Approach to a patient with Vasculitis

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Internal medicine

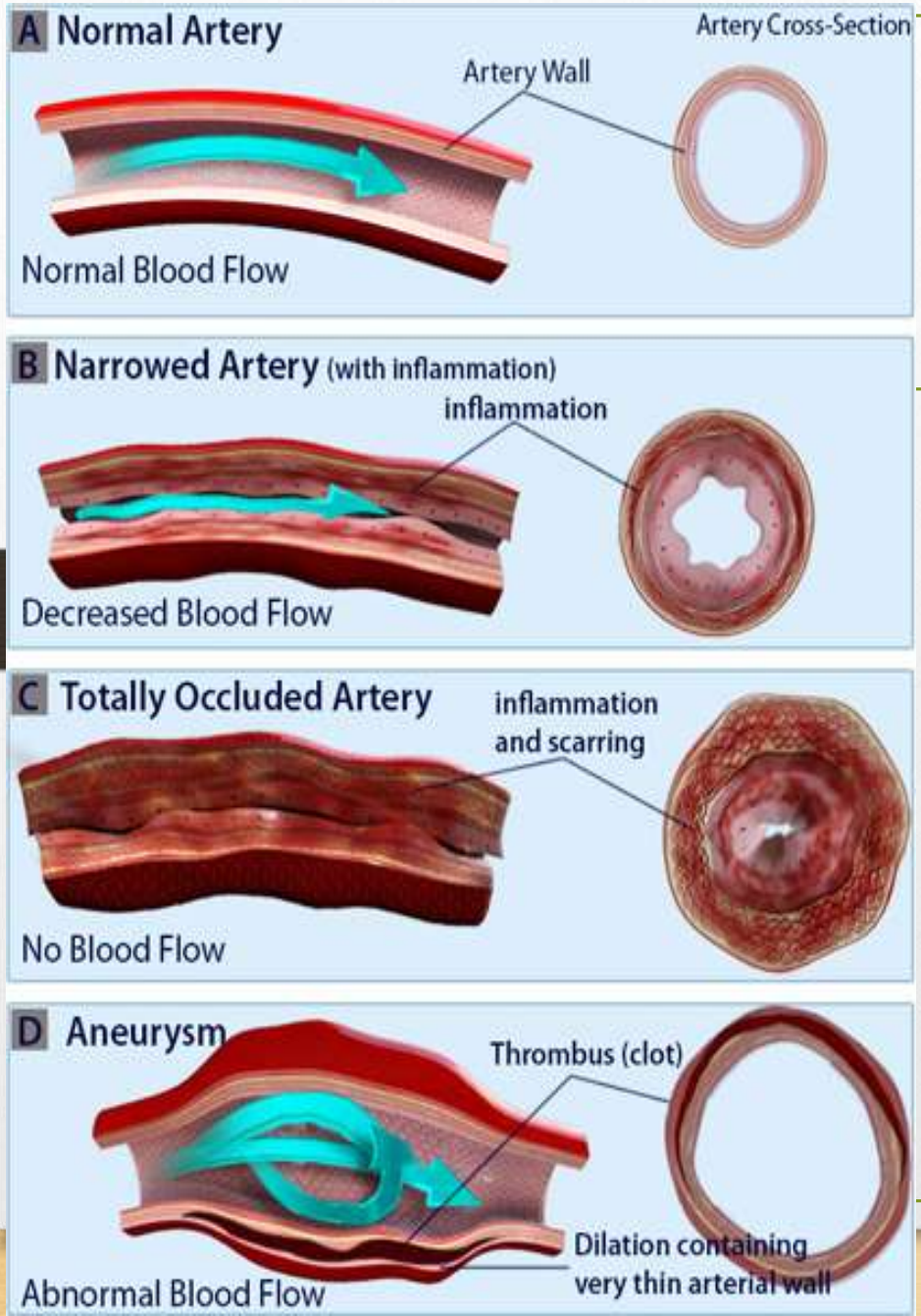
BSMMU

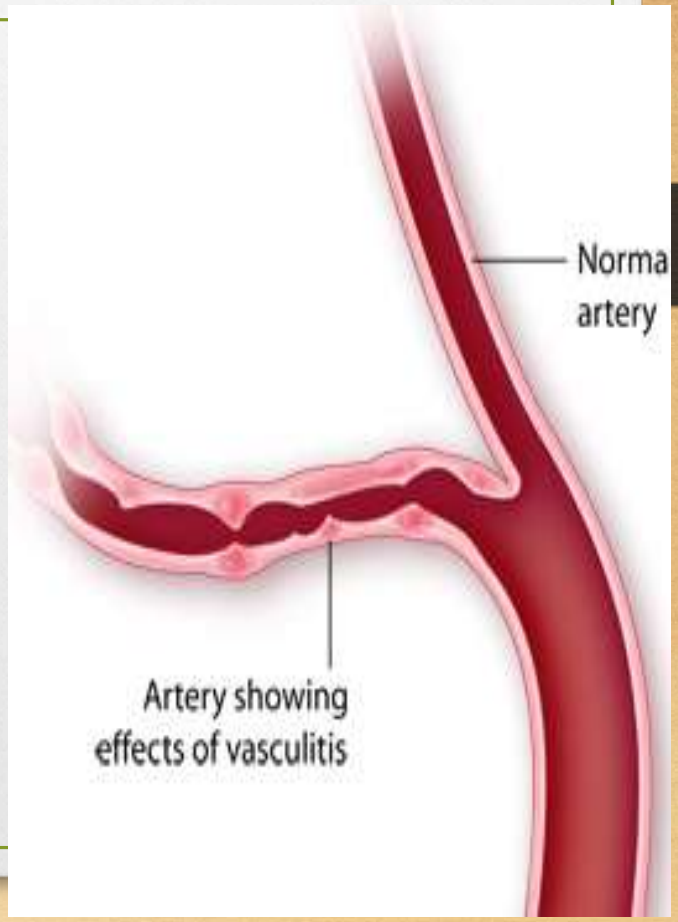
What does vasculitis mean ?

- Vasculitis means inflammation and damage to the blood vessel wall
- Any type of blood vessel in any organ can be affected
- Patients can present with a wide spectrum of clinical manifestations ranging from isolated cutaneous vasculitis to multisystem involvement
- Vasculitis can occur as a primary disorder or secondary to various medical conditions.

PATHOLOGICAL CHANGES

- Systemic inflammatory response
- Thinning of vessel wall
- Narrowing or complete occlusion of affected vessel


A Normal Artery
Artery Cross-Section
Artery Wall
Normal Blood Flow
B Narrowed Artery (with inflammation)
inflammation
Decreased Blood Flow
C Totally Occluded Artery
inflammation
and scarring
No Blood Flow
D Aneurysm
Thrombus (clot)
Dilation containing
very thin arterial wall
Abnormal Blood Flow


Norma
artery
Artery showing
effects of vasculitis

PATHOGENESIS

1. Immune complex formation
2. ANCA mediated
