VASCULITIS & VASCULAR TUMORS

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Arteritis/Angiitis/Vasculitis

CLASSIFICATION OF VASCULITIS:
(1)NON-INFECTIOUS ARTERITIS :
1. Large-Vessel vasculitis [Aorta, large vessels to extremities,head & neck]
eg.(A) Temporal (Giant cell) arteritis
(B) Takayasu's arteritis (pulseless disease)
2. Medium-Vessel vasculitis [Visceral arteries & branches]
eg.(A) Polyarteritis nodosa
(B) Kawasaki's disease
3. Small-Vessel vasculitis [Arterioles, venules, capillaries] *eg*
(A) Wegener granulomatosis (granulomatosis with angitis)
(B) Churg-Strauss syndrome
(C) Microscopic polyangiitis(leucocytoclastic)

Mechanisms of Non Infectious arteritis

- ***IMMUNE COMPLEX DEPOSITION :*** *(A) SLE, PAN assoc with immune complex mediated vasculitis. Circulating Ag-Ab complexes seen. (B) Drug hypersensitivity assoc with immune complex deposition (C) Viral infections, Ab to viral proteins forms immune complexes*
- ***ANTINEUTROPHIL CYTOPLASMIC ANTIBODIES:*** *ANCAs autoAb against neutrophil primary granules, endothelial cells. (A) MPO-ANCA / p- ANCA seen in microscopic polyangiitis & Churg-Strauss syndrome (B) PR3-ANCA / c-ANCA seen in Wegener granulomatosis*

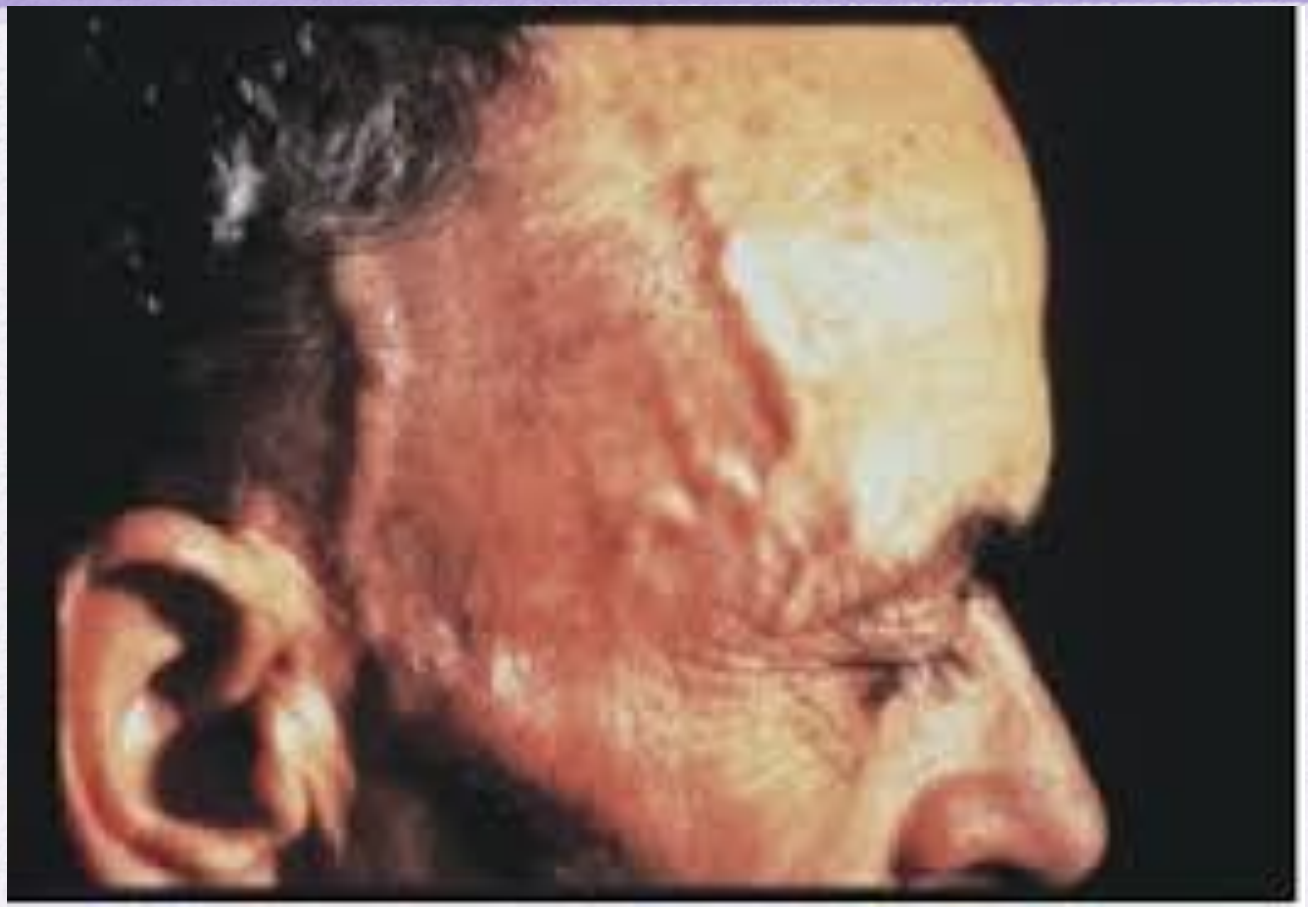
Mechanisms of Non Infectious arteritis

- ***How ANCA acts:*** *Drugs or Bacterial antigens induce ANCA formation → Subsequent infection →Release of cytokines(surface expression of PR3 & MPO)*
  ANCA's react with cytokine activated cells leading to direct injury (of endothelial cells / further activation of neutrophils)
- *Increased ANCA titres associated with Disease activity*
- ***ANTI-ENDOTHELIAL CELL ANTIBODIES :*** *(A) have been identified in Kawasaki disease.*

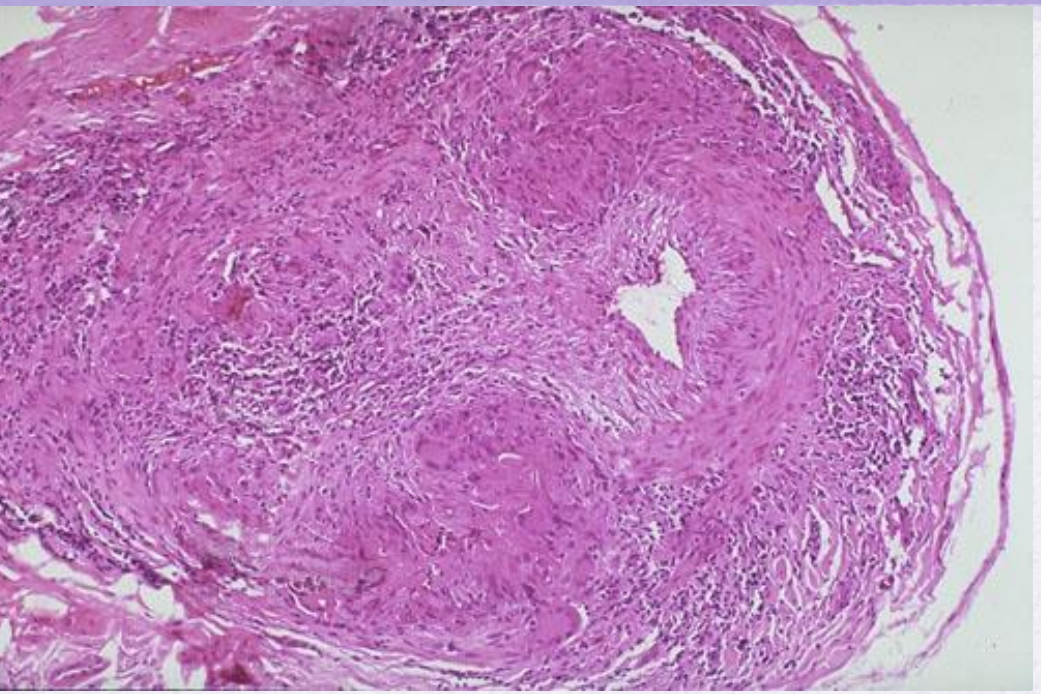
Giant cell/ Temporal Arteritis

- *Granulomatous inflammation of large arteries of the head esp Temporal, also vertebral, ophthalmic arteries.*
- *Morphology: nodular thickening. Granulomatous inflammation of the media with fragmentation of the internal elastic lamina.*
- *Pathogenesis: T cell mediated immune response against Ag in vessel wall.*
- *Clin Features : Elderly patients. Constitutional symptoms. Facial pain, intense headache along the course of the Superficial Temporal artery.*

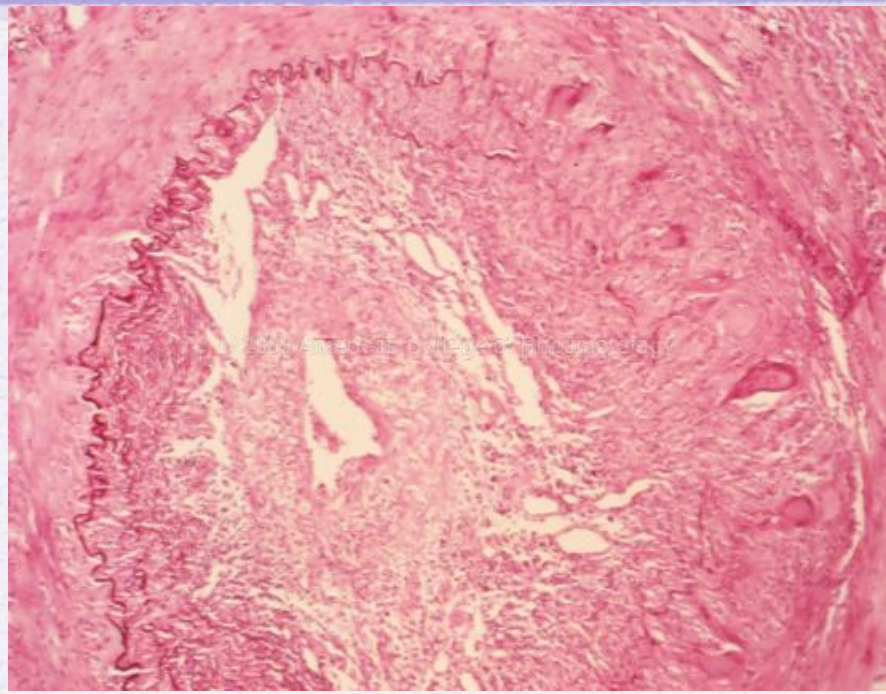
Giant cell Arteritis(Nodular thickening of the Superficial Temporal Artery)



