SHO Teaching
Vasculitis – Renal medicine

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OUTLINE

• What is vasculitis
  – Causes
  – Classification

Brief look into ANCA Associated Vasculitis (AAV)
  – Clinical presentation
  – Diagnosis
  – Treatment
What is vasculitis?

Inflammation of vessels

How does it cause damage?

- Inflammatory leucocytes in vessel walls
  - Loss of vessel wall integrity
  - bleeding
  - lumen occlusion
  - tissue ischaemia and necrosis
Cause of vasculitis?

- Can be primary or secondary → vessel inflammation
- Exact mechanisms variable and in some case unclear
- Affected vessels vary in size, type and location
Classification of Vasculitis

Chapel Hill Consensus Criteria
Nomenclature update 2012
Suspicion....

- Delayed diagnosis – variable presentation
- Mononeuritis multiplex
- Palpable purpura
- Pulmonary-renal involvement
ANCA Associated Vasculitis (AAV)

Types:

- GPA – Granulomatosis with polyangiitis (Previously called WEGENER’s Granulomatosis)
- MPA – Microscopic polyangiitis
- Limited Vasculitis
- Churg-strauss (Eosinophilic Granulomatosis with PolyAngiitis)
ANCA

- Antineutrophil cytoplasmic antibody
- Antibodies directed against intracellular antigens
- cANCA – PR3 (Proteinase 3)
- pANCA – MPO (Myeloperoxidase)
- +ve ANCA
  - 99% specificity and 70% sensitivity
  - RIGHT CLINICAL CONTEXT
Spectrum of disease

GPA

- Destruction in Upper Respiratory Tract
- and/or cavities in Lower Respiratory Tract
- and/or granulomatosis on biopsy of any organ

MPA

Significant overlap in signs and symptoms and in ANCA serologies

Chapel Hill Consensus Conference

Increase risk of relapse

anti-PR3

Better predictive value
- Long term outcome
- Relapse propensity

anti-MPO

GPA or MPA

Clinical presentation

• Predominantly older patients
• male = female

• Constitutional symptoms
  – Fever, migratory arthralgia, malaise, anorexia and weight loss
  – Prodromal symptoms – weeks/months before organ specific damage
• **ENT**
  
  – 90% GPA vs 35% MPA
  – Nasal crusting, sinusitis, persistent rhinorrhea, bloody discharge, oral/nasal ulcers, conductive and sensorineural hearing loss
  – GPA – more likely to have evidence of bony / cartilage destruction

• **Pulmonary disease**
  
  – Hoarseness, cough, dyspnoea, stridor, wheezing, haemoptysis or pleural pain
  – Tracheal / subglottic stenosis
  – Pulmonary haemorrhage – GPA
• Renal disease
  – Common in GPA and MPA
  – Features of glomerulonephritis
    • NIH – GN only present in 18% of patients at presentation but 77-85% of patient will go on to develop GN within 2 years

Asymptomatic haematuria
AKI
Subnephrotic proteinuria
Rapidly progressive GN

– Histology – severity of renal biopsy findings generally parallel severity of clinical presentation
• Skin
  – ½ of GPA or MPA patients
  – Leukocytoclastic vasculitis → purpura (usually legs), focal necrosis and ulceration
  – Urticaria, livida reticularis and tender nodules

• Eyes
  – Conjunctivitis, corneal ulceration, episcleritis/scleritis, optic neuropathy, retinal vasculitis and uveitis

• CNS
  – Mononeuritis multiplex, cranial nerve involvement and hearing loss
  – Multiple ischaemic (or haemorrhagic) lesions in white matter of brain
  – Granulomatous inflammation of CNS
GPA or MPA

Diagnosis

• Prompt diagnosis – you need to consider it...
  – Early initiation of Rx could be life / organ saving

• Careful History
  – vague constitutional symptoms

• Examination – Rash
  – Urine Dipstick

• Lab investigations
  – Routine blood tests inc CRP
  – ANCA serology
  – ANA, C3 & C4, cryoglobulins, hepatitis serology, HIV screen, anti-GBM antibody
  – Blood cultures (if temp ? IE)
• **Tissue biopsy .....(don’t delay treatment!)**
  
  – Usually renal but can be other organs involved (lungs)
  
  – Renal – Pauci-immune GN
    
    • Few or no immune deposits in glomeruli on IF and EM
    
    • Pauci-immune crescentic GN
  
  • Histology can be used to predict renal outcomes
Limited disease (Lung or Renal)

– Lung
  • GPA
  • Isolated clinical findings related to URT or lungs
  • Usually younger women
  • More likely to have a chronic, recurring disease – destructive URT disease (saddle-nose deformity)
  • 80% will eventually develop GN

– Renal
  • Part of the GPA/MPO spectrum
  • Usually present later
  • Eventually develop extrarenal manifestations
Eosinophilic granulomatosis with polyangiitis (EGPA)
Churg-stauss

- Chronic rhinosinusitis
- Asthma
- Eosinophilia

- Vaculitis of small and medium sized arteries
- Predominantly involves lung
  - CV, Renal, skin and CNS

- Can present in similar way to GPA/MPA – constitutional symptoms.

- Positive ANCA in 40-60% of cases
  - MPO-ANCA
  - More likely to have renal involvement (less likely to have cardiac involvement)
Differential

- Anti-GBM disease
- EGPA (churg-stauss syndrome)
- ? PAN
- ? IE
- Drugs – Propylthiouracil, carbimazole, Hydralazine, minocycline, allopurinol, penicillamine, procainamide, phenytoin, rifampicin, cefotaxime, isoniazid and indomethacin.
- Cystic fibrosis – non-MPO P-ANCA
Treatment ANCA Assoc Vasculitis (AAV)

- Immunosuppressive therapy greatly improved survival
- Biphasic and tailored
  - Induction of remission – rapid disease control (3 - 6 months)
  - Maintenance of remission – prevent relapse (>18 months)

- Relapses are frequent
- Significant short and long-term adverse effects
  - Patients in 1st year of treatment 3X more likely to die of adverse effect of treatment than disease itself
  - Increase risk of infection, CV events and malignancies
Relapse

• Risk factors
  – PR3-ANCA
  – Sub-optimal intensity induction therapy
  – Early withdrawal of therapy
  – Chronic nasal carriage of *staph aureus*
  – Rising ANCA titre ??
Treatment of relapse

• Increase steroids

• RAVE trial – Rituximab superior to cyclophosphamide in relapsing disease

• RITAZAREM – looking at Rituximab vs Azathioprine in relapsing disease
Summary

- Vasculitis complex condition with different aetiologies
- Vague non-specific symptoms
  - Life threatening
- Need suspicion for diagnosis
- Increased awareness and better multicentred studies have improved the management - AAV
- Chronic disease – frequent relapses
- Toxicity of treatment needs to be considered