Vasculitis)

Medium Vessel Vasculitis
Polyarteritis Nodosa
Kawasaki Disease

Anti-GBM Disease

ANCA-Associated Small Vessel Vasculitis
Microscopic Polyangiitis
Granulomatosis with Polyangiitis
(Wegener’s)
Eosinophilic Granulomatosis with Polyangiitis
(Churg-Strauss)

Large Vessel Vasculitis
Takayasu Arteritis
Giant Cell Arteritis
ANCA Associated Vasculitis
AAVs

• ANCA-associated vasculitis (AAV) includes
  – GPA (Granulomatosis with Polyangiitis),
  – MPA (Microscopic Polyangiitis),
  – EGPA (Eosinophillic GPA), and
  – renal-limited pauci-immune glomerulonephritis
• Associated with necrotizing vasculitis.
• Predominantly affecting small vessels
• Associated with myeloperoxidase ANCA, or proteinase-3 ANCA.
Granulomatosis with Polyangiitis

Granulomatous inflammation involving the respiratory tract and necrotizing vasculitis affecting small to medium-sized vessels
EULAR/PReS classification criteria for GPA

• Any three of:
  – Histological evidence of granulomatous inflammation.
  – Upper airway involvement.
  – Laryngotracheobronchial involvement.
  – Pulmonary involvement (Xray or CT scan)ANCA positivity.
  – Renal involvement.
Airways Disease in Granulomatous Polyangiitis

- Sinusitis: 60%
- Epistaxis: 50%
- Saddle Nose Deformity: 25%
- Oral Ulcers: 20%
- Otitis Media: 30%
- Subglottic Stenosis: 30%
- Pulmonary Hemorrhage: 30%

*Akikusa et al.* (Arthritis Rheum 2007)
### Systems Affected in 65 Children with Wegener’s Granulomatosis

<table>
<thead>
<tr>
<th>System</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>ENT</td>
<td>94%</td>
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<tr>
<td>Pulmonary</td>
<td>80%</td>
</tr>
<tr>
<td>Renal</td>
<td>67%</td>
</tr>
<tr>
<td>Joint</td>
<td>58%</td>
</tr>
<tr>
<td>Ocular</td>
<td>54%</td>
</tr>
<tr>
<td>Skin</td>
<td>51%</td>
</tr>
<tr>
<td>Venous Thrombosis</td>
<td>(16%)</td>
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</tbody>
</table>

*Akikusa et al.* (Arthritis Rheum 2007)
Granulomatosis with Polyangiitis

Limited Disease
• Confined to upper airways and lungs

Systemic/severe Disease
• Rapidly progressive glomerulonephritis
• Pulmonary hemorrhage
• Mononeuritis Multiplex
• Scleritis or peripheral ulcerative keratitis
EGPA (Churg Strauss syndrome)

• Eosinophilic granulomatous inflammation of respiratory tract.

• Often associated with
  – Late onset asthma,
  – Eosinophilia

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<th>Diagnosis requires 4 of the following:</th>
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<td>1  History of asthma</td>
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<td>2  History of allergies (seasonal, foods, contact)</td>
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<td>3  Peripheral eosinophilia greater than 10%</td>
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<tr>
<td>4  Mono- or polyneuropathy</td>
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<tr>
<td>5  Migratory pulmonary infiltrates</td>
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<tr>
<td>6  Paranasal sinus pain or radiographic opacification</td>
</tr>
<tr>
<td>7  Biopsy demonstrating extravascular eosinophils</td>
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</table>
Polyarteritis nodosa (PAN)

- Necrotizing vasculitis of medium & small arteries.
- Cutaneous PAN: skin involvement but no major organs affected.
- Aneurysm formation along vessel walls.
- 3rd most common childhood vasculitis after IgA vasculitis and Kawasaki.
- Peak age 7-11 years.

Aetiology

- Some cases especially in adults associated with Hep B infection.
- Strep infection associated with cutaneous PAN.
- Familial cases of PAN may be caused by recessive, mutations in CECR1 gene.
- CERC1 is a gene encoding the enzyme adenosine deaminase 2 (ADA2).
PAN: Clinical 1

- **Systemic:**
  - fever,
  - weight loss,
  - myalgia, arthritis.

