Vasculitis

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- Inflammation of the walls of vessels is called *vasculitis*

- It is encountered in diverse clinical settings.

- Vessels of any type in virtually any organ can be affected.

Clinical manifestations often include:

1. constitutional signs & symptoms: e.g., fever, myalgias, arthralgias, & malaise.
2. local manifestations of downstream tissue ischemia.

Several vasculitides tend to affect only vessels of a particular size or location, but Most vasculitides affect small vessels; from arterioles to capillaries to venules

- 20 primary forms of vasculitis → classification schemes → according to: vessel diameter, role of immune complexes, presence of specific autoantibodies, granuloma formation, organ specificity, & even population demographics
- The two most common mechanisms of vasculitis are:
  - direct invasion of vascular walls by infectious pathogens
  - Immune-mediated mechanisms .
- Physical & chemical injury, such as irradiation, mechanical trauma, & toxins can also cause vascular damage.

Pathogenesis of Noninfectious Vasculitis

Immunologic injury in noninfectious vasculitis may be caused by:

(1) Immune complex deposition

(2) Antineutrophil cytoplasmic antibodies (ANCA)

(3) Anti-endothelial cell antibodies. (Anti-EC)

(4) Autoreactive T cells

Immune Complex–Associated Vasculitis

- ✓ This mechanism is supported by the fact that the vascular lesions resemble those found in experimental immune complex - mediated conditions.
- ✓ Also in some cases contain readily identifiable antibody and complement.
- ✓ is a diagnostic challenge; rarely is the specific antigen responsible for immune complex formation known, & in most instances it is not clear whether the pathogenic antigen-antibody complexes are deposited into the vessel wall from the circulation or form in situ.
- **Systemic lupus erythematosus & polyarteritis nodosa**

ANCA associated

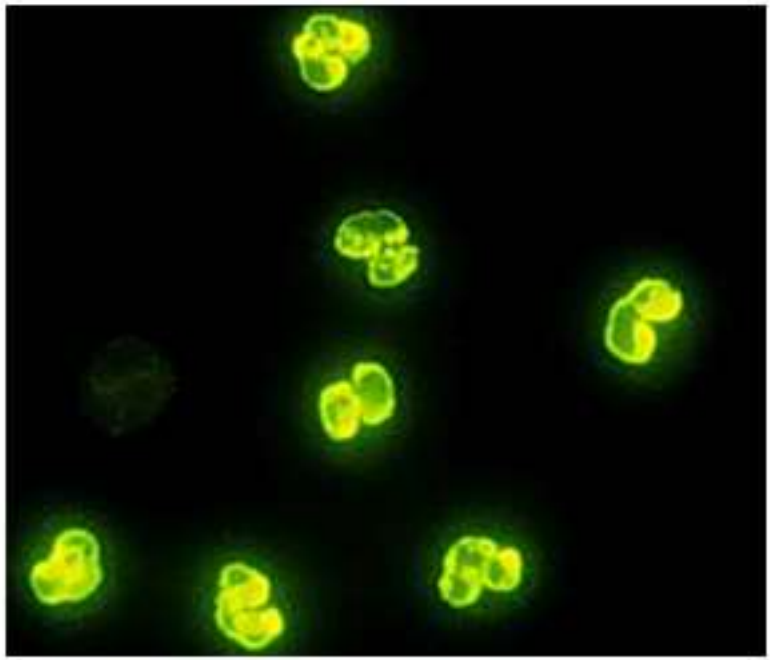
- Patients have circulating antibodies react with neutrophil cytoplasmic antigens *(antineutrophil cytoplasmic antibodies (ANCAs)*.
- ANCAs are a heterogeneous group of autoantibodies directed against constituents (usually enzymes) of neutrophil primary granules, monocyte lysosomes.
- Two main patterns are recognized by IF studies:

1. **Cytoplasmic** localization of the staining (c-ANCA), target antigen is proteinase-3 (PR3), a neutrophil granule constituent. *(Anti-proteinase-3)* → **granulomatosis with polyangiitis**

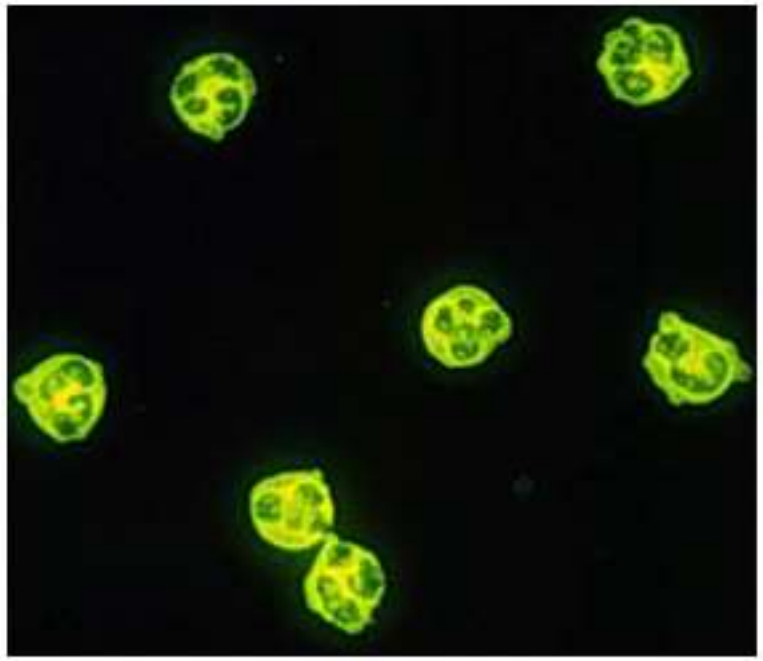
2. **Perinuclear** staining (p-ANCA) & target antigen is myeloperoxidase (MPO). (*Anti-myeloperoxidase)* ***microscopic polyangiitis & Churg-Strauss syndrome***

ANCA associated

These auto-antibodies are directed against cellular constituents without circulating immune complexes. Lesion does not contain antibody and complement; so often described as **"pauci-immune."**



P-ANCA Pattern



C-ANCA Pattern

Anti-Endothelial Cell Antibodies & Autoreactive T Cells

- Antibodies to ECs underlie certain vasculitides, such as **Kawasaki disease**
- Autoreactive T cells cause injury in some forms of vasculitides characterized by formation of granulomas.