3. T lymphocyte mediated - with Granuloma formation

Immune complex formation

- Henoch Schonlein purpura- IgA mediated
- SLE & other collagen vascular diseases- ANA
- Polyarteritis Nodosa- Hepatitis B ag
- Essential Mixed Cryoglobulinaemia- Hepatitis C virion

ANCA

- p-ANCA (anti-proteinase 3)-

✓ Wegener's Granulomatosis

- c-ANCA (anti-MPO)

✓ Churg Strauss vasculitis

✓ Microscopic Polyangiitis

Granuloma formation (T lymphocyte mediated)

- Giant cell arteritis
- Takayasu's arteritis
- Wegener's granulomatosis
- Churg Strauss vasculitis

Classification

- Primary
- Secondary

Primary Vasculitis

- Large vessel vasculitis
  - Giant cell arteritis
  - Takayasu's arteritis

- Medium vessel Vasculitis
  - Poly Arteritis Nodosa
  - Kawasaki's disease

Small vessel Vasculitis

- Wegener’s Granulomatosis
- Churg Strauss syndrome
- Microscopic Polyangiitis
- Henoch Schonlein Purpura
- Essential Mixed Cryoglobulinemia

Other primary vasculitis

- Thromb Angiitis Obliterans
- Behcet's disease
- Idiopathic Cutaneous vasculitis
- Isolated Vasculitis of CNS
- Relapsing Polychondritis
- Polyangiitis overlap syndromes (features of more than 1 vasculitis)