Giant cell Arteritis



Granulomas in the Arterial wall



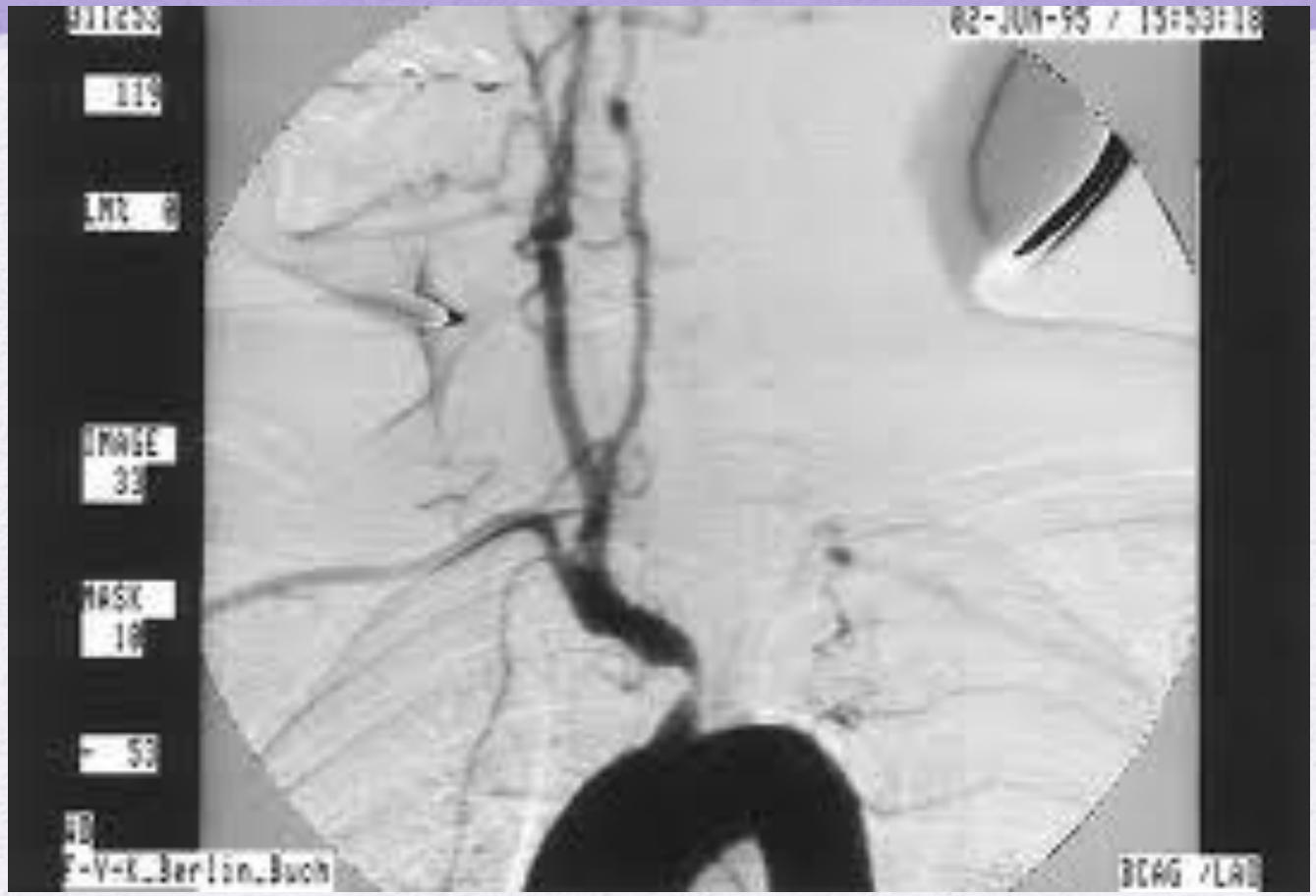
Destruction of the Internal Elastic Lamina on Giant cell arteritis

Takayasu Arteritis

- Granulomatous arteritis of medium & large arteries. Ch by transmural fibrous thickening of the aorta(a.arch & great vessels) with severe luminal narrowing of the branches

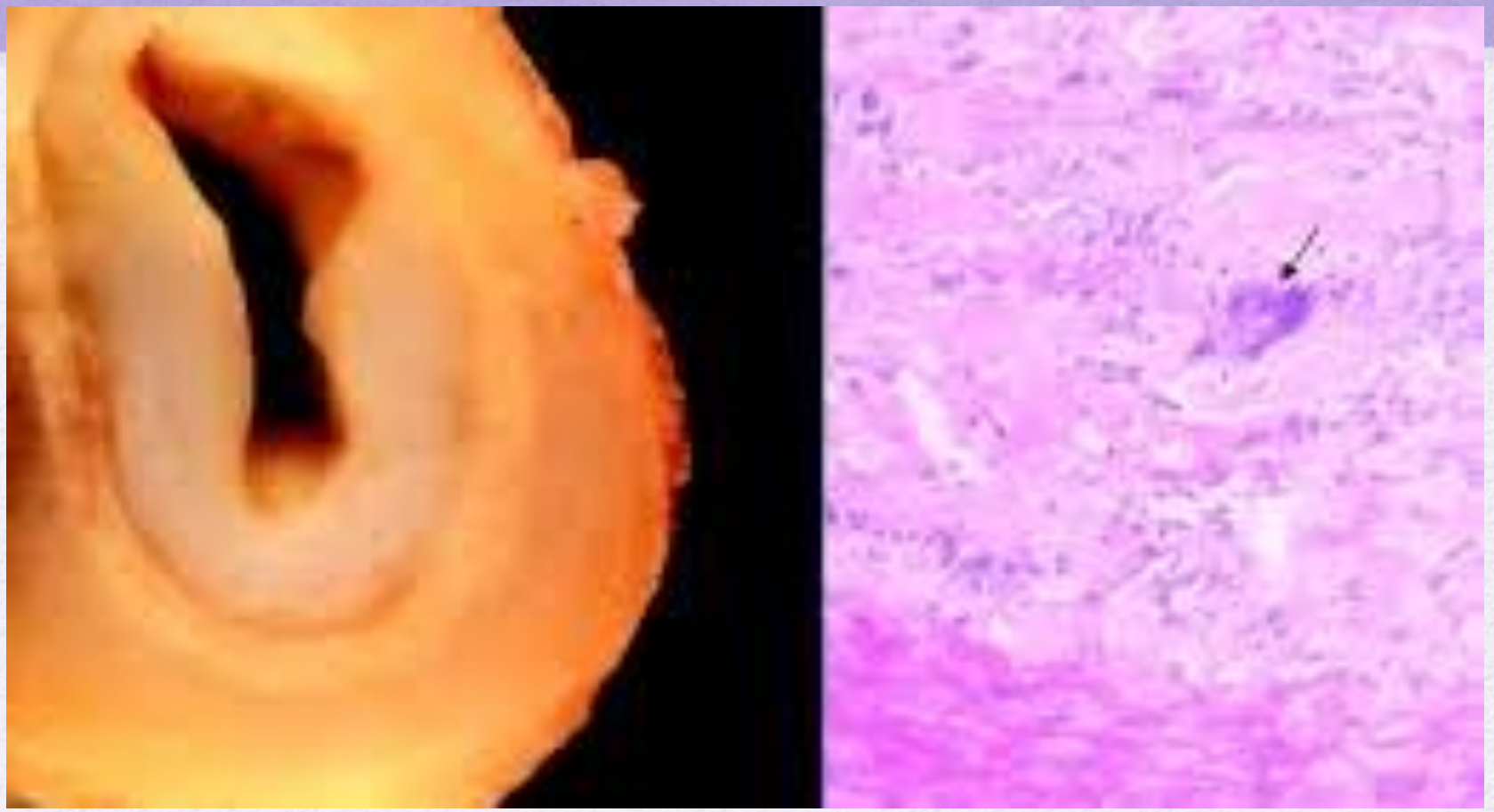
- **Clin Feat:** Fever, easy fatiguability, Vascular symptoms: reduced blood pressure, weakened pulses in upper extremities(pulseless disease), visual defects, blindness, neurologic defects.
  Distal aorta➔Intermittent claudication
  Coronary ostia➔ Myocardial infarction
  Renal artery ➔Systemic hypertension

Takayasu arteritis



Contrast enhanced Angiography showing critical narrowing in Takayasu arteritis

Takayasu arteritis



Gross & Histological picture of Innominate Artery in Takayasu arteritis

POLYARTERITIS NODOSA

- Necrotising vasculitis involving medium sized muscular and small arteries of multiple organs & tissues.
- Organs usually affected are kidneys, heart, liver, GIT, muscle , pancreas, testes, nervous system & skin. ***LUNG IS SPARED***
- Symptoms depend on the organ of involvement: renal(albuminuria, hematuria, renal failure) GIT(abdominal pain, malena) peripheral neuritis, hypertension.
- Pathogenesis: Deposition of Immune complexes(HbsAg-HbsAb complexes seen in 30% patients) & tumor related antigens

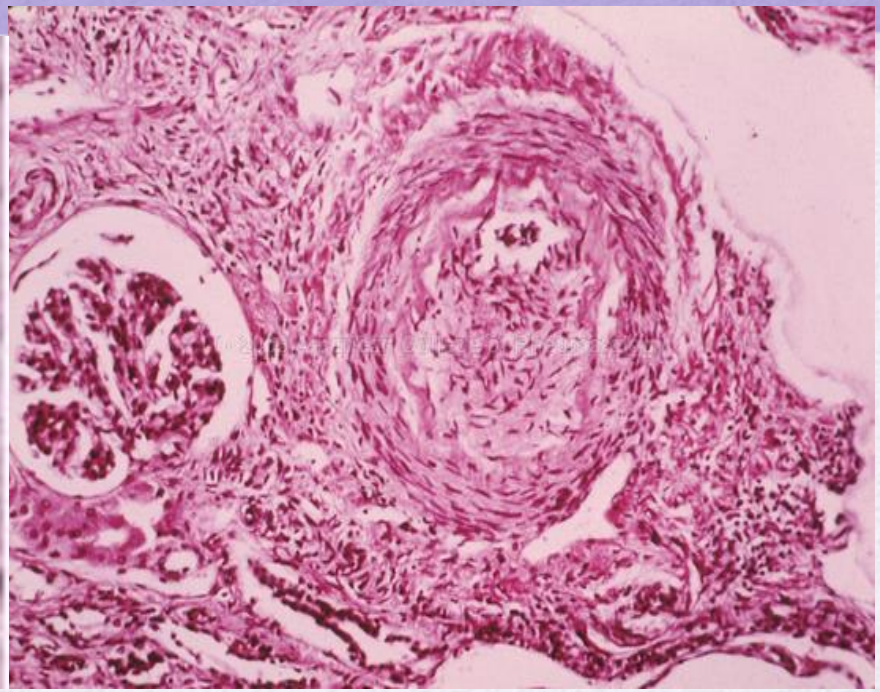
PAN (contd)

- *Gross appearance*: Segemental involvement of vessels , Beaded appearance

- *Microscopic appearance:* 3 stages. **(i)Acute Stage:** Fibrinoid necrosis in the media along with acute inflammatory cells. Periarteritis. Thrombus in the lumen
  (ii) Healing Stage : Marked fibroblastic proliferation producing nodularity. Lymphocytes, plasma cells & macrophages seen.
  (iii) Healed Stage: Thickened arterial wall due to dense fibrosis. Internal elastic lamina is fragmented/lost. Hemosiderin laden macrophages & organised thrombus.

PAN(contd)