Classification of Vasculitis

Vessel	Disease	summary
Large	Giant-cell arteritis	F, >50. Arteries of head.
	Takayasu arteritis	F, <40. “Pulseless disease”
Medium	Polyarteritis nodosa	Young adults. Widespread.
	Kawasaki disease	<4. Coronary disease. Lymph nodes.
Small	Wegener granulomatosis	Lung, kidney. c-ANCA.
	Churg-Strauss syndrome	Lung. Eosinophils. Asthma. p-ANCA.
	Microscopic polyangiitis	Lung, kidney. p-ANCA.

Temporal (giant cell, cranial) arteritis

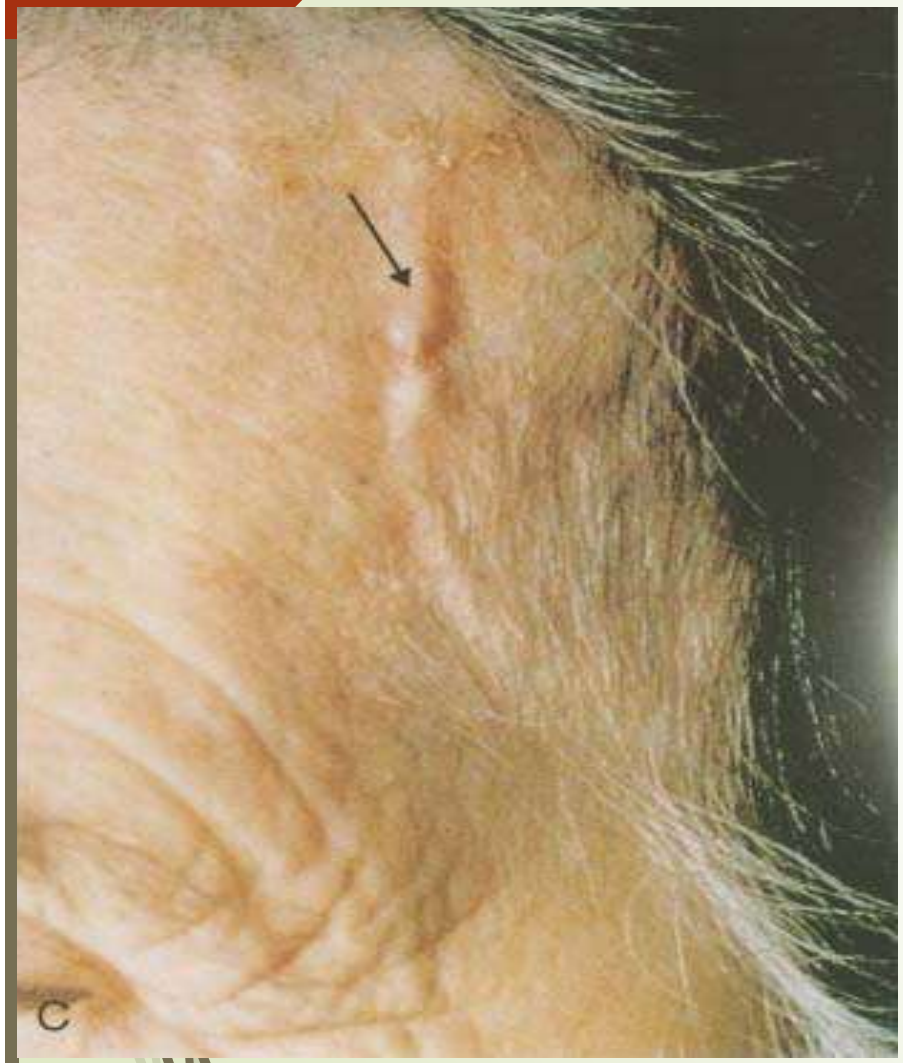
- A **chronic inflammatory disorder** affects principally **large- to small-sized arteries in the head (**the temporal, vertebral, ophthalmic arteries**)**, also affect the aorta, & may cause thoracic aortic aneurysm**.**
- It is the most common form of vasculitis among older adults in developed countries.
- Ophthalmic arterial involvement may lead to permanent blindness. Therefore, giant cell arteritis is a medical emergency that requires prompt recognition & treatment.

Temporal (giant cell, cranial) arteritis

- **Histology**
  - granulomatous inflammation
  - chronic non-specific panarteritis
  - fragmentation of the internal elastic lamina
- **Pathogenesis**
  - T Cell mediated immunity