- **Abdominal pain,**

- **Skin:**
  - livedo reticularis,
  - tender subcut nodules,
  - skin infarction.
PAN: Clinical 2

- Renal: hypertension, proteinuria, haematuria.
- GIT: GI haemorrhage, pain
- Neurologic: focal defects, hemiplegia
- Other: testicular pain.
EULAR/PReS classification criteria for childhood polyarteritis nodosa (PAN)\(^8\)

*Systemic inflammation with evidence of necrotizing vasculitis or angiographic abnormalities of medium or small-sized arteries plus one of the following:*

1. Skin involvement (livedo reticularis, nodules, infarcts)
2. Myalgias
3. Hypertension
4. Peripheral neuropathy
5. Renal involvement (proteinuria, hematuria, or impaired function)
Takayasu’s arteritis

• Chronic granulomatous, large vessel vasculitis.
• Mainly affects the aorta & its major branches.
• Named after Japanese ophthalmologist who described retinal vasculitis with absent pulses.
• Vessel Inflammation associated with stenosis, as well as dilatation with aneurysms.
Fig. 1 Angiogram of the aortic arch demonstrating a fusiform aneurysm of the descending portion (thick arrow). There is also a stenotic lesion involving the left subclavian artery (long thin arrow).
Takayasu: clinical, acute

- Systemic:
  - fever,
  - weight loss, malaise,
  - Arthritis, arthralgia, myalgia.

- Skin: Rash, erythema nodosum, pyoderma gangrenosum.

- Hypertension

- Thrombosis, myocardial infarction.
Takayasu: clinical, chronic

- Asymmetric or absent pulses
- BP difference of >10mmHg on 4 limb BP
- Systemic hypertension, CCF.
- Arterial bruits
- Claudication, Abdominal pain
- CNS: Dizziness, headaches, seizures, TIA, stroke......from ischaemia and hypertension.
Takayasu: clinical, chronic

- Eye: diplopia, blurred vision.
- Renal: renovascular hypertension, renal failure.

EULAR/PReS classification criteria for childhood-onset Takayasu arteritis (TA)^8

Characteristic angiographic abnormalities of the aorta or its main branches and pulmonary arteries plus one of the following:

1. Absent peripheral pulses or claudication
2. Blood pressure discrepancy in any limb
3. Bruits
4. Hypertension
5. Elevated acute phase reactants
Differential Diagnoses

- Other vasculitides
- Fibromuscular dysplasia
- Williams syndrome
- Aortic stenosis.
- Syphilis.
- TB and other granulomatous infections.
Vasculitis: investigations

- Inflammatory markers: Increased ESR, CRP.
- Urine dipstick: Proteinuria, hematuria.
- Renal function, liver function.
- ANCA, ANA, dsDNA.
- Biopsy: renal, respiratory tract, skin etc
- Radiology: pulmonary cavities, nodules.
- CT/Xray of sinuses: erosions; ECG, CXR, Echo
- MRA, CTA, Angiography.
Management of vasculitides

- **Supportive:** pain, BP, Aspirin
- **Induction:** prednisone; cyclophosphamide.
- **Maintenance:** Azathioprine, MMF, prednisone, aspirin.
- **Other:** Biologic therapy- rituximab, anti-TNF.
- **Kawasaki:** IVIG, Aspirin; Biologics-infliximab.
- **Takayasu:** surgery.
Complications

• Renal failure
• Tissue/ digital gangrene
• Stroke (thrombotic/ hypertensive).
• Treatment related
  – Steroid toxicity
  – Gonadal failure: cyclophosphamide
SUMMARY

- Primary vasculitides are rare in children.
- IgA vasculitis, Kawasaki disease are the most common.
- Diagnosis includes finding systemic features of malaise, weight loss, fever, myalgia, arthralgia, arthritis and .....
- Clinical features specific to each condition.
- Management involves an induction phase usually 6 months; and maintenance phase.
Thanks