PAN, Early stage showing fibrinoid necrosis & thrombus

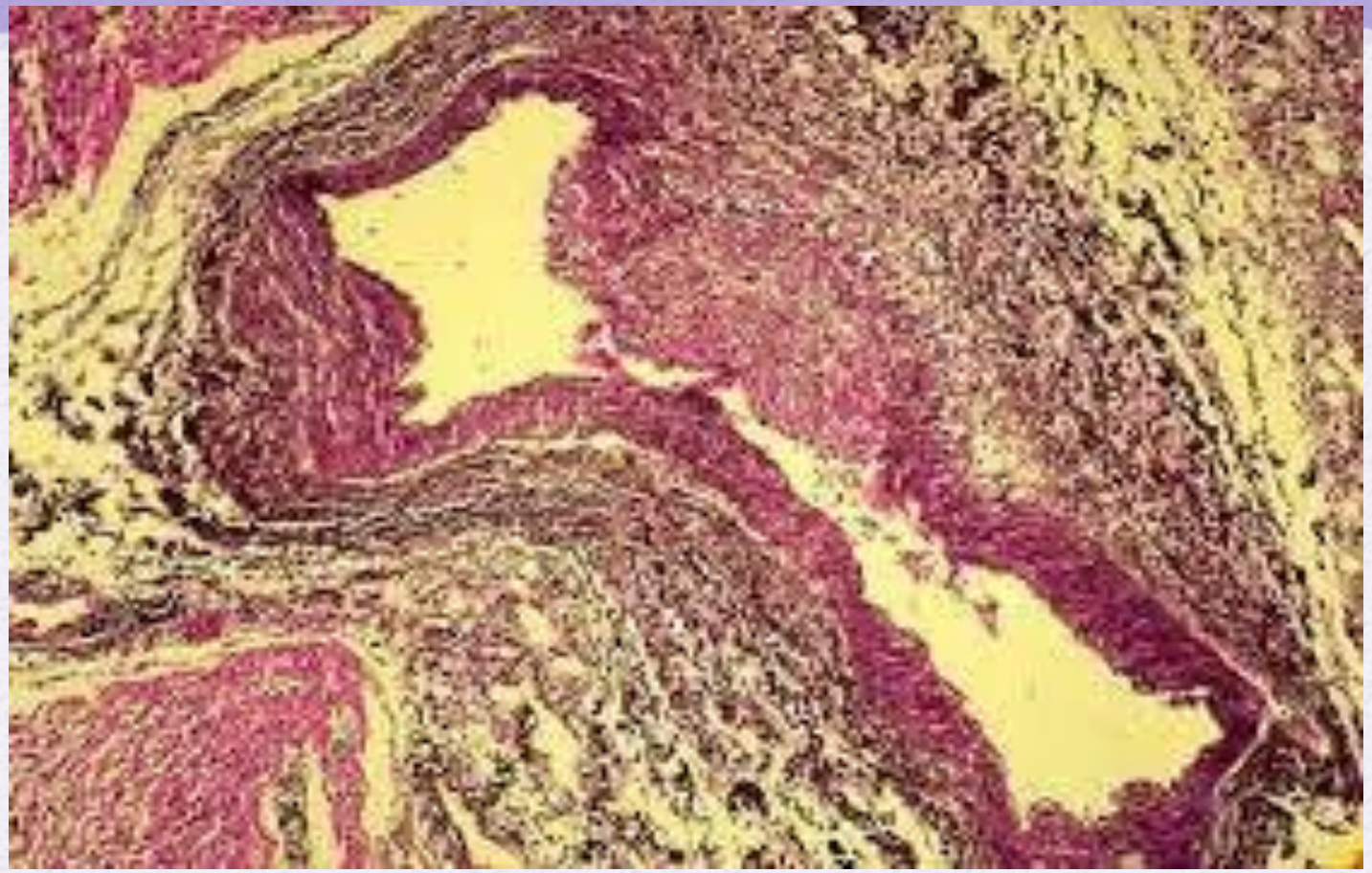


PAN, Healing stage with focal interruption of the Internal Elastic lamina

Kawasaki disease

- Vasculitis of medium sized & small arteries
- Prediliction for coronary arteries, in children
  Coronary arteritis ➔ Aneurysm formn, thrombosis➔ Myocardial infarction.
  Associated with erythema, desquamative rash & cervical lymphnode enlargement.
- Pathogenesis: Unknown Ag(infectious agent/virus)➔Act of T cells, Prodn of cytokines, Polyclonal B cell activation ➔ AutoAb to endothelial cells & smooth muscle cells➔ Acute vasculitis

Kawasaki disease



Kawasaki disease in a Coronary artery showing Segmental necrosis & inflammation

Microscopic polyangiitis

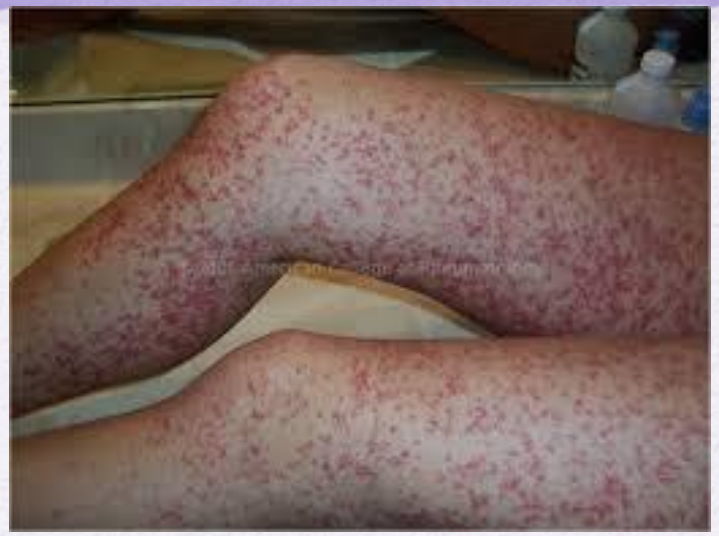
- ***Hypersensitivity vasculitis / Leucocytoclastic vasculitis***
- *Necrotizing vasculitis affecting capillaries, arterioles & venules*
- *Involves: Skin, mucous membranes, lungs, brain, heart, GIT, muscle, kidneys.[**Clin Feat:** hemoptysis, hematuria, purpura, abdominal pain, muscle weakness]*
- *Disorders like **Henoch-Schonlein purpura, Essential mixed cryoglobulinemia,** Vasculitis associated with connective tissue disorders, **Necrotizing glomerulonephritis.***

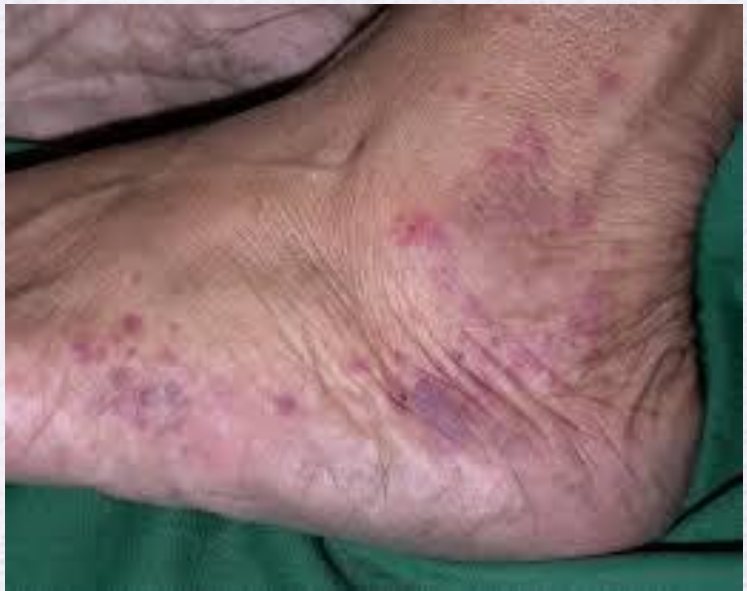
Microscopic polyangiitis

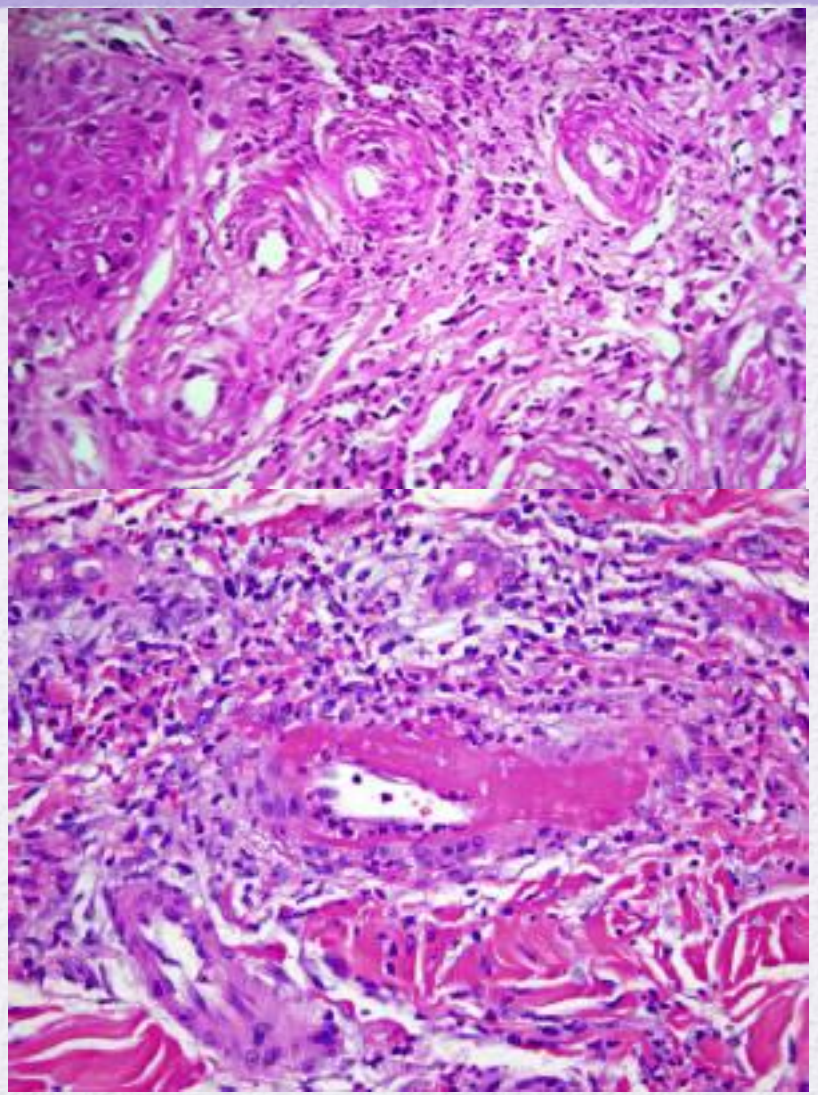
- **Pathogenesis:** Offending Ag, eg drug(penecillin), micro organism(Streptococci)➔Immune complex deposition or Sec immune response eg formation of p-ANCA➔ activation & influx of neutrophils.

- **Morphology:** (1) Infiltration & fragmented neutrophils in walls of small vessels(leucocytoclastic)
  (2) Segmental fibrinoid necrosis of the media with focal transmural necrosis.

Microscopic polyangiitis







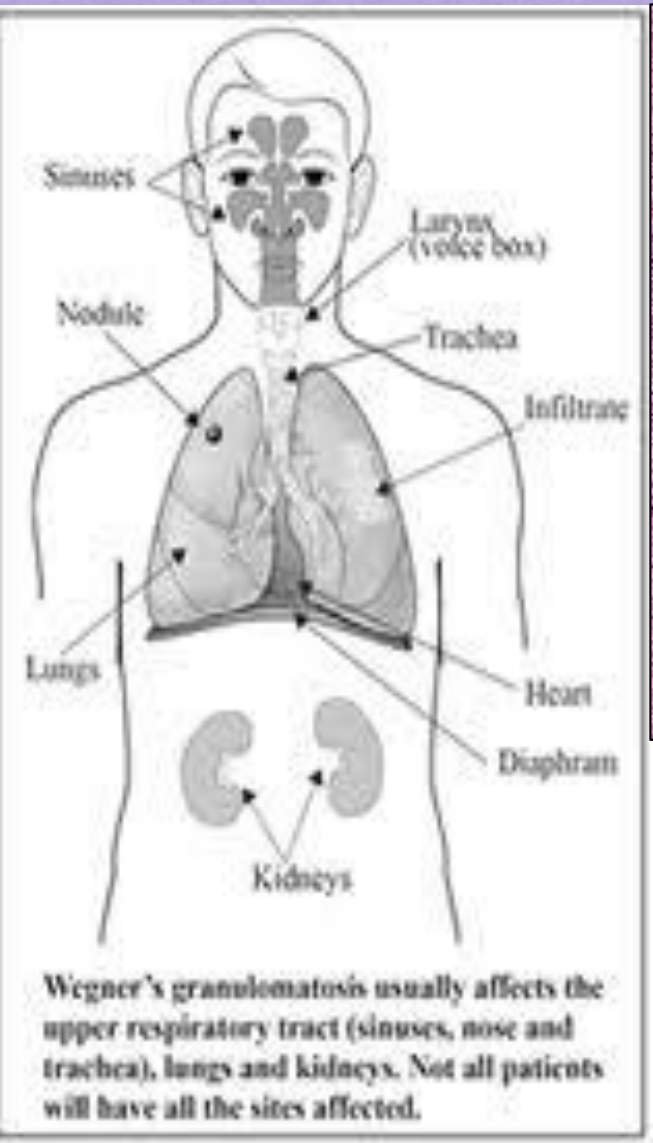
Wegener granulomatosis

- *Necrotizing vasculitis characterized by*
  (1) Acute necrotizing granulomas upper resp tract(nose, sinuses, throat) lower respiratory tract(lung)
  (2) Necrotizing/granulomatous vasculitis affecting small to medium sized vessels(lungs & upper airways)
  (3) Renal- Focal, necrotizing, cresentric glomerulonephritis