Temporal (giant cell, cranial) arteritis

- **Clinical features**
  - Females > males (~X4)
  - > 50 years (rare before 50 years of age)
  - non-specific constitutional symptoms
  - Headache, local facial pain & tenderness
  - ocular symptoms, 50 % (range from diplopia to blindness)
- **Diagnosis**
  - Biopsy (at least 1cm)→ Could be negative (very focal involvement)
  - Rx: corticosteroids are effective.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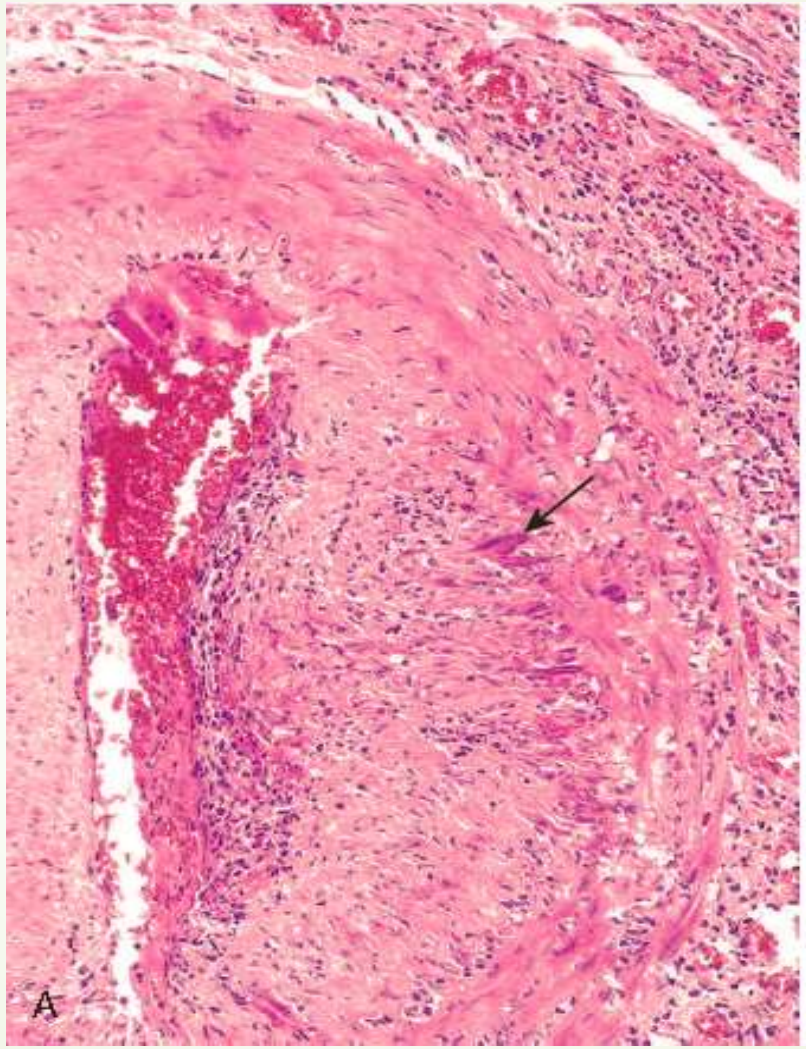
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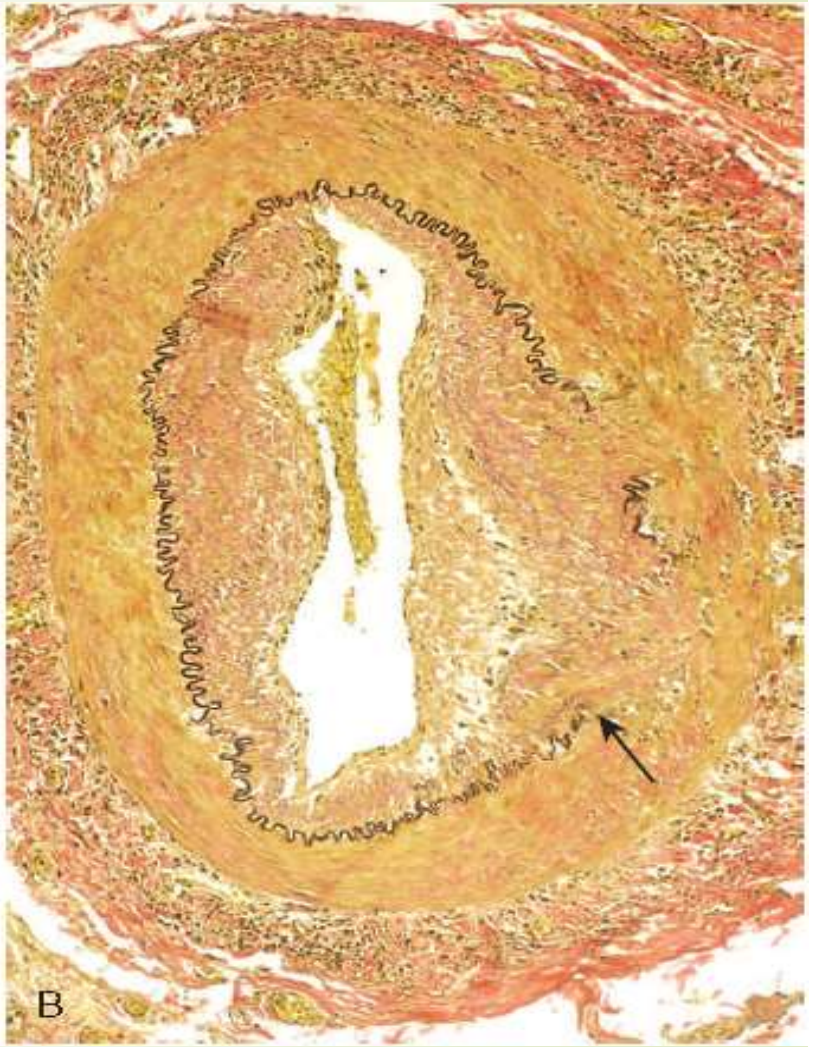
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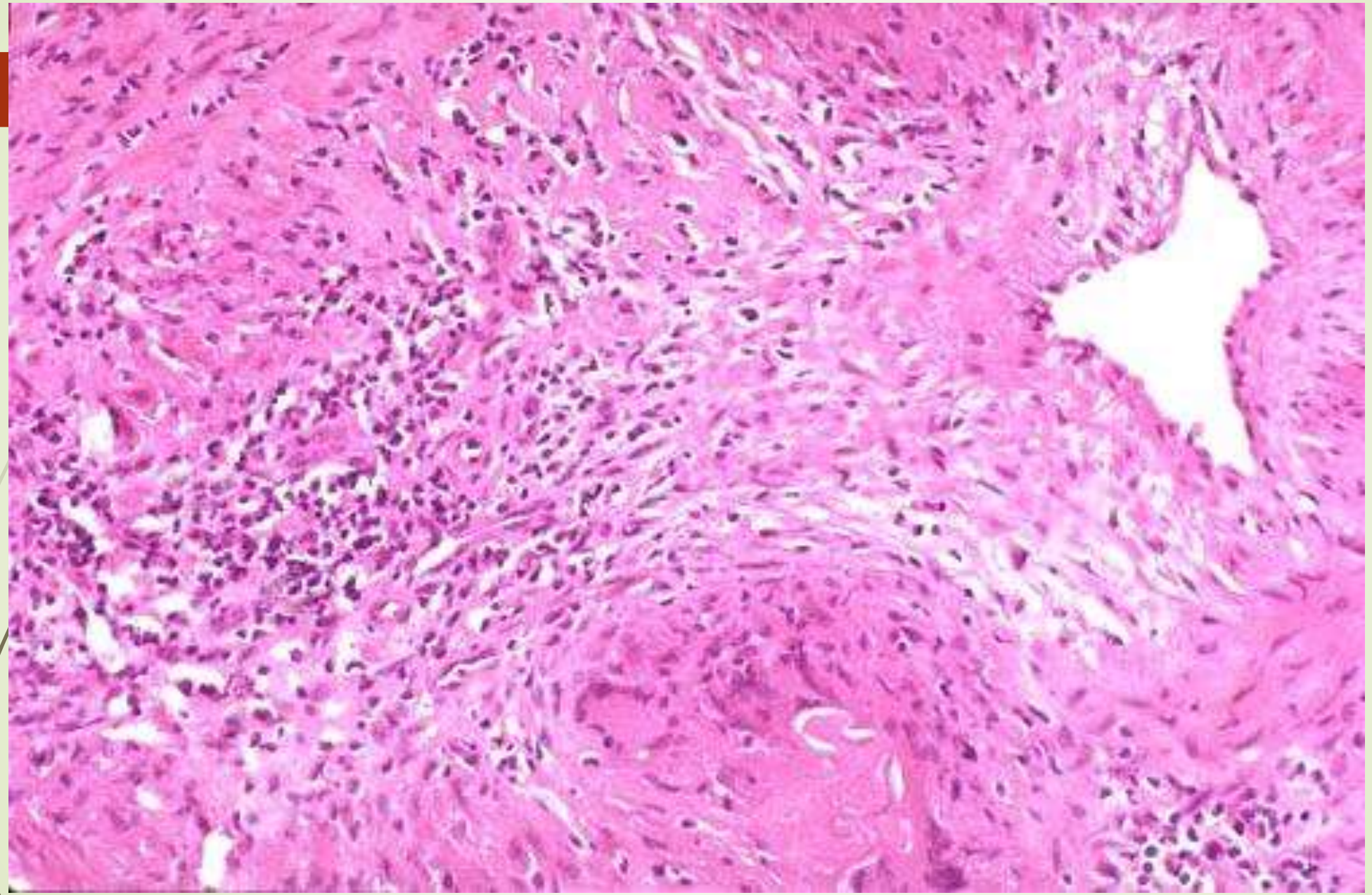
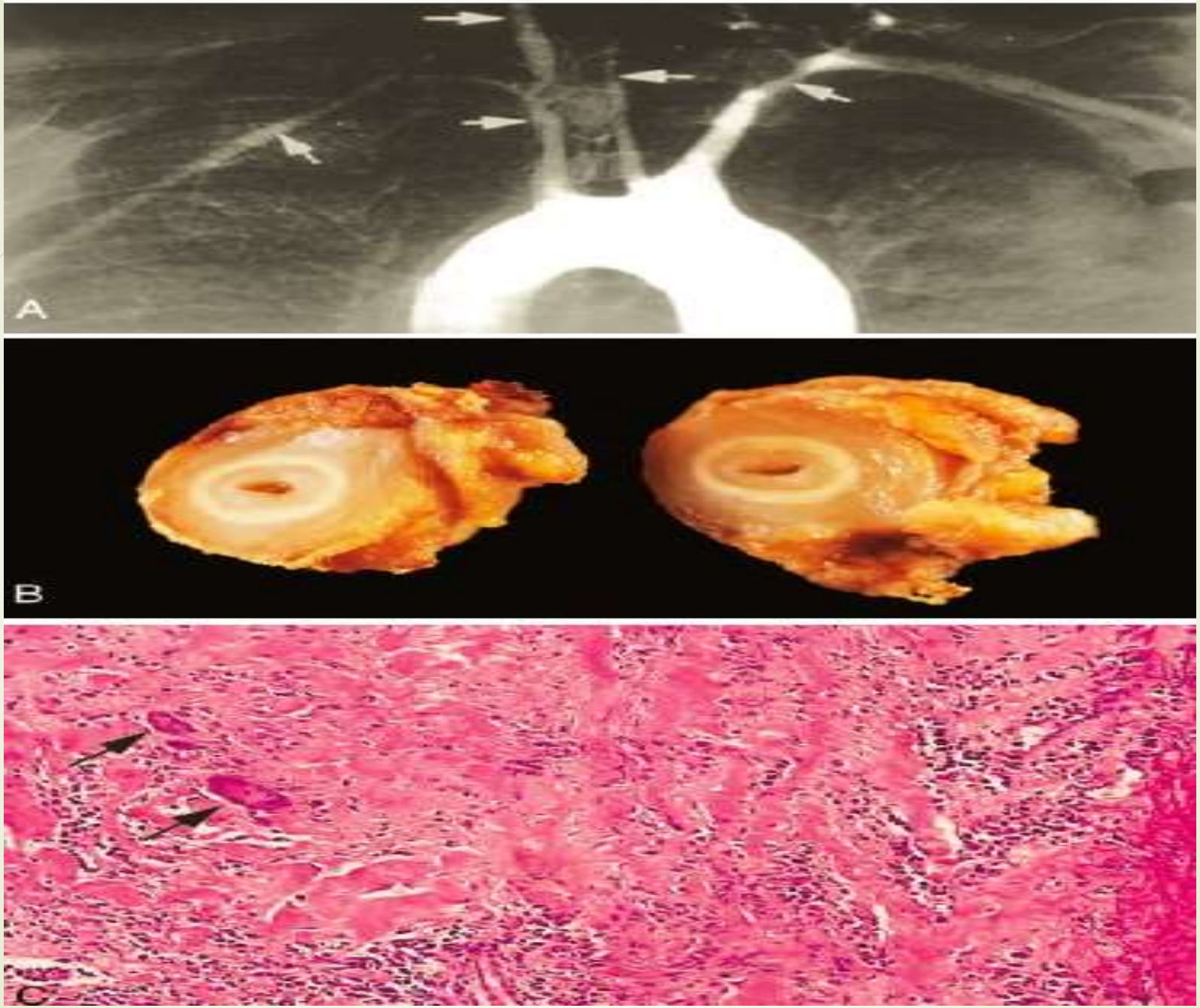