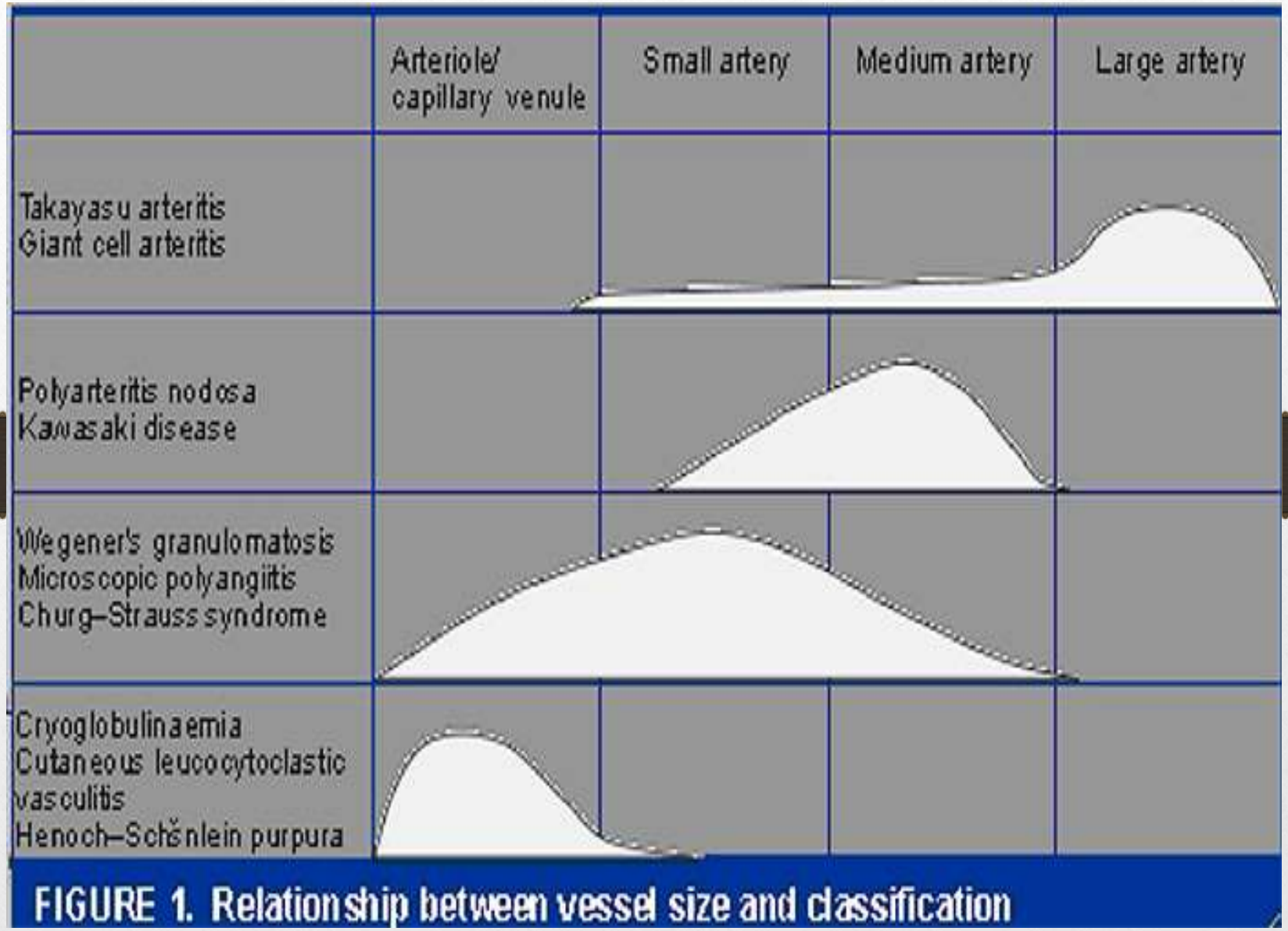


FIGURE 1. Relationship between vessel size and classification

Secondary Vasculitis

- Connective tissue disorders
  - rheumatoid vasculitis,
  - lupus erythematosus,
  - Sjögren's syndrome,
  - inflammatory myopathies
- Inflammatory bowel disease
- Paraneoplastic
- Infection
- Drug-induced vasculitis