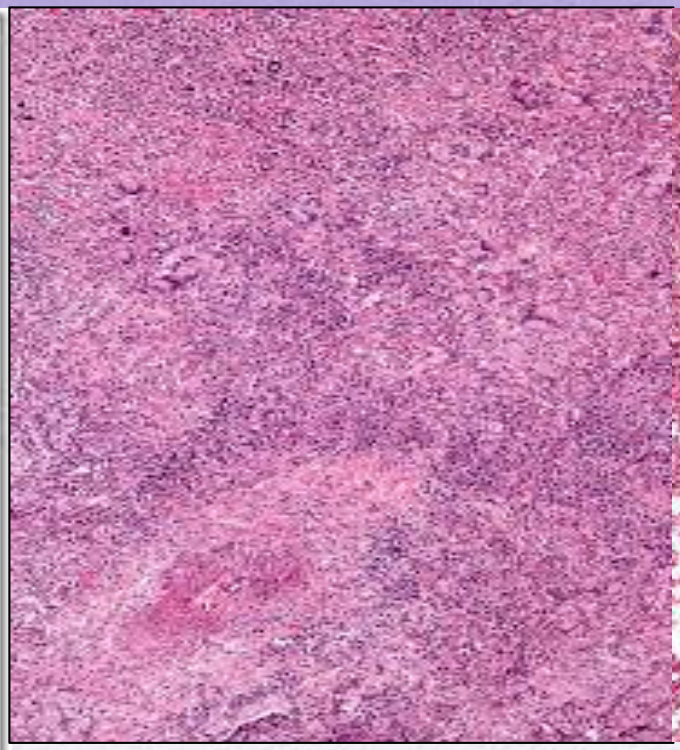
- ***Pathogenesis:*** *T cell mediated hypersensitivity reaction to an inhaled infectious / environmental agent*
  PR3-ANCA (c-ANCA) detected in most cases

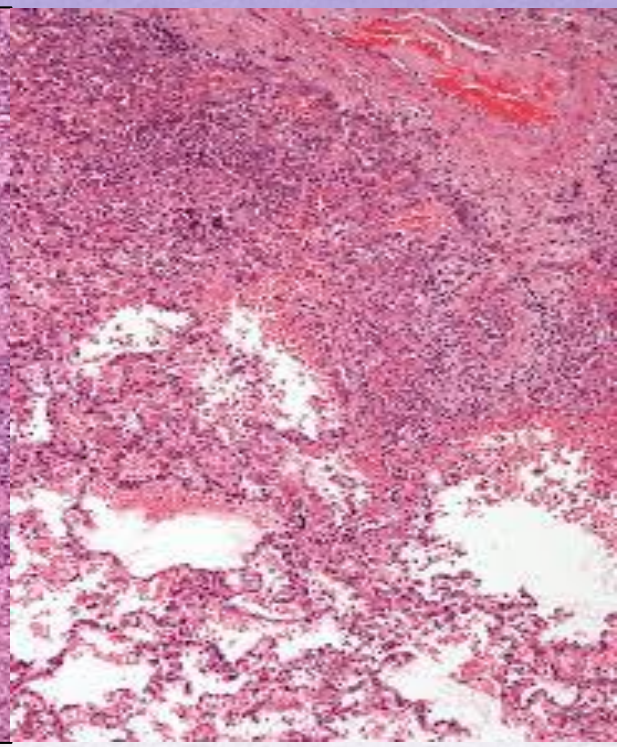
- ***Morphology:*** *Necrotizing granulomas, vasculitis, geographic patterns of necrosis*

Wegener granulomatosis



Wegner's granulomatosis usually affects the upper respiratory tract (sinuses, nose and trachea), lungs and kidneys. Not all patients will have all the sites affected.



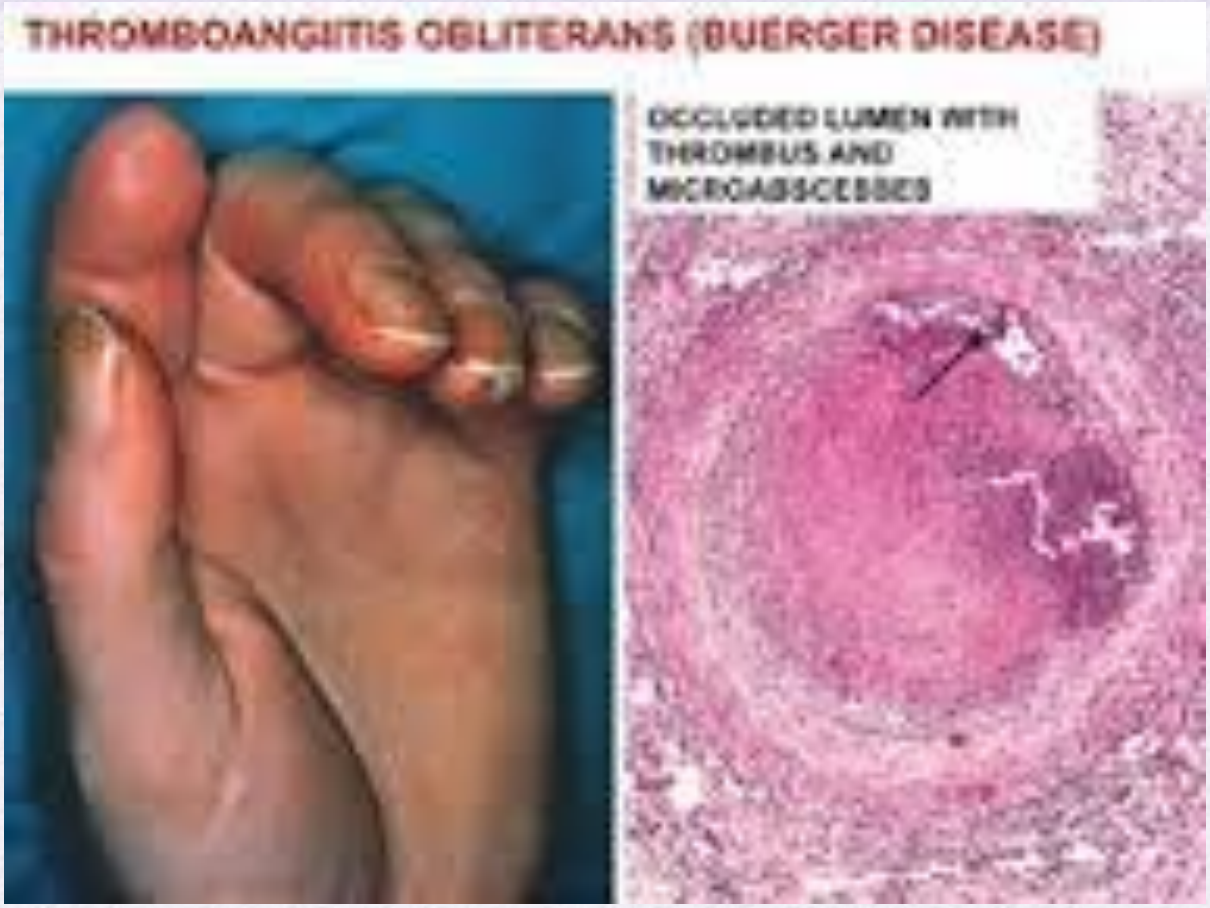


Necrotizing granulomas with multinucleated giant cells & vasculitis

Thromboangitis obliterans(Buerger disease)

- *Acute inflammatory occlusion ofsmall/medium sized arteries(tibial & radial) extending to veins & nerves*
- *Associated with heavy cigarette smoking. Direct endothelial cell toxicity*
- *Clinical features: Nodular phlebitis, Raynaud's phenomenon, severe pain, even at rest → Peripheral vascular insufficiency*
- *Morphology: Acute/chronic inflammation in the vessel wall & luminal thrombus formation with microabscesses*

Thromboangiitis Obliterans



Churg-Strauss syndrome

- ***Allergic granulomatosis & angiitis***
- *Small vessel necrotizing vasculitis associated with asthma, eosinophilia, lung involvement, necrotizing granulomas. MPO-ANCA (p-ANCA) seen in some cases.*
- *Involves skin, GIT, kidney, heart.*
  Clinical Features: *Purpura. GI bleeding, proteinuria, hematuria, cardiomyopathy*

Infectious Arteritis

- ***INFECTIOUS ARTERITIS***
  1. Endarteritis Obliterans : *non specific inflammatory response of arteries & arterioles seen close to peptic/duodenal ulcer sites, chronic lung abscesses, chronic meningitis etc.* ***Ch by obliteration of vessel lumina.***

- ***2. Non-syphilitic infective arteritis:*** *Invasion of vessel wall by bacteria/fungi eg Mucormycosis* ***Ch by vessel wall inflammation, obliteration & ischemic necrosis of the tissue supplied.***

- ***3. Syphilitic arteritis:*** *Ascending aorta & aortic arch* ***Ch by endarteritis & periarteritis of the vasa vasorum.***

VASCULAR TUMORS

- Tumors – Benign/Intermediate/Malignant

(A) Endothelial cells

(B) Pericytes

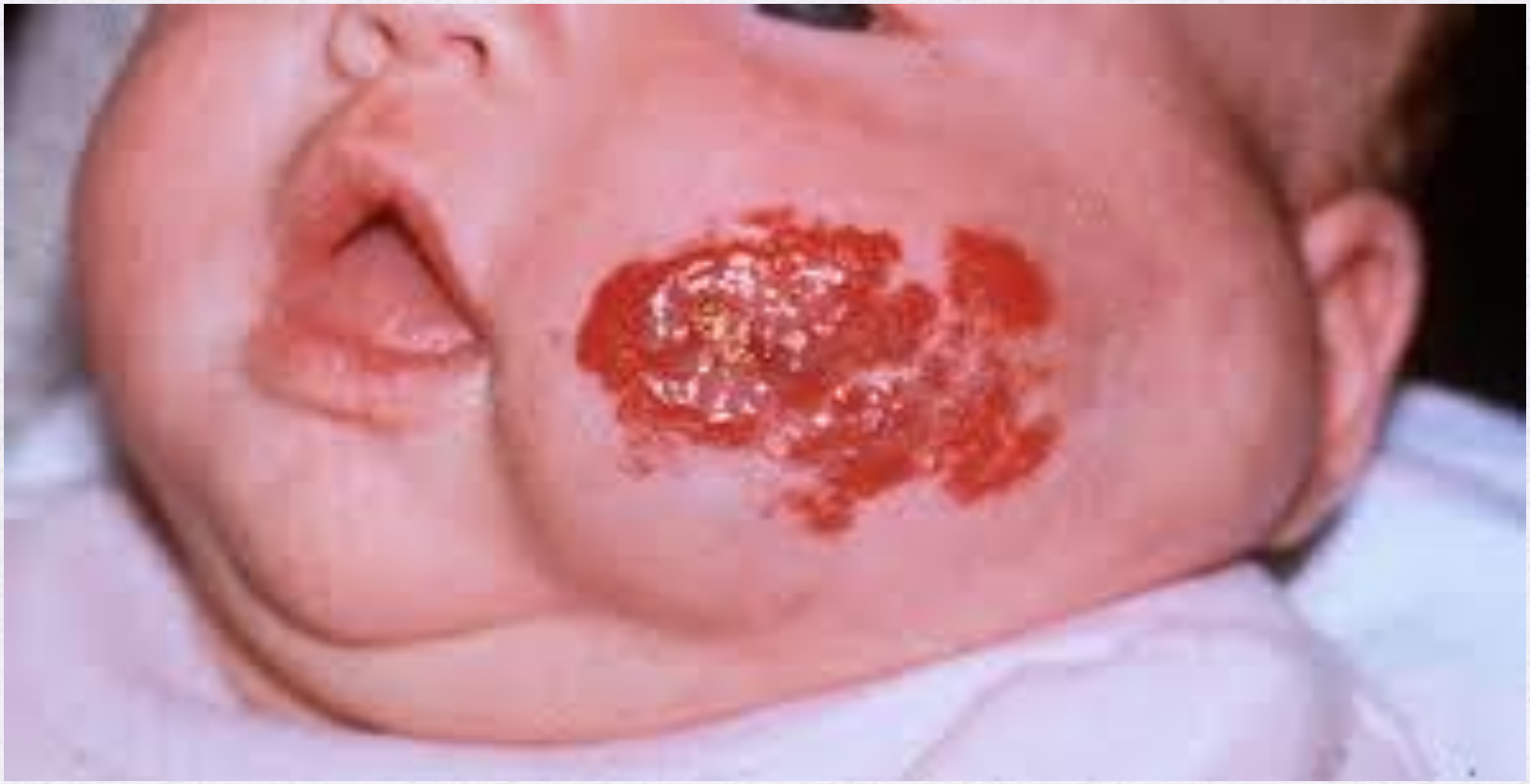
(C) Glomus body

- Congenital malformations
- Tumor like conditions: Ectasias
- Reactive vascular proliferations