Takayasu Arteritis (pulseless disease)

- A granulomatous vasculitis of **medium & larger** arteries affects mainly arch of aorta.
- Characterized by transmural fibrous thickening & obliteration of aortic arch & great vessels → luminal narrowing of the major branch vessels → the origin of great vessels.
- Symptoms are secondary to luminal narrowing:

ocular disturbances & marked weakening of the pulses in the upper extremities →(pulseless disease).

- More common in females younger than 40 years and more frequently in Asian countries.
- Course of disease is variable ,may enter in quiescent stage.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Polyarteritis nodosa (PAN)

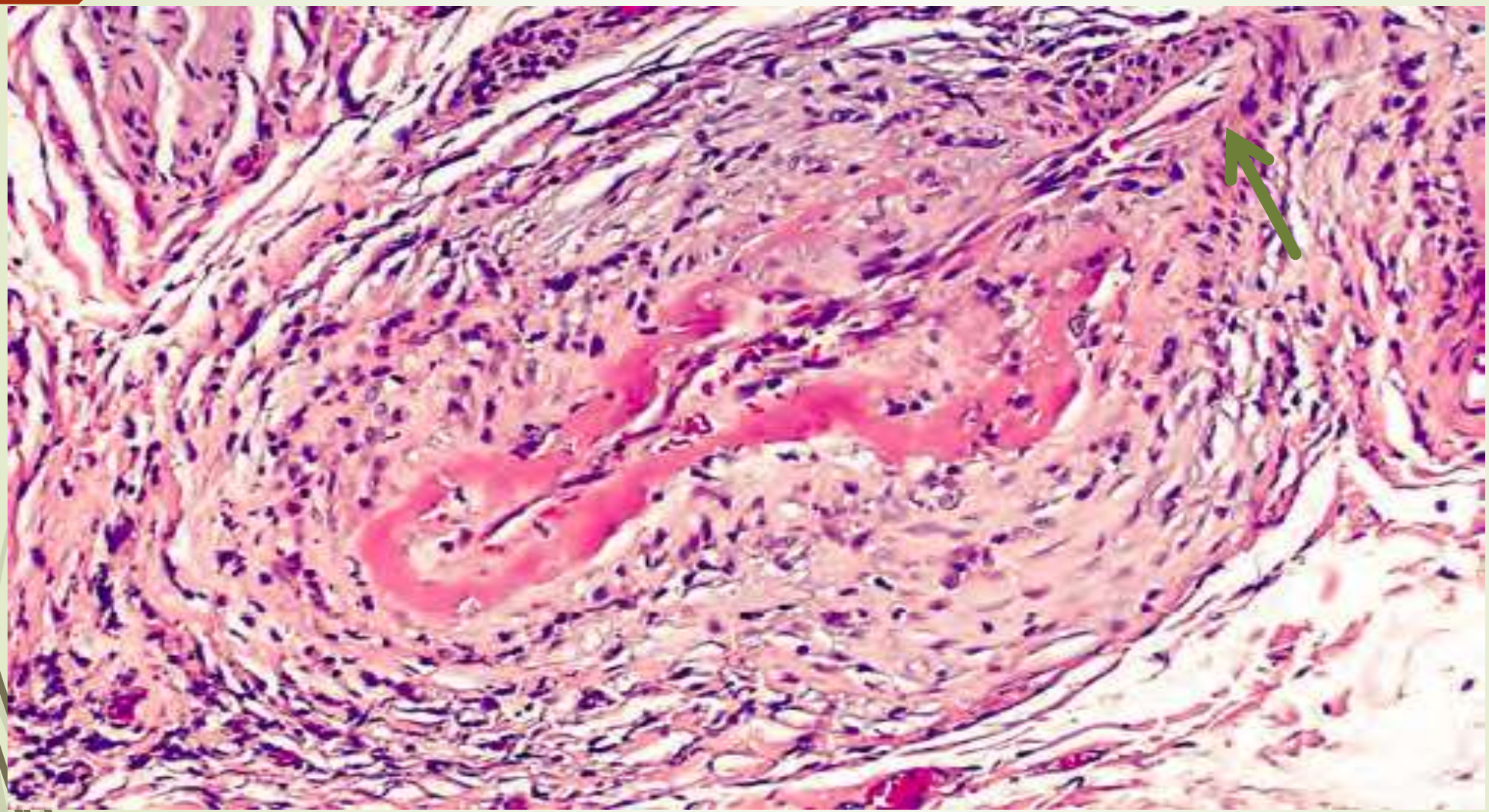
- A systemic disease characterized by necrotizing inflammation of **small - to medium - sized arteries** throughout the body (renal and visceral), sparing the pulmonary circulation.
- The involvement of the vessels is **focal, random & episodic.**
- It often produces irregular aneurysmal **dilatation (coz it weakens the arterial wall)** nodularity, and vascular **obstruction leading to infarctions.**
- Acute lesions show **segmental transmural necrotizing inflammation** extending around the vessel.

Polyarteritis nodosa (PAN)

- Healed lesions show marked fibrotic thickening of the arterial wall ,with associated elastic lamina fragmentation.
- All stages of activity may coexist in different vessels or even in the same vessel and this is so characteristic of PAN → ongoing and recurrent insults.
- Clinical features

young adults, males > females , vascular involvement is widely scattered → clinical picture can be varied & puzzling.

- Diagnosis .... Biopsy
- Rx … immunosuppression



Kawasaki disease (mucocutaneous lymph node syndrome)

- Acute febrile illness, **large- to medium-sized vasculitis** of infants & children (< 4 years) characterized by

  - Fever,
  - Lymphadenopathy,
  - Skin rash
  - Oral / conjunctival erythema.