STEP 1

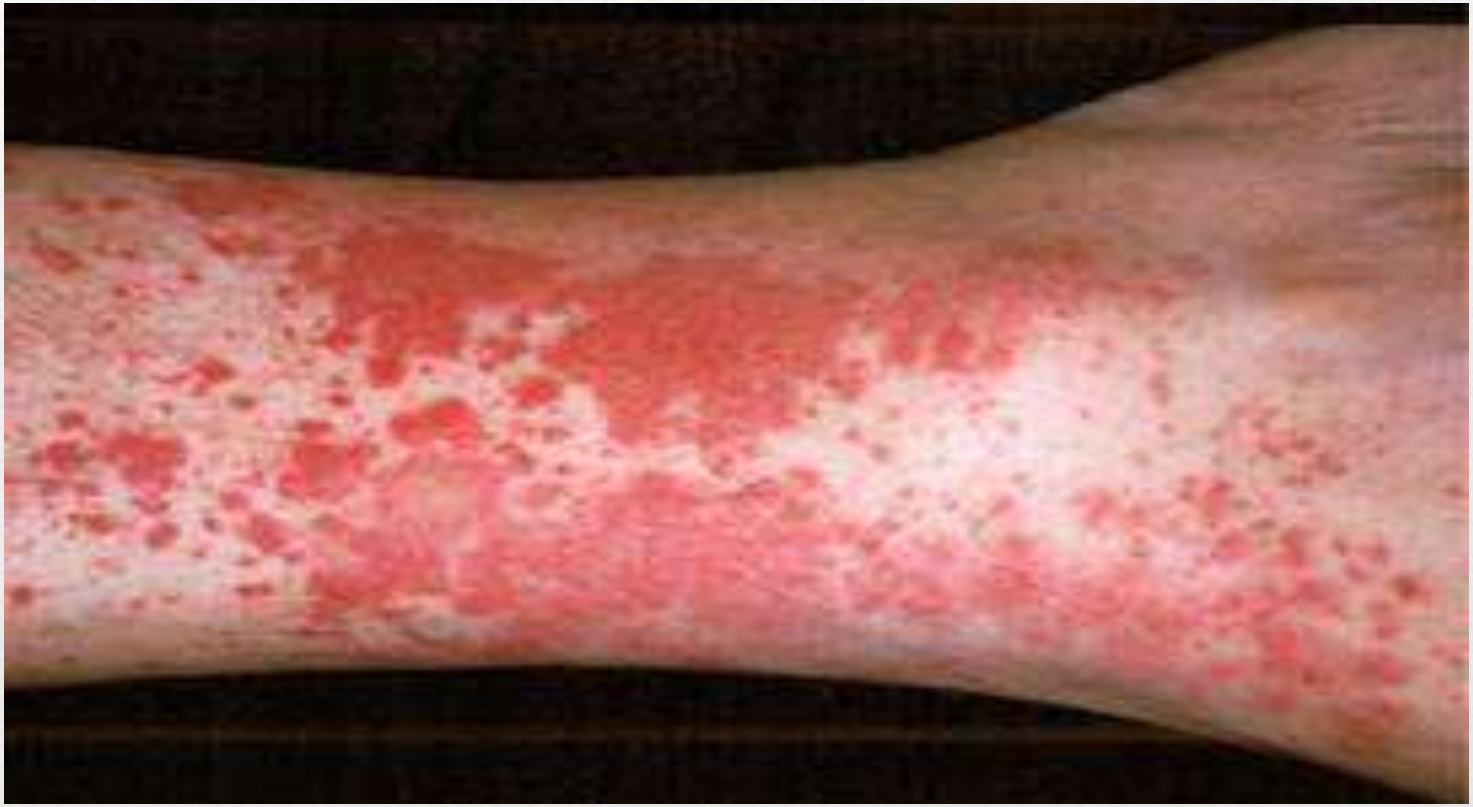
When to suspect vasculitis

- Multi-system involvement
- Unexplained fever, weight loss.
- Unexplained raised ESR or CRP
- Occlusive arterial disease or hypertension in young adults.
- Cerebrovascular/cardiovascular events in young.
- Unexplained proteinuria with or without casts.
- Splinter haemorrhages in nails

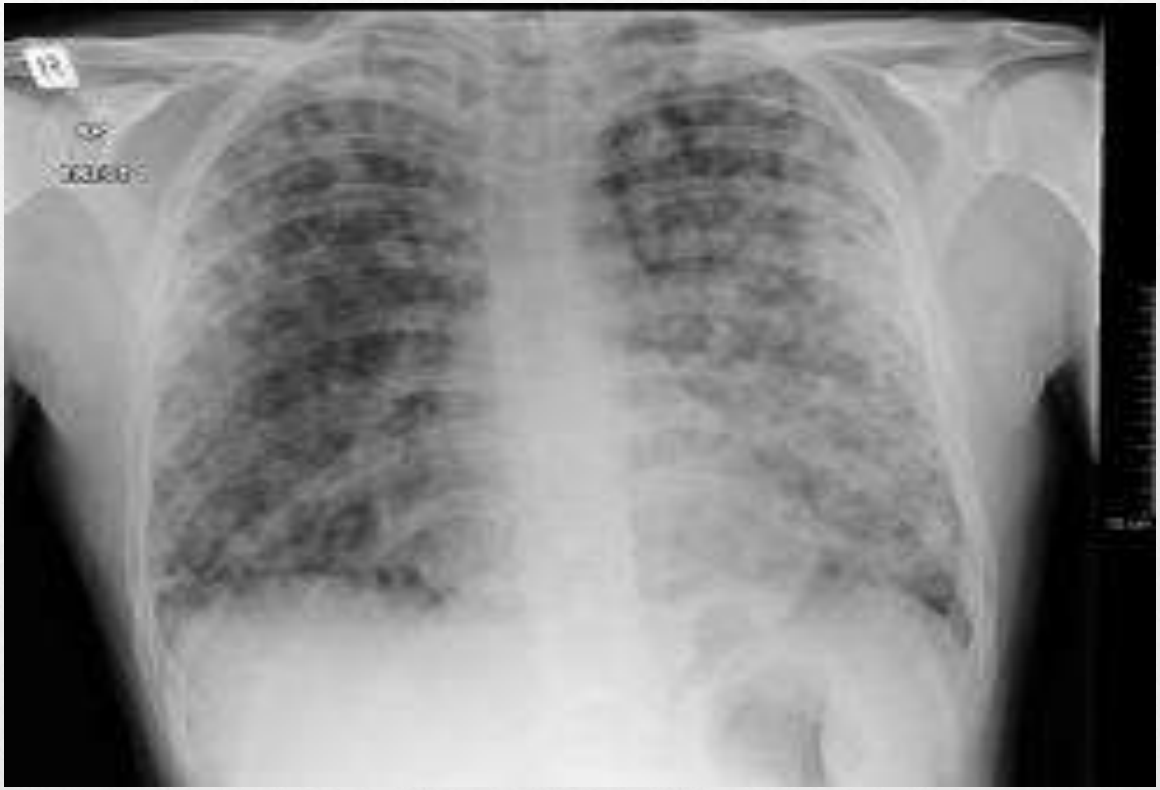
- Cutaneous lesions - palpable purpura, erythema, subcutaneous nodules or urticaria.
- Sudden retinal vascular disease without hypertension or diabetes