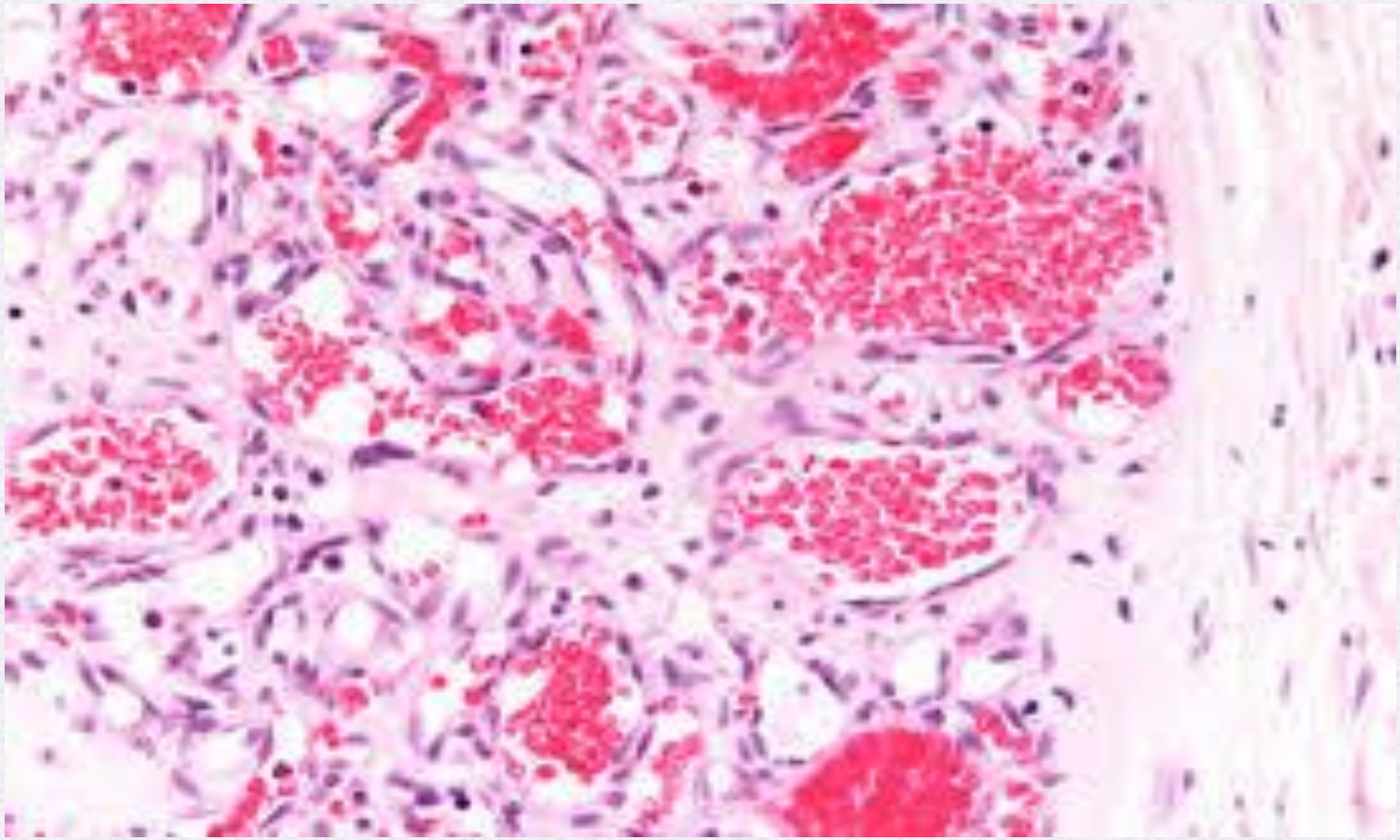
Benign Tumors & Tumor-like lesions

(1) Hemangiomas : *Increased numbers of normal or abnormal vessels filled with blood. Superficial locations like head & neck. Internal organs eg liver. Histologic variants:*
(a) Capillary Hemangioma*. Skin/mucus membranes 7% of all benign tumors of infancy. Spontaneous regression. Morphology: Closely packed thin walled capillaries with flattened endothelial cells, filled with rbc's.*
(b) Cavernous Hemangioma: *Large dilated vascular channels, seen in organs like liver & brain.Thrombus formn/Dystrophic calcific, Do not regress spontaneously. "von Hippel Lindau disease" in which cav hemangiomas are seen in cerebellum, retina, liver, pancreas*

Gross app: *Capillary Hemangioma*

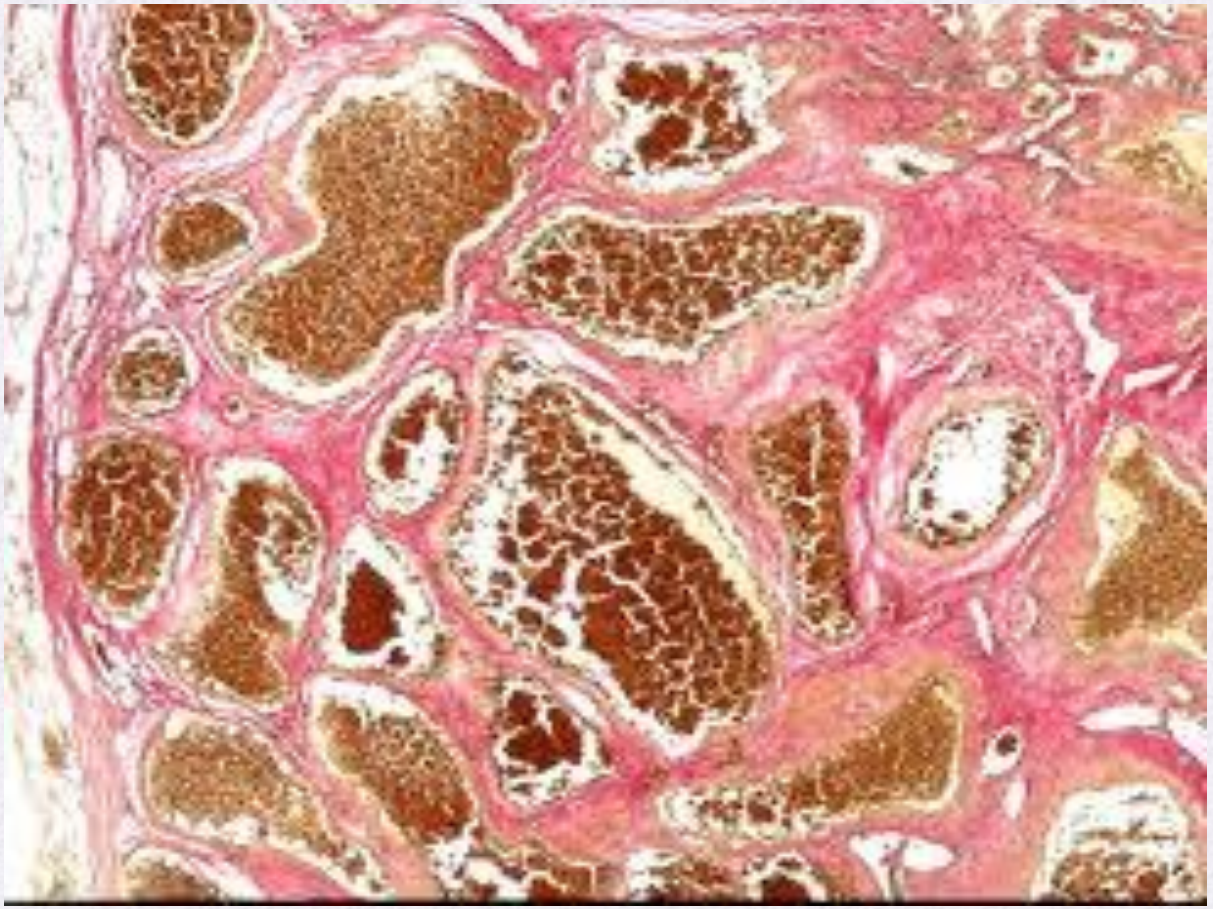


Histology:*Capillary Hemangioma*



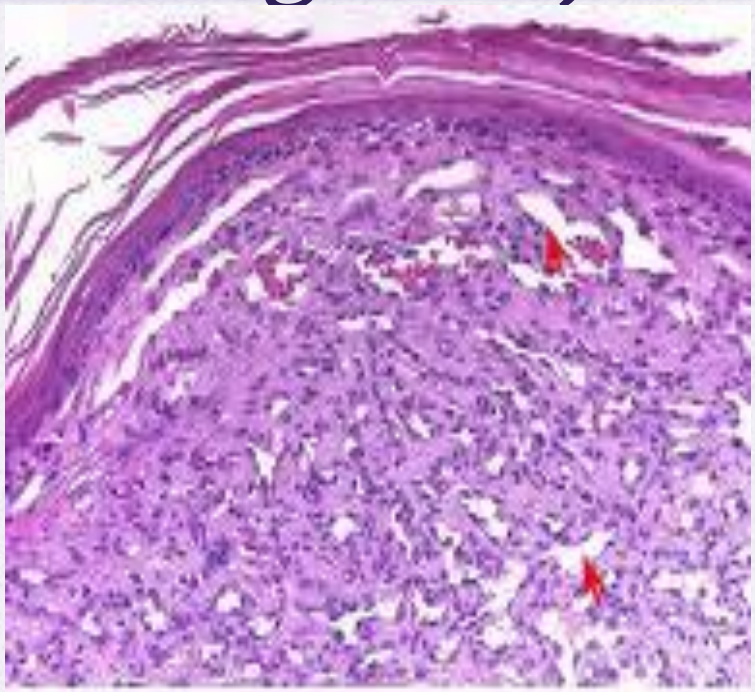
Gross App: *Cavernous Hemangioma, brain*