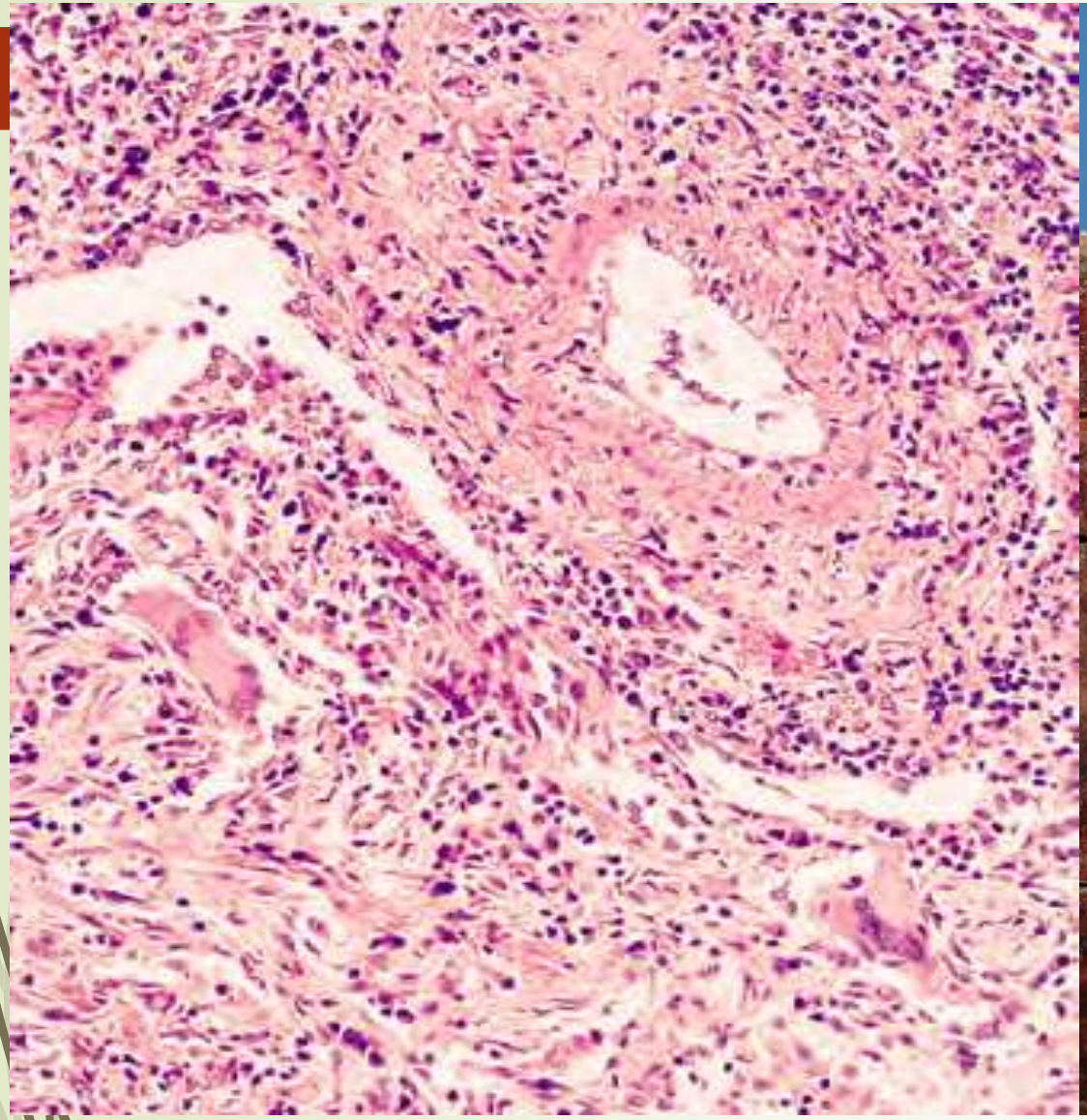
- 20% have coronary vasculitis ,often with aneurysm.
- Histology like PAN
- Etiology ; unknown (auto-antibodies to ECs)
- Self-limited disease, rarely fatal(1%) → complications of coronary involvement.

Granulomatosis With Polyangiitis

- Previously called *Wegener granulomatosis*.
- Classical cases consist of a triad:
  1. Granulomatous or necrotizing vasculitis mainly in the **lung** & upper respiratory tract.
  2. Necrotizing granulomas of upper &/or lower respiratory tract
  3. Renal involvement
     - focal necrotizing glomerulonephritis
     - rapidlly progressive glomerulonephritis
- Clinical picture
  - overlaps with PAN
  - Males > females, peak at 5th decade

Granulomatosis With Polyangiitis

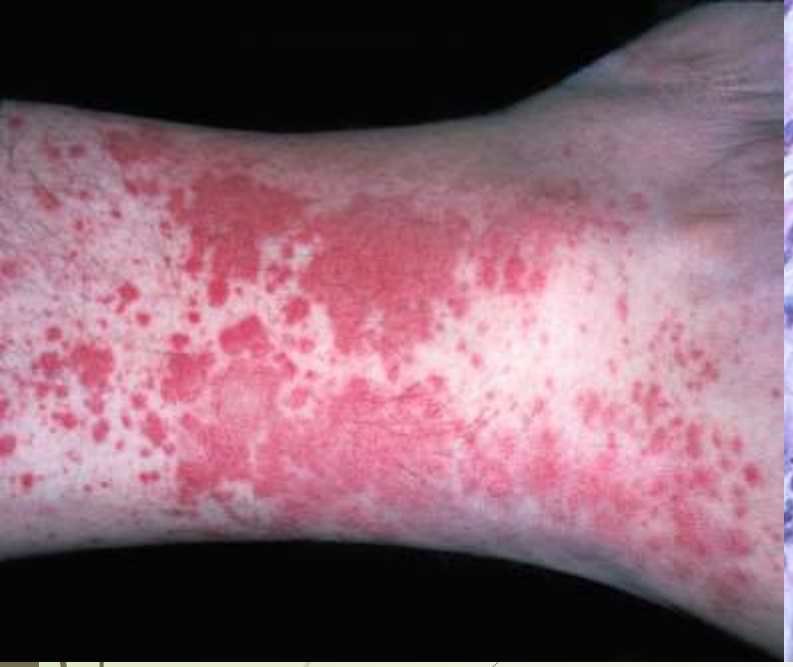
- Diagnosis
  - Lung biopsy, kidney biopsy, or nasal biopsy,
- Prognosis
  - 80% die within a year (if not treated)
  - 90% respond to treatment
- Pathogenesis
  - T Cell Mediated.
  - > 95% PR3-ANC positive (Mirrors the clinical coarse)