- Sudden appearance of peripheral neuropathy - wrist drop, foot drop.
- Unexplained finding of pulmonary nodular/cavitatory lesions.
- Persistent headache with sudden visual impairment (monocular blindness) in elderly.
- Jaw claudication

Palpable purpura

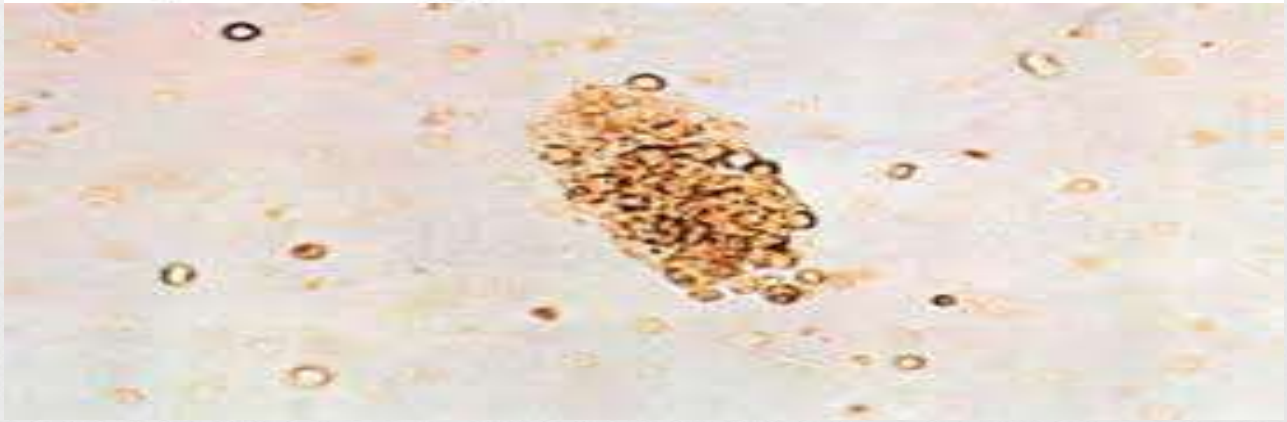


Pulmonary infiltrates



Microscopic hematuria

Bladder symptoms manifested as gross hematuria is an obvious reason to quickly visit the urology specialists.



STEP 2

RULE OUT DISEASES THAT MIMIC VASCULITIS

- Infections
- Malignancies
- Thrombotic Microangiopathies
- Drugs
- Others

Infections

- Bacterial endocarditis
- Gonococcal Infection
- Syphilis
- Rickettsial diseases
- Histoplasmosis
- Coccidiomycosis
- Whipple’s
- Lyme’s

Malignancies

- Atrial Myxomas
- Carcinomatosis
- Lymphomas

Thrombotic Microangiopathies

- TTP
- HUS

Drugs

- Cocaine
- Phenytoin
- Sulfa drugs
- Penicillins
- Hydralazine
- Allopurinol
- Propylthiouracil
- Thiazides

Others

- SLE
- Amyloidosis
- Sarcoidosis
- Atheroembolic Disease

STEP 3

THE PATTERN OF VESSEL INVOLVEMENT

(Large vessel, Medium vessel, Small vessel)

Clinical features of vasculitis on the basis of size of the affected blood vessel

Size of blood vessel	Blood vessel involved	Clinical features
Small vessel vasculitis	▪ Cutaneous post-capillary venules ▪ Glomerular capillaries ▪ Pulmonary capillaries	• Palpable purpura • Haematuria, red cell casts, proteinuria, and decline in renal function • Lung haemorrhage manifesting as breathlessness, haemoptysis and widespread alveolar shadowing on chest radiograph