Histo: *Cavernous Hemangioma*



Gross: *Pyogenic Granuloma(Lobular capillary hemangioma)*

Histo: *Pyogenic Granuloma(Lobular capillary hemangioma)*



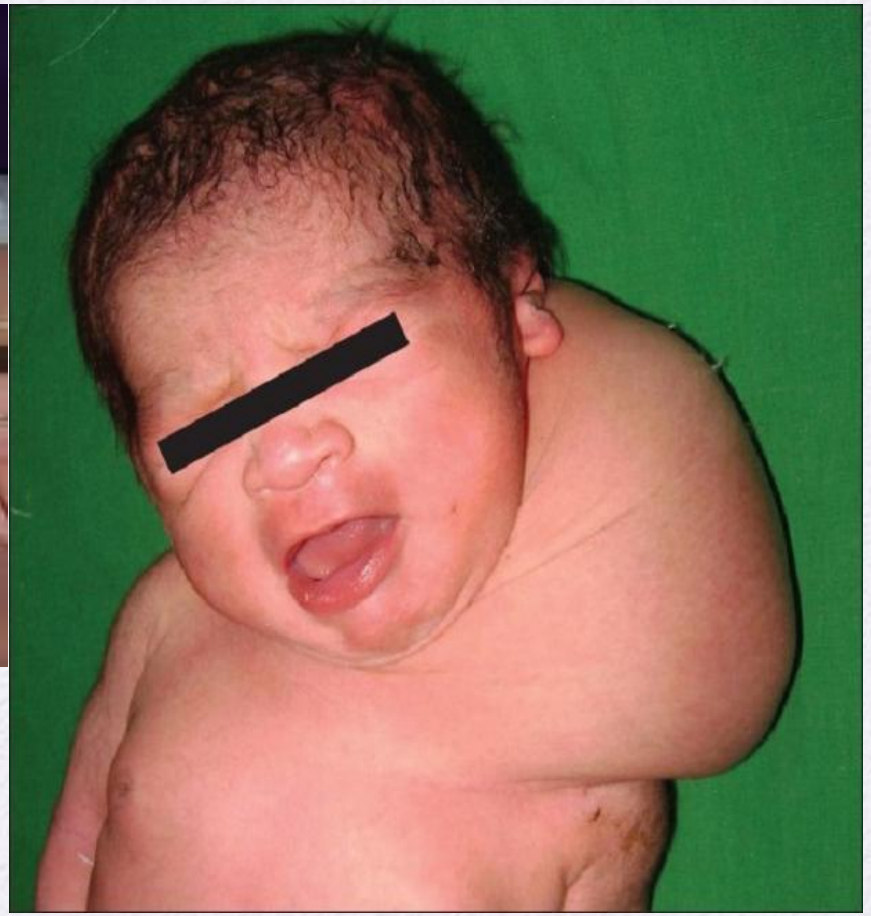
Capillary vessels

Lymphangiomas

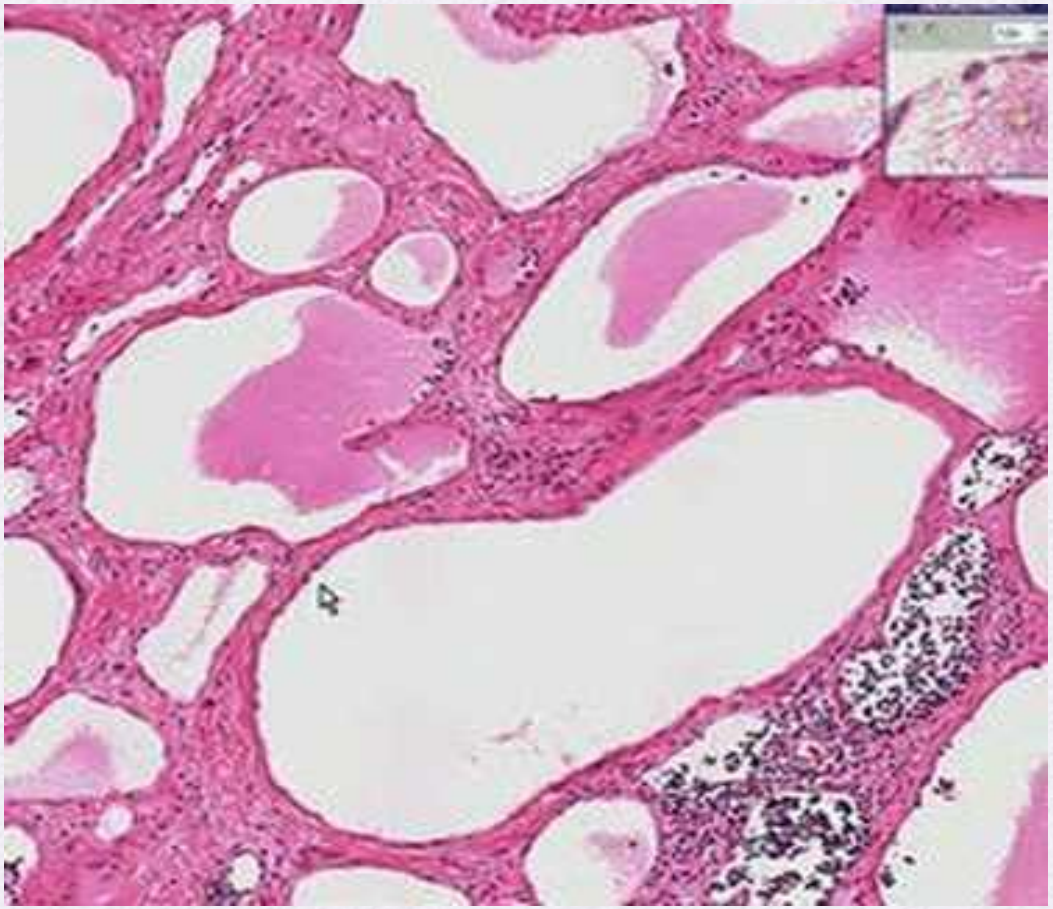
1. ***Capillary(Simple) Lymphangiomas*** *– seen in head, neck & axilla. Distinguished from Capillary Hemangioma by the absence of RBC's.*

2. ***Cavernous Lymphangiomas(Cystic Hygroma)*** *– Neck or Axilla of children, can be large producing deformities in the neck. Morphology: Dilated lymphatic spaces lined by flattened endothelial cells with lymphoid aggregates in the walls. Turner's syndrome*

Gross App: *Cystic Hygroma(Cavernous Lymphangioma)*



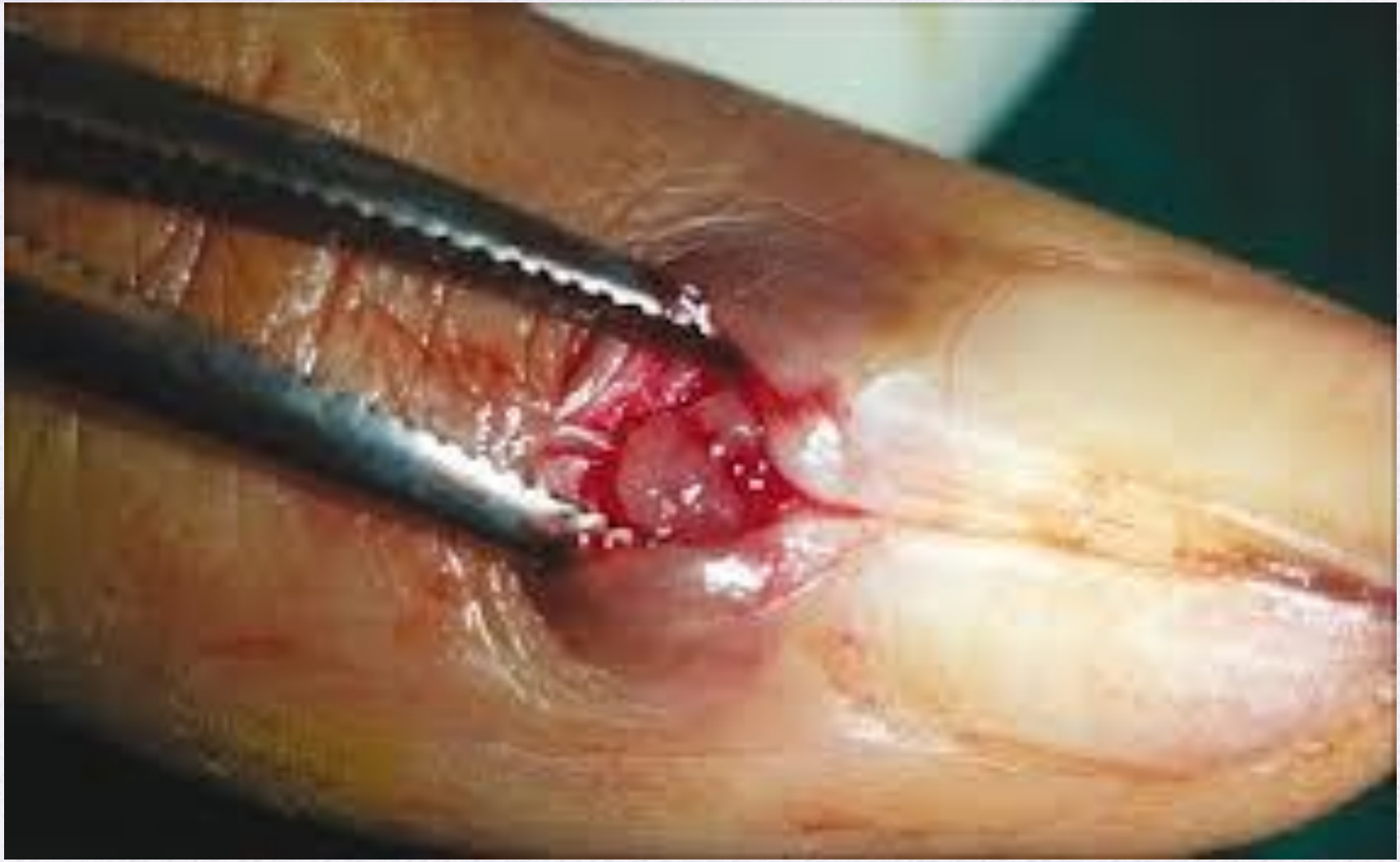
Histology: *Cystic Hygroma(Cavernous Lymphangioma)*



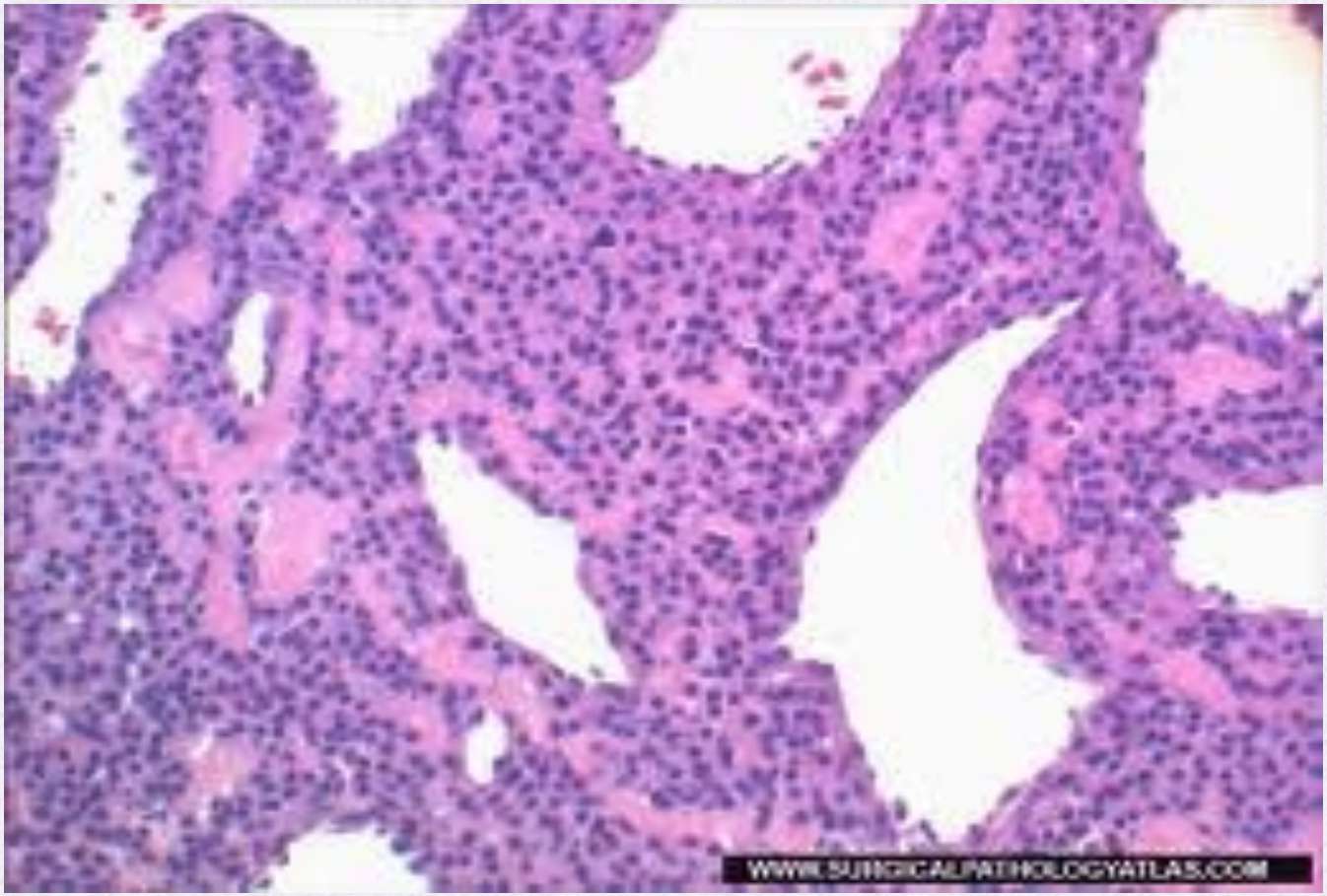
Glomus tumor (Glomangioma)

- Small solitary painful lesion arising from ***Glomus body*** (present in dermis – role in temperature regulation)
- Location: hand, foot under fingernails & on tympannic membrane
- Morphology: Aggregates & nests of specialized glomus cells closely related to branching vascular channels.

Gross: *Glomus tumor(Glomangioma)*



Histology: *Glomus tumor (Glomangioma)*



Bacillary Angiomatosis(BA)

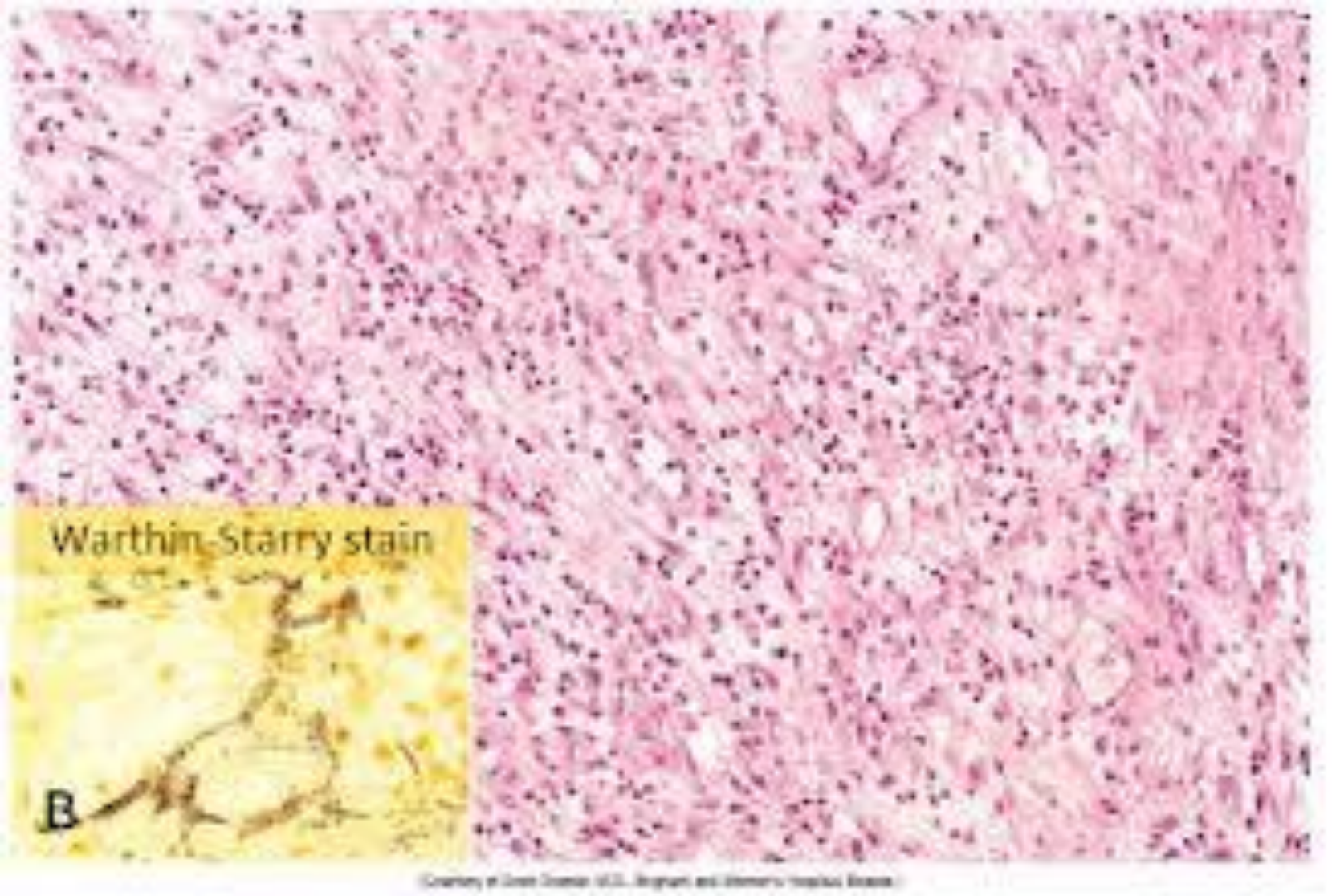
- BA is a vascular proliferation/angiomatosis assoc with infection of the ***'Bartonella'*** genus.
- Caused by ***Bartonella henselae*** – mostly transmitted by cat scratch/bite(*Causative org-Cat Scratch disease*)***Bartonella quintana***-transmitted by human body lice (*Causative organism of Trench fever*)
- Seen in AIDS & immunocompromised pts.
- Characterized by tumor like masses formed by the proliferation of blood vessels in the skin & organs like bone, brain.

Bacillary Angiomatosis(BA)

- **Clinical presentation:** Papules/ Nodules which are red, globular, non-blanching. Lichenoid plaques. Subcutaneous nodules.
- **Microscopic picture**: Proliferation of capillaries with plump endothelial cells showing mitosis. Neutrophils, nuclear debris see. Causal organism seen on special stains (Warthin-Starry)
- **Mechanism:** Bacteria➔ Induction of host *Hypoxia inducible factor 1 alpha* ➔VEGF production➔ capillary proliferation.

Gross App: *Bacillary Angiomatosis*

Histology:*Bacillary Angiomatosis*



Intermediate grade tumors- Kaposi Sarcoma (KS)

- KS: *'AIDS defining illness'* 4 forms are known
- **(1) Chronic/ Classic KS :** Not associated with AIDS. East European, plaques/skin nodules l limbs. Remain localized
- **(2) Lymphadenopathic/ African KS:** Younger pts.Not assoc with AIDS. Assoc with lymphadenopathy. Aggressive form of KS which involves the viscera.
- **(3) Transplant-associated KS:** in solid organ transplantation when the pt is immunosuppressants
- **(4) AIDS associated/ Epidemic KS**: Most common malignancy in AIDS patients. Involves lymph nodes, viscera, wide dissemination.

Kaposi Sarcoma (KS)

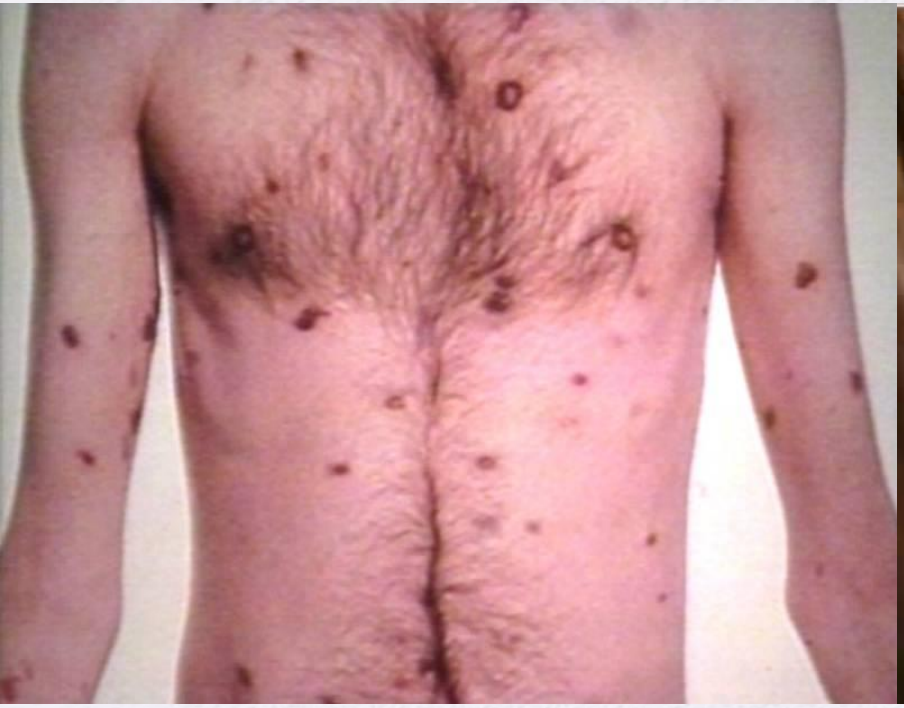
- **Pathogenesis:** Human herpesvirus-8(HHV-8) or KS associated herpesvirus(KSHV) identified in cutaneous KS lesion in AIDS. Also in 95% of all KS lesions.

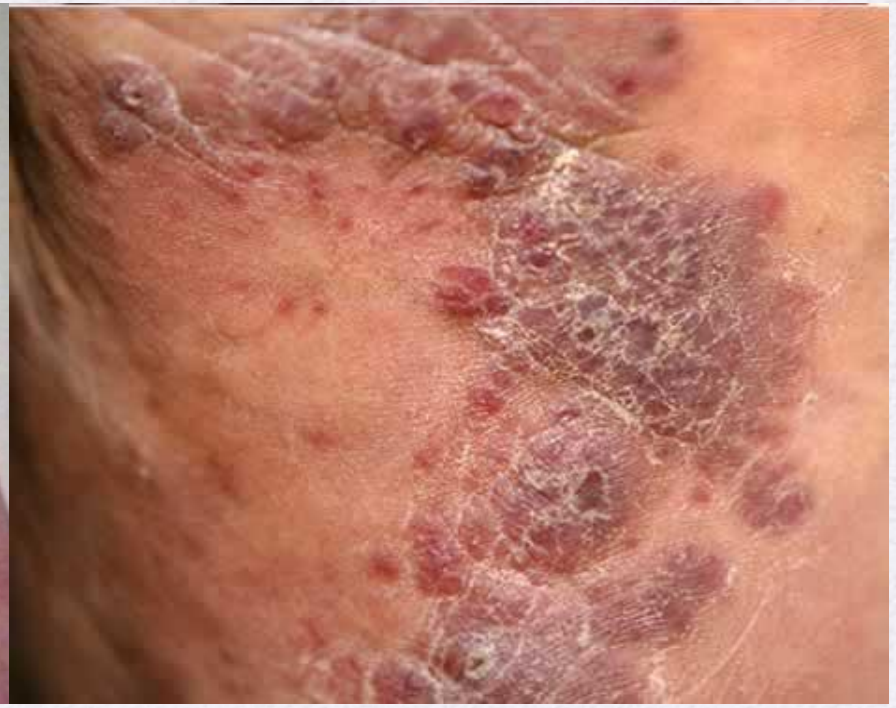
- Induction of a lytic & latent infection in endothelial cells
  (a) Lytic infection➔ Release of cytokines from HIV infected T cells. Induction of VEGF by virally coded G protein
  (b) Latent infection➔ Disruption of proliferation controls by KSHV proteins

Kaposi Sarcoma (KS)

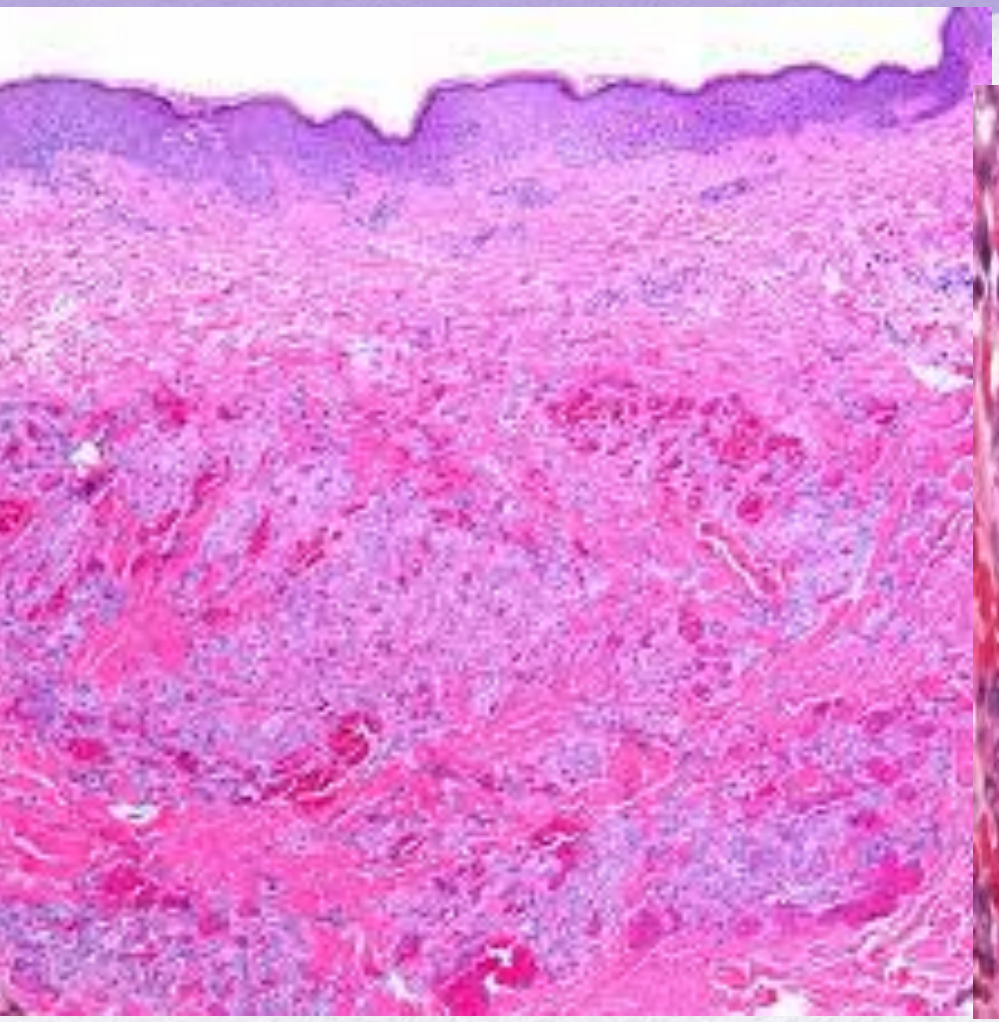
- **Morphology:** 3 stages- Patch, Plaque, Nodule
- **Patch stage:** reddish, purple patches in lower limbs showing dilated irregular vascular spaces lined by endothelial cells, inflammatory cells, Can be confused with granulation tissue.
- **Plaque stage:** Large violaceous raised plaques ch by dilated irregular vascular channels surrounded by plump spindle cells. Inflammatory cells, extravasated rbc's & hemosiderin laden macrophages
- **Nodule stage:** Plump, proliferating spindle cells, slit like vessels with rbc's, inflammatory cells, hemorrhages, hemosiderin pigment

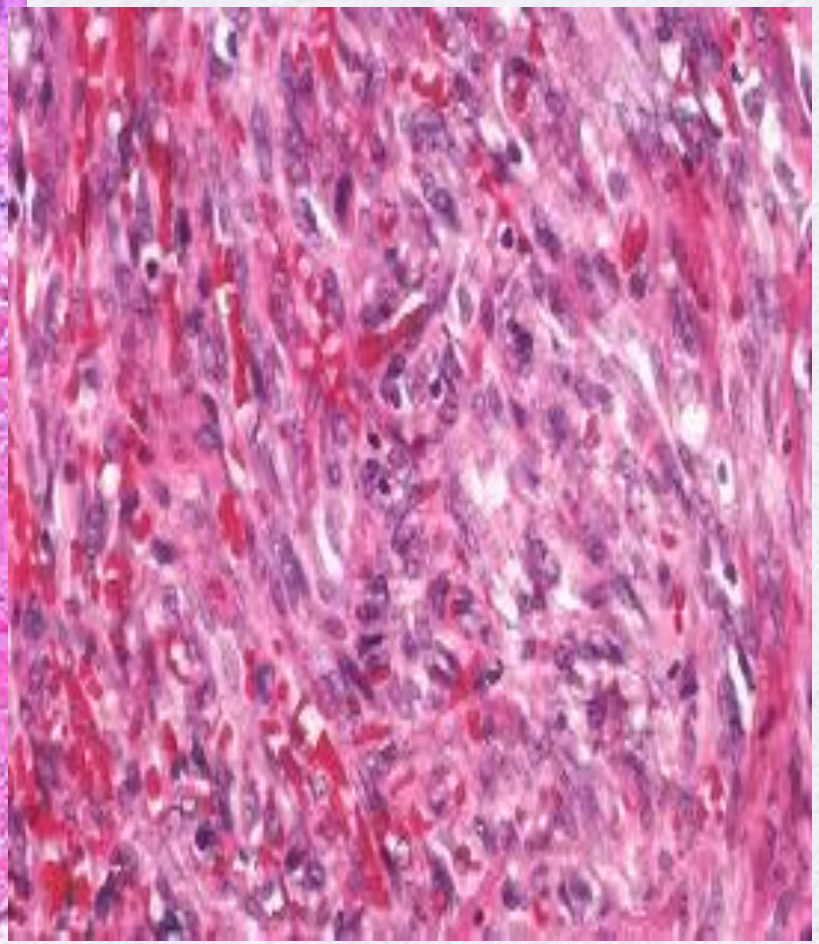
Gross App:*Kaposi Sarcoma (KS)*





Histology: *Kaposi Sarcoma (KS)*





Intermediate grade & Malignant Vascular Tumors

- HEMANGIOENDOTHELIOMA Intermediate grade
- ANGIOSARCOMA:(malignant tumor of endothelial cells) common sites are skin, soft tissues, breast, liver.
- HEMANGIOPERICYTOMA:(malignant tumor of the pericytes) common sites are retroperitoneum and lower extremities.

Aneurysms

- Localized abnormal dilatation of a blood vessel.
- (1) True Aneurysm (saccular)
- (2) True Aneurysm (fusiform)
- (3) False Aneurysm/Dissecting Aneurysm – defect in vascular wall➔ extravascular/pulsating hematoma
- (4) Dissection – dissecting hematoma between the layers of the vessel wall

Aneurysms

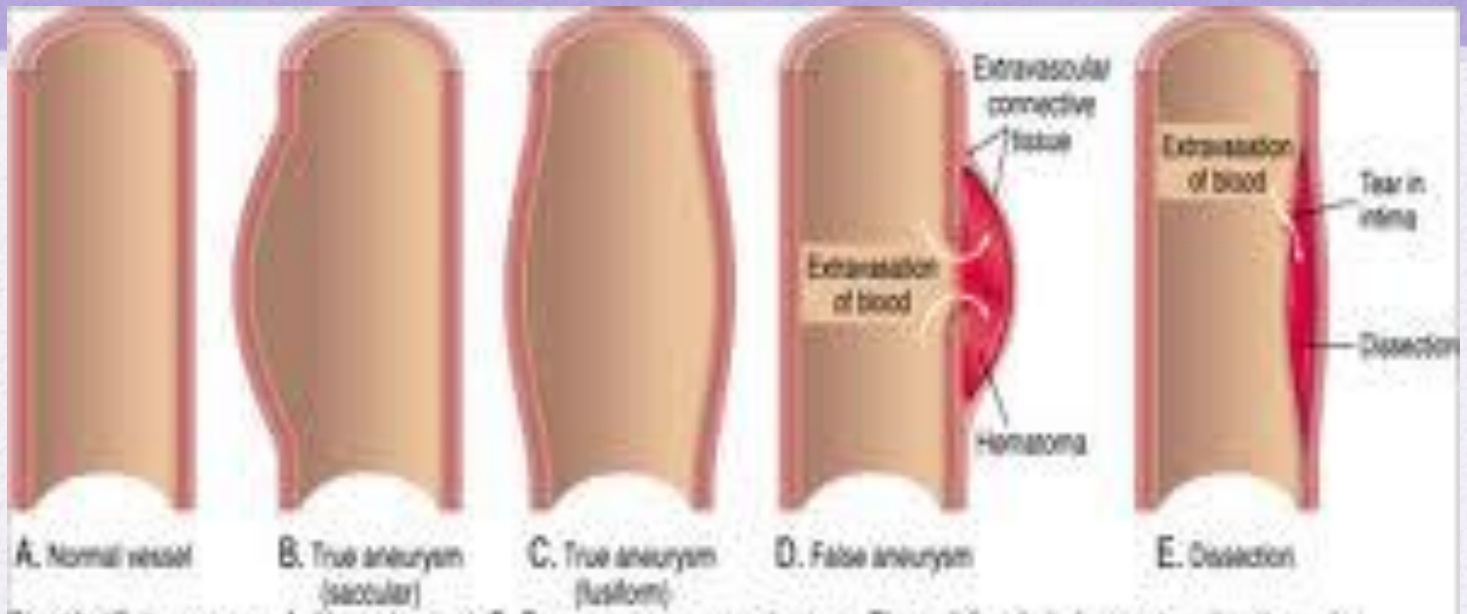
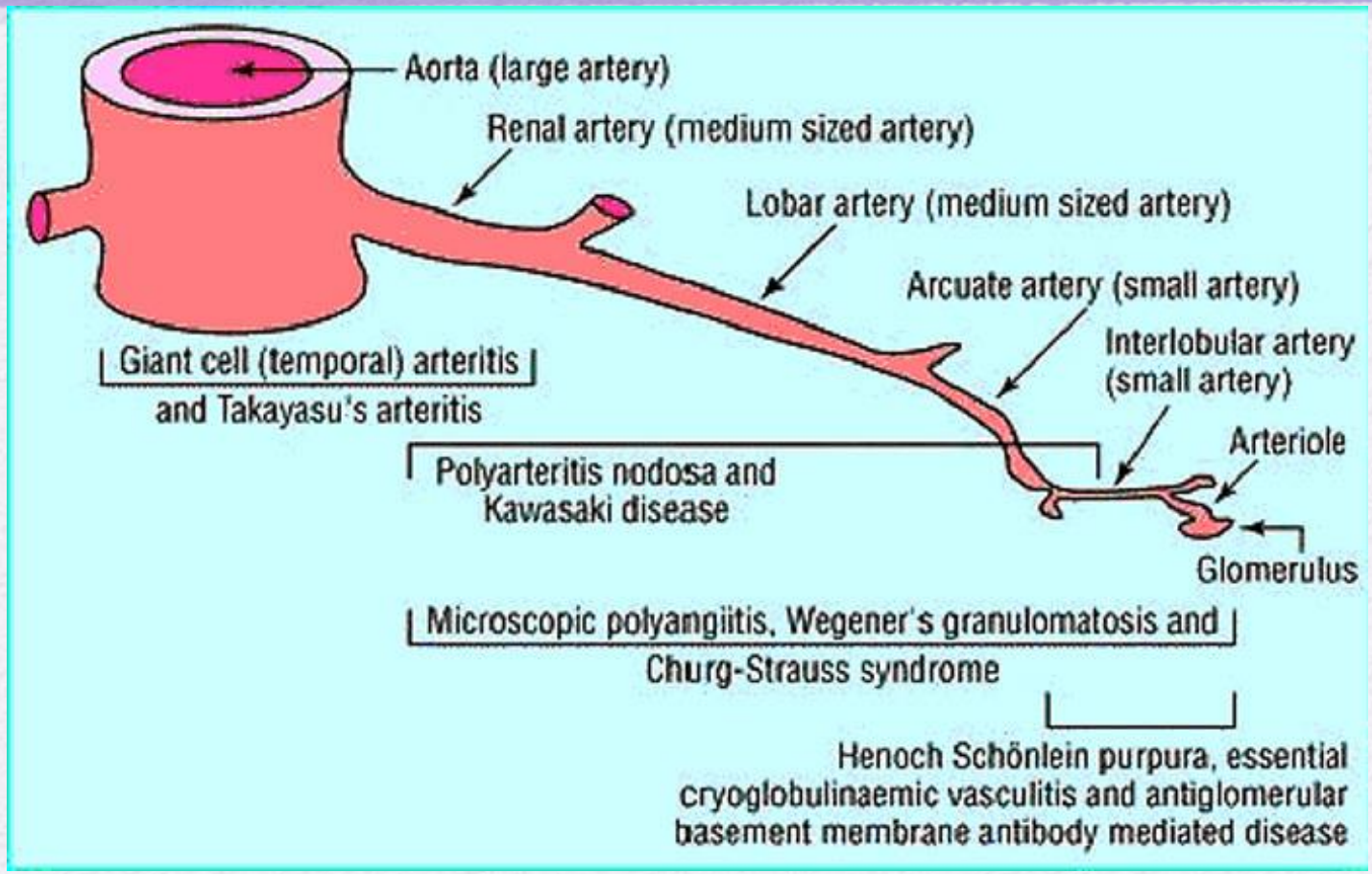


Fig. 10–17. Aneurysms. **A**, Normal vessel. **B**, True aneurysm, saccular type. The wall focally bulges outward and may be attenuated but is otherwise intact. **C**, True aneurysm, fusiform type. There is circumferential dilation of the vessel, without rupture. **D**, False aneurysm. The wall is ruptured, and there is a collection of blood (hematoma) that is bounded externally by adherent extravascular tissues. **E**, Dissection. Blood has entered (dissected) the wall of the vessel and separated the layers. Although this is shown as occurring through a tear in the lumen, dissections can also occur by rupture of the vessels of the vaso vasorum within the media.

Aneurysms

- **Pathogenesis: (1) Atherosclerosis**(abdominal aorta)
  (2) Hypertension (ascending aorta)
  (3) Cystic Medial Degeneration eg ***Marfan's syndrome*** (defective synthesis of protein *fibrillin* with weakened elastic tissue) ***Ehlers- Danlos syndrome*** (defective Type II collagen synthesis) ***Scurvy*** (altered collagen cross-linking)
  (4) Other conditions which weaken vessel walls- ***Vasculitis***, ***Congenital defects*** (berry aneurysms in the Circle of Willis), ***Mycotic aneurysms*** (infective origin)

Classification of Arteritis



Diagrammatic Representation of the Classification of Arteritis