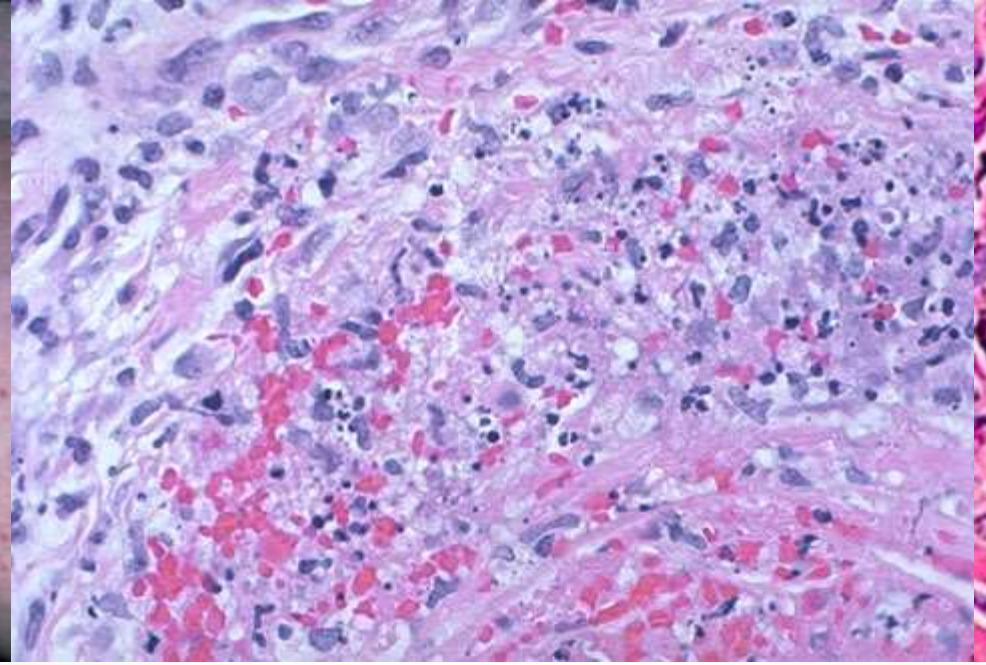


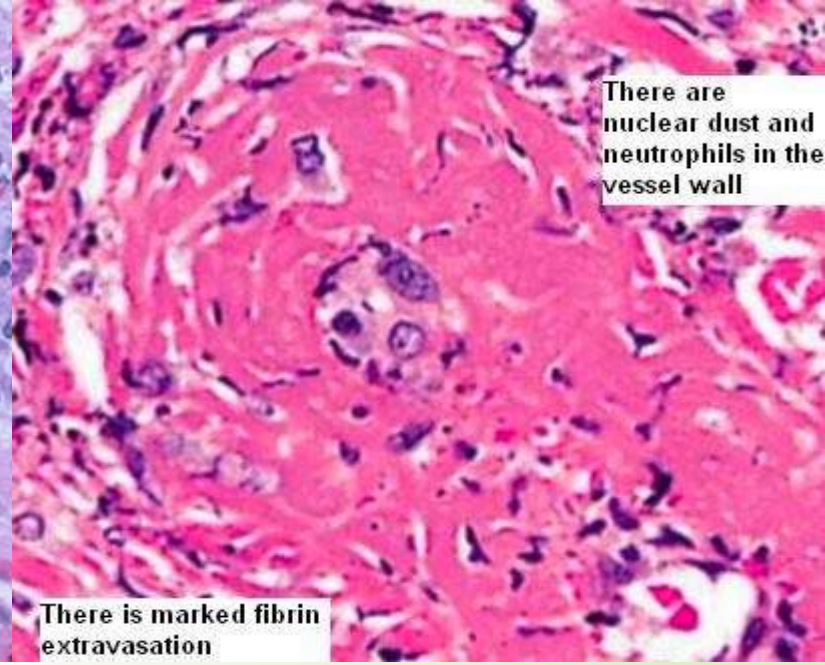

HÔPITAL
SAINTE-JUSTINE
1
2
3
cm

Microscopic polyangiitis (microscopic polyarteritis)
or
HYPERSENSITIVITY vasculitis
OR
LEUKOCYTOCLASTIC vasculitis

Most cases of microscopic polyangiitis are associated with MPO-ANCA , Although immunoglobulins and complement components can be demonstrated in early skin lesions, most lesions are “pauci-immune”