Size of blood vessel	Blood vessel involved	Clinical features
Medium vessel vasculitis	▪ Small cutaneous arteries	▪ Necrotic lesions and ulcers, nail fold infarcts
	▪ Epineural arteries	▪ Mononeuritis multiplex
	▪ Mesenteric artery	▪ Abdominal pain, gastrointestinal bleeding and perforation because of gut infarction
	▪ Branches of coeliac artery	▪ Infarction of liver, spleen, or pancreas
	▪ Renal artery	• Renal infarction
	▪ Coronary arteries	▪ Myocardial infarction or angina, coronary artery aneurysm, ischaemic cardiomyopathy
	▪ Small pulmonary arteries	▪ Necrotic lesions leading to cavitating lung shadows on chest radiograph
	▪ Small arteries in ear, nose and throat region	▪ Nasal crusting, epistaxis, sinusitis, deafness, stridor because of sub-glottic stenosis

Size of blood vessel	Blood vessel involved	Clinical features
Large vessel vasculitis (aorta and its branches)	▪ Extracranial branches of carotid artery	▪ Temporal headache (temporal artery), blindness (ophthalmic artery), jaw claudication (vessels supplying muscles of mastication)
	▪ Thoracic aorta and its branches	▪ Limb claudication, absent pulses and unequal blood pressure, bruits, thoracic aortic aneurysms

STEP 4

Learn the characteristic presentations of each vasculitis

Giant Cell Arteritis

- Can occur exclusively but often seen with PMR
- Rare: 15/100,000
- Age >50
- Cause unknown
- Involves the large blood vessels of the head and neck including the blood vessels that supply the optic nerve

