VASCULITIS: Challenges in treatment

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VASCULITIS

• Vasculitis: A clinicopathologic process characterized by inflammatory destruction of blood vessels that results in occlusion or destruction of the vessel and ischemia of the tissues supplied by that vessel.

• Vasculitis can involve vessels of any size and can affect any organ system.
Mr TNH, 50 yo Chinese man

March 2002

Livedo reticularis

Palpable purpura and ulcerations
April 2002

Diagnosis: Cutaneous Vasculitis secondary to PAN
Management

• Prednisolone
• IV methyl prednisolone
• IV Immunoglobulin
• Immunosuppressive drugs
  (cyclophosphamide, azathioprine, cyclosporine)
• Antibiotics
• Occlusive dressing
• Surgical debridement
Ulcers worsen
Vasculitis

Classification based on:

- Vessel size
  
  (Chapel Hall Consensus Conference 2012)

- Clinical & Histologic criteria
  
  (American College of Rheumatology criteria 1990)

- Type of cellular infiltrate on histology

- Aetiology
Classification of Vasculitis

Chapel Hill Consensus Criteria
Nomenclature update 2012

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
Vasculitis - Aetiology

- **Drugs** (Beta-lactam antibiotics, NSAID, diuretics)
- **Infection**
  - Bacterial: β-haemolytic Strep, Staph aureus, Borrelia, etc
  - Mycobacterial
  - Viral: hepatitis B and C, HSV
  - Fungal: Candida
  - Protozoa: *Plasmodium malariae*
- **Connective tissue disease**
  - SLE, RA, Sjogren’s syndrome, dermatomyositis
- **Granulomatous disease**
  - Behcet’s disease, sarcoidosis, inflammatory bowel disease
- **Cryoglobulinaemia**
- **Malignancy**
  - haematological: lymphoprolif, paraproteinaemias, AML, solid tumour
- **Idiopathic (~50%)**
Pathogenesis

1. Antigen stimulates antibody formation

2. Immune complexes in circulation

3. Deposit at certain sites and activates complement pathway
   - Degranulation of mast cells

4. Neutrophils attach to endothelial cells
   - Migrate to perivascular tissue
   - Phagocytose and degrade immune complexes

5. Neutrophils disintegrate
   - Release lysosomal enzymes

6. Damage vascular endothelium
General approach

• History (patient’s story)
• Examination (Body’s story)
• Investigations: should aim to
  – Establish diagnosis
  – Assess organ involvement
  – Assess disease activity
• Management; multidisciplinary esp with multiorgan involvement
Common Clinical Manifestations

- **Systemic**
  - Fever, sweats, weight loss

- **Skin**
  - Palpable Purpura

- **Neurologic**
  - Mononeuritis Multiplex

- **Musculoskeletal**
  - Arthralgia / arthritis
  - Muscle pain / claudication

- **Respiratory**
  - Sinusitis / Epistaxis
  - Pulmonary infiltrates

- **Gastrointestinal**
  - Abdominal Pain
  - Bloody stools

- **Renal**
  - Glomerulonephritis
  - Hypertension
Clinical Presentation Of Cutaneous Vasculitis

Palpable purpura
Clinical Presentation of Cutaneous Vasculitis

Livedo reticularis
Clinical Presentation of Vasculitis

Urticarial vasculitis
Clinical Presentation of Cutaneous Vasculitis

Digital infarcts

Nodular vasculitis
• Are there additional tests which could help confirm this suspicion?
  
• Serologic tests
• Tissue biopsy
• Imaging studies
Serologic Tests

• ANCA
• Hepatitis B surface antigen
• Hepatitis C
• HIV
• ANA
• ACA, “lupus” anticoagulopathy panel
Tissue biopsy: Histopathology of Skin

Superficial and deep perivascular infiltrates of neutrophils
Leucocytoclastic Vasculitis

Fibrinoid necrosis of vessel wall
Neutrophil infiltration
Nuclear dust formation
Imaging studies

- Sinus CT scan
- Chest CT scan
- CT/MR angiography
Mimickers of Vasculitis

• Infective Endocarditis
• Atrial Myxoma
• Cholesterol embolism
• Antiphospholipid antibody syndrome
• Vasoconstrictive drugs eg. cocaine, amphetamines, ergot poisoning
Polyarteritis Nodosa

- Necrotizing vasculitis of medium & small arteries
- Age ~ 40s; M > F
- Constitutional symptoms are common
  - fever 50%
  - weight loss 50%
- Vasculitis can be variable in distribution making diagnosis difficult
Polyarteritis Nodosa
ACR Criteria (3 of 10)

- Wt loss > 4 kg
- Livedo reticularis
- Testicular pain
- Myalgias, weakness or leg tenderness
- Mononeuropathy or polyneuropathy
- Diastolic BP > 90
- ↑ BUN or Creatinine
- Hepatitis B virus
- Arteriographic abnormality
- Biopsy of small or medium artery containing PAN
Classic PAN: Manifestations

- Mononeuritis multiplex 50%
- Renal involvement: 60%
  - Hypertension (more common)
  - Glomerulonephritis (uncommon)
- Abdominal involvement 45%
- Arthralgias/Myalgias/Myositis 64%
- Testicular pain 25%
- Pulmonary involvement rare
Polyarteritis Nodosa

- Association with Hepatitis B (surface antigen)
- Classic PAN is NOT associated with ANCA
Management of Cutaneous PAN

- **Colchicine** 0.5mg bd or tds
  - inhibit neutrophil chemotaxis
  - found to be effective in many studies
  - recent double-blind study failed to show benefit

- **Dapsone** 50-100mg daily
  - patients with only cutaneous involvement
  - esp useful in erythema elevatum diutinum

- **Systemic corticosteroids:** prednisolone 1mg/kg/day
  - systemic involvement
  - ulcerated lesions

- **Immunosuppressive agents:** azathioprine, cyclophosphamide, methotrexate, CSA
  - steroid-sparing effect, steroid resistant
  - systemic involvement, systemic vasculitis
  - rapid progressive course

- **Plasmapheresis**
Management of PAN

Adjunctive treatments:

• Antiplatelet agents: aspirin, dypiridamole, ticlopidine
  • livedoid vasculitis
  • concomitant arterial disease

• Pentoxyphylline 400mg tds
  • reduce blood viscosity, inhibit platelet aggregation
Management of PAN

New treatments:

• Intravenous immunoglobulin
  • cases which failed conventional therapy
  • reduces circulating pro-inflammatory cytokines, inhibitis action of ANCA
  • requires further studies

• Monoclonal antibodies: Campath-1H, rat CD4 228
Management

- Corticosteroids (Pred. 80mg/d and 2 courses of iv methyl pred.)
- Immunosuppressive drug (cyclophosphamide, azathioprine, oral cyclosporine)
- IV Immunoglobulin
- Antibiotics
- Surgical debridement
  - Condition worsen with more ulcers and infections
  - Planned for below knee amputation – pt refused
Topical Cyclosporine

• 1990 - Cyclosporin mouth wash effective in oral lichen planus

• Local action by inhibiting T-cell proliferation and release of lymphokines.

• May have an antibacterial effect
Right foot

Pre topical CyA

6/12
Left foot

Pre topical CyA

6/12
Right heel

Sep 2002

Pre topical CyA

Mar 2003
Conclusion

• Vasculitis are chronic diseases, characterized by relapse and remission with multiorgan involvement
• Achieving remission requires intense monitoring by a multidisciplinary team
• Even after achieving disease remission, patients will continue to suffer from the chronic, irreversible consequences of both the disease and side-effects of its therapies
THANK YOU

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