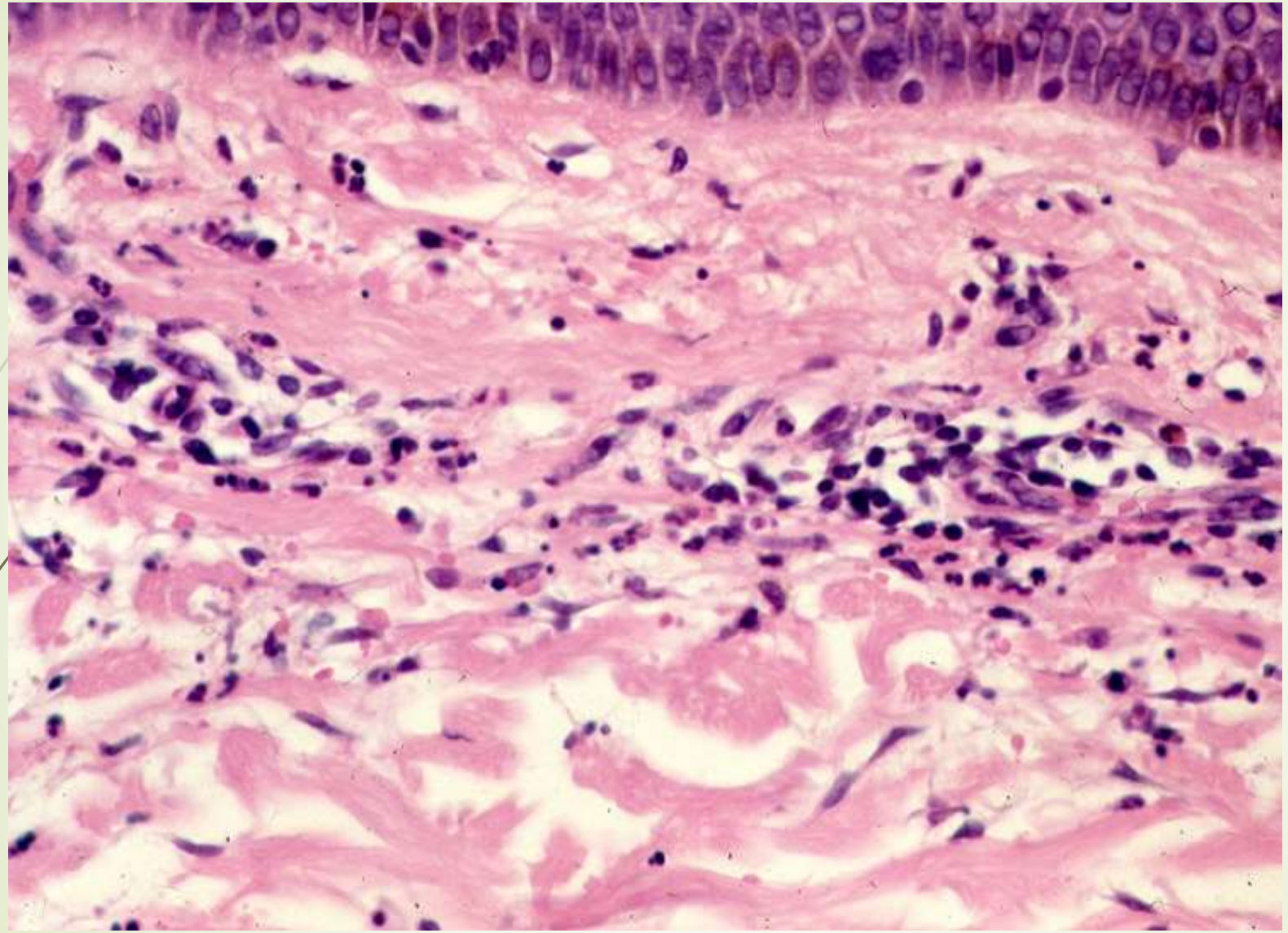




- Involvement of small vessels (arterioles, capillaries, & venules).
- all lesions of the same stage/age.
- Skin, mucous membranes, lungs, brain, heart, GIT, kidney & muscles.
- In contrast to PAN, necrotizing glomerulonephritis (90%) & pulmonary capillaritis are common

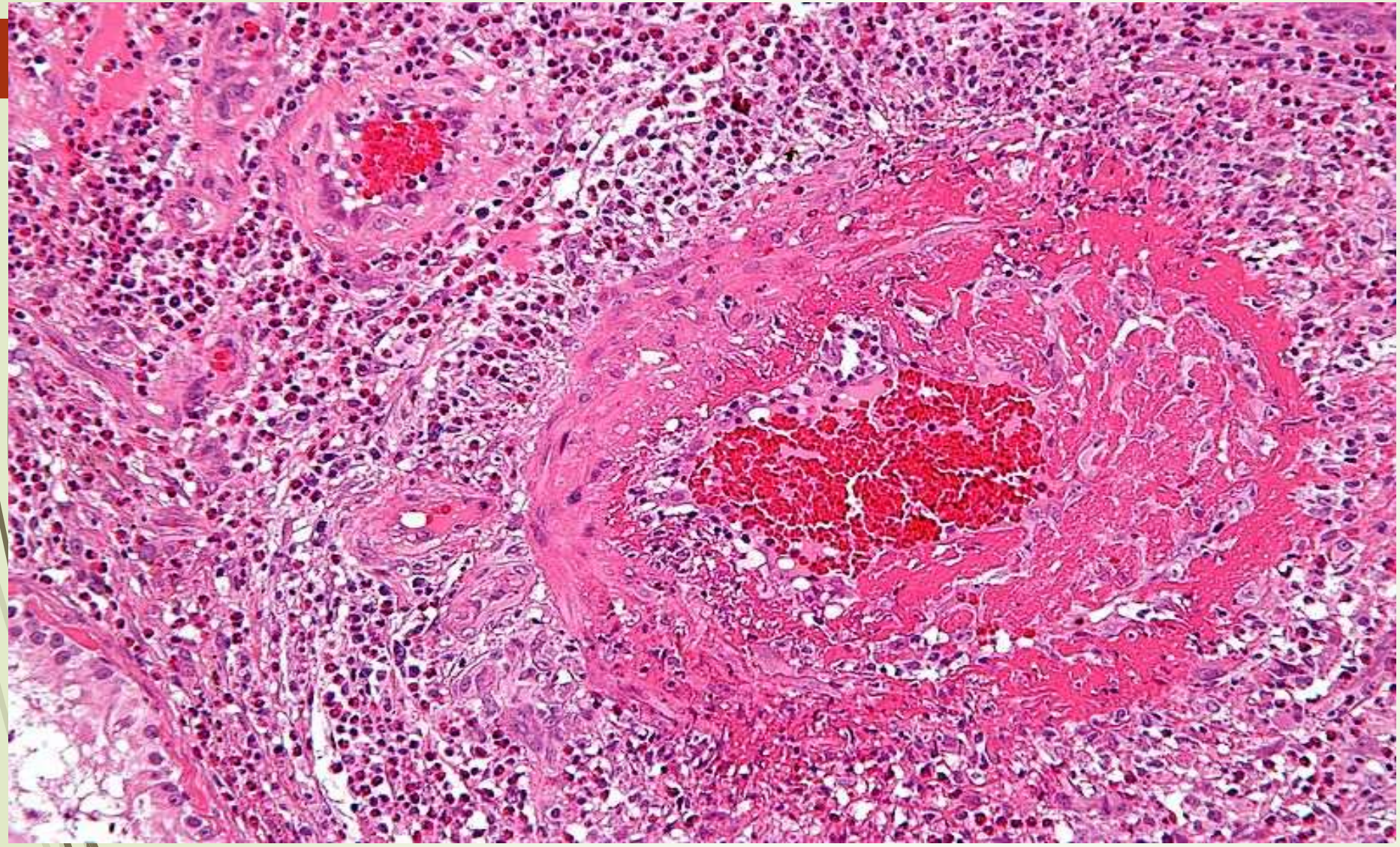
- Segmental fibrinoid necrosis of media.
- No granulomatous inflammation
- Sometimes limited to infiltration of vessel wall by neutrophils with **nuclear fragmentation (leucocytoclasia), leukocytoclasatic vasculitis.**
- A reaction to an Ag such as drugs, microorganisms or hetrologous protein in a previously sensitized patients.

- Clinical: hemoptysis, arthralgia, abdominal pain, hematuria, proteinuria, hemorrhage, & muscle pain or weakness.
- Except in brain or renal involvement most patients respond to removal of offending antigens & immunosuppression.
- Ass : Henoch -schonlein purpura, essential mixed cryoglobulinemia, vasculitis with malignancy



In allergic granulomatosis and angiitis (Churg-Strauss syndrome)

- Rare disease characterized by
  - necrotizing vasculitis accompanied by granulomas with **eosinophilic** necrosis.
  - p-ANCAs are present in A minority of patients.
  - There is a strong association with allergic rhinitis, bronchial asthma, and peripheral eosinophilia.
  - Coronary arteritis & myocarditis are the principal causes of morbidity and mortality.



Thromboangiitis obliterans (Buerger's Disease)

- A condition marked by segmental, **thrombosing**, acute & chronic inflammation of intermediate & small arteries & veins in the limbs with extension to accompanying nerves.
- Exclusively seen in heavy smokers males before the age of 35.
- Instep claudication followed by pain at rest, might end in gangrene.
- Etiology ? Endothelial cell injury by toxins in tobacco.