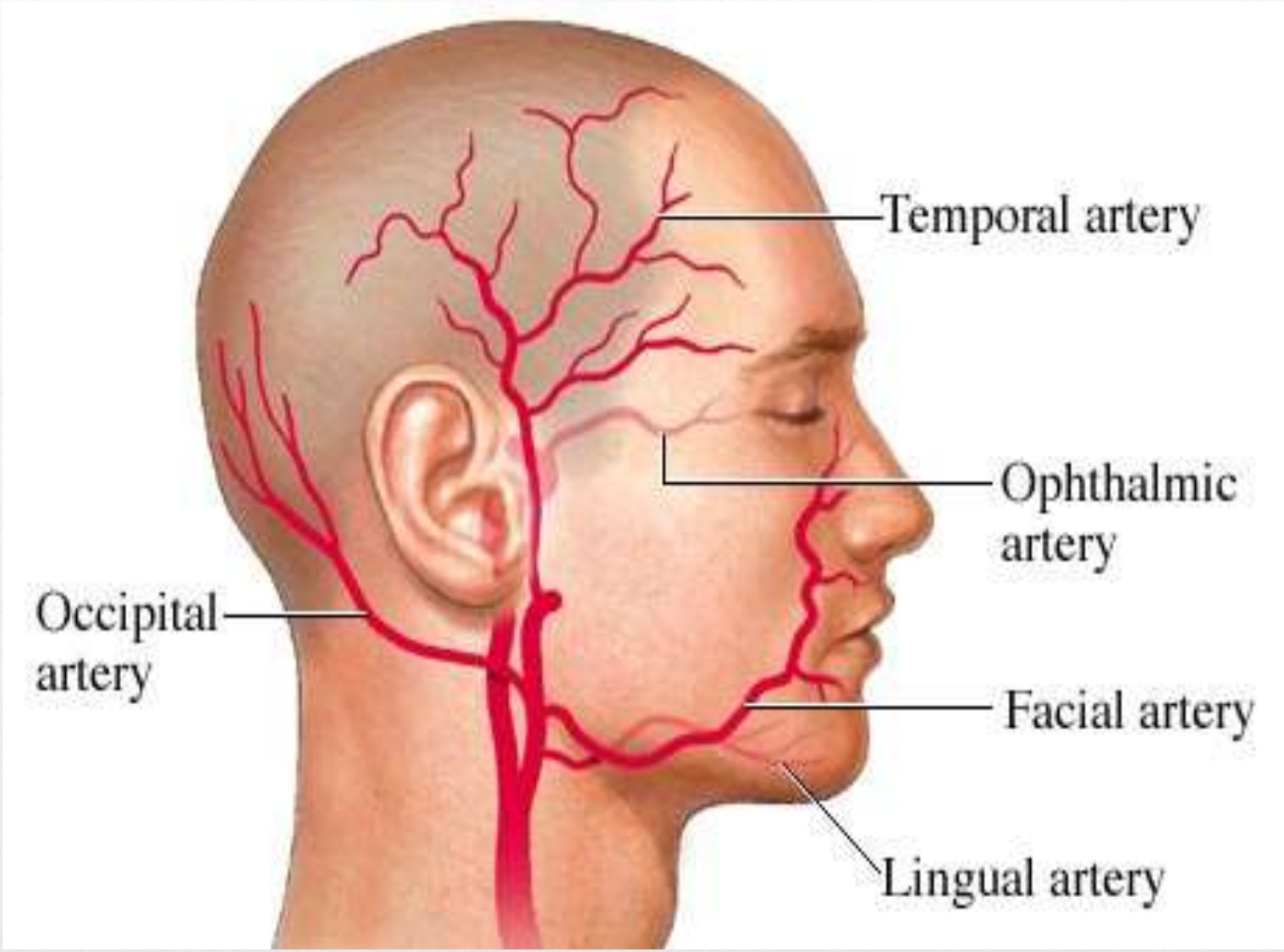
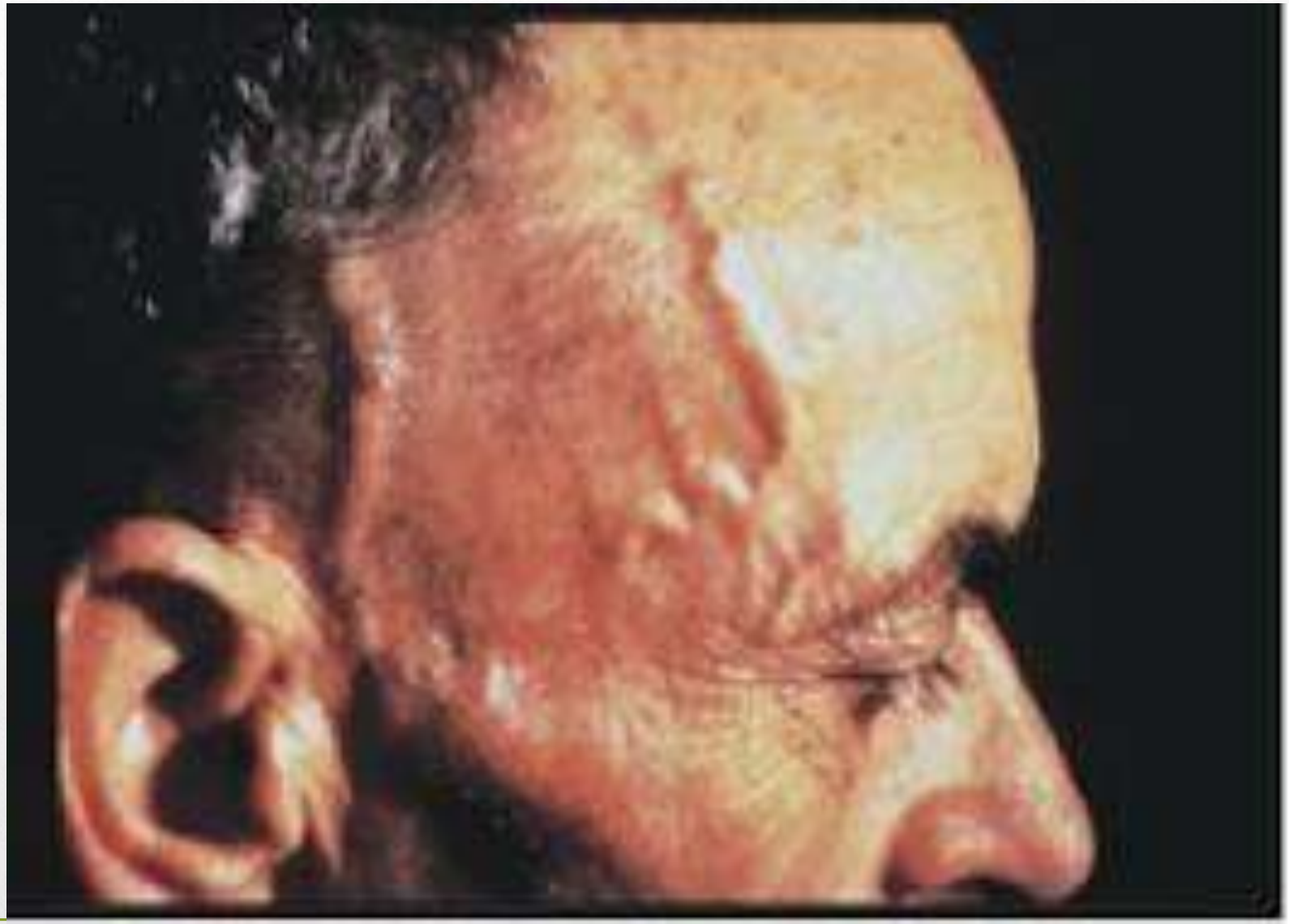

Temporal artery
Ophthalmic artery
Occipital artery
Facial artery
Lingual artery

TABLE 1

Symptoms in giant cell arteritis*

Category	Symptoms
Symptoms due to involvement of cranial vessels	Headache Jaw claudication (pain on chewing) Scalp tenderness Loss of vision Abnormalities of the temporal artery (pain, nodules, absence of pulse)
Symptoms due to involvement of great vessels (aorta and branches of aorta)	Claudication of extremities (especially arm)
Symptoms due to systemic inflammation	Fever, night sweats, weight loss
Polymyalgia rheumatica	Mainly proximal myalgia and stiffness of the neck and shoulder and pelvic girdles

* modified from (3, 11, 12, 39)



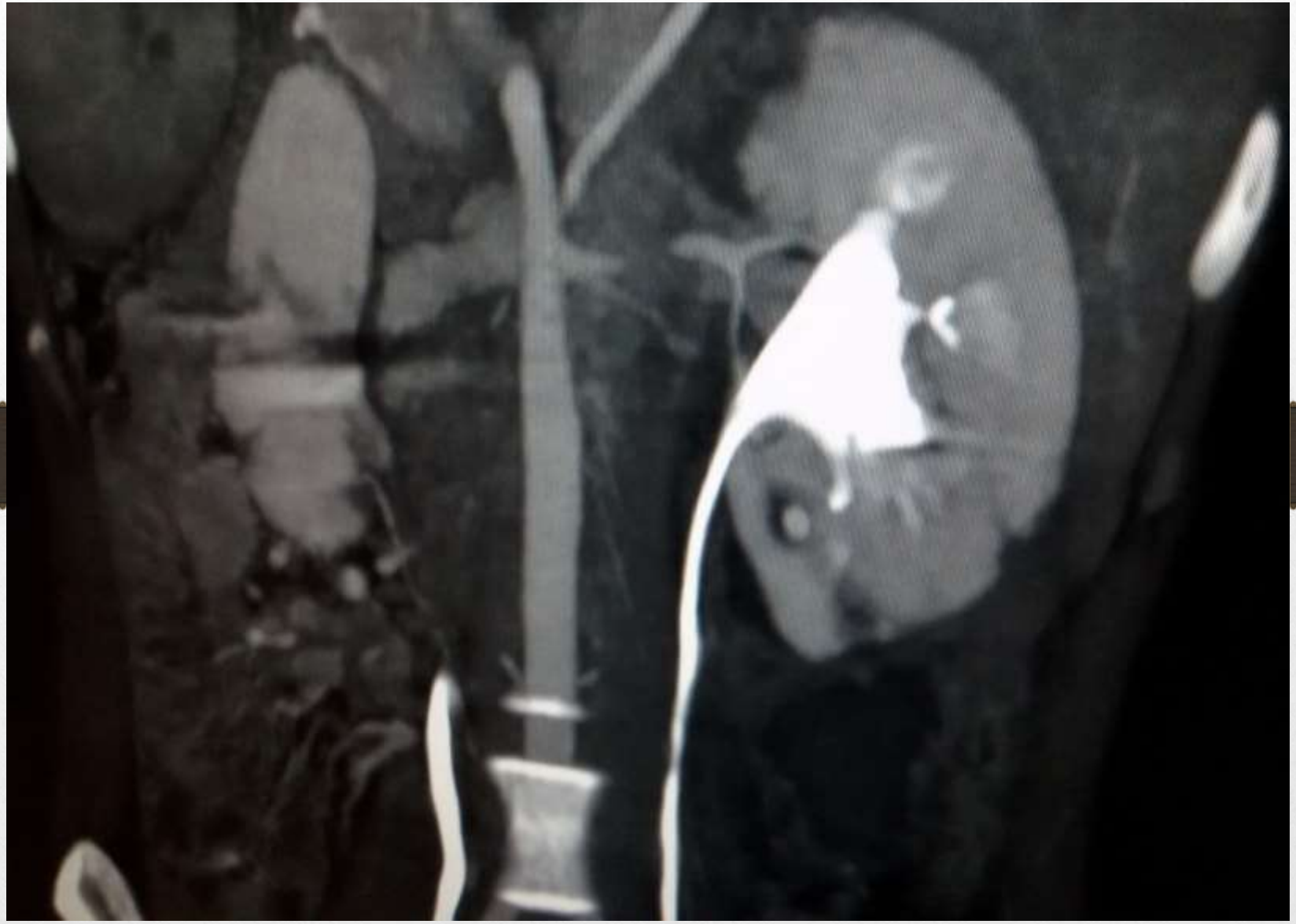
MEDIUM VESSEL VASCULITIS

