



Wegener's Granulomatosis

Key features:

Granulomatous inflammation. If you see inflamed venules, its more likely to be a microscopic polyangiitis.

- **Not eosinophilic-** eosinophilia suggests Churg-Strauss syndrome
- **Not whole-length;** segmental, involving mainly bifurcations.

SYMPTOMS: weird and non-specific

- fever
- weight loss
- malaise
- weakness
- myalgias, especially calves;
- mononeuritis, most commonly foot drop
- abdominal pain – worse after eating (“bowel claudication”)
- headache
- OCCASIONALLY: hematuria, hypertension (sent in by GP)

PAN very rarely involves the lung.

Definitive diagnosis: TISSUE. You need a biopsy.

SIGNS: weird and non-specific

- Rash and purpura
- **LIVEDO RETICULARIS:** bizarre mottling of the skin, in a fishnet-like pattern
- Cutaneous infarcts
- Raynauds phenomenon

Blood tests:

- Anaemia
- High WCC with neutrophils
- High ESR, CRP
- Most likely, ANCA-negative
- Could have either liver, kidney, or pancreatic failure (due to infarcts)
- For some reason, 30% of these people are Hep B positive

Expected complications

- Hypertension
- Bowel infarcts and perforations
- Ischaemic heart disease
- Renal failure

Management:

- Prednisone and cyclophosphamide
- If there is Hep B, use antiviral drugs.
- Rate of relapse- 10%
- Rate of untreated survival ~ 10% over 5 years

Pathophysiology

Whole thickness of the vessel wall is involved. Acutely, neutrophils swarm in and infiltrate the vessel wall, and involve the surrounding perivascular tissues. This results in intimal proliferation, and the vessel wall begins to degenerate. Soon after, monocytes become the predominant species in the wall, and fibrinous necrosis ensues, which produces much greater wall thickening. This occasionally results in downstream infarction. As the lesions heal, there is collagen deposition, and this occludes the lumen even more. Because this happens most frequently at bifurcations, it tends to produce aneurysms.

Cyclophosphamide

A hideous DNA alkylating agent; the damage done to DNA resembles that caused by radiation. Derived in the 1950s from the nitrogen mustards which the great warring nations stockpiled (and for some reason never found a good opportunity to use).

-metabolized by the liver into the active ingredient, phosphoramidate mustard. Some is turned into the bladder-toxic **acrolein**, which causes hemorrhagic cystitis

- the cells most damaged are those with low levels of Aldehyde Dehydrogenase (ALDH) which transforms the phosphoramidate mustard into an inactive metabolite.

-side effects are nausea, vomiting, darkening of the skin, alopecia lethargy and bone marrow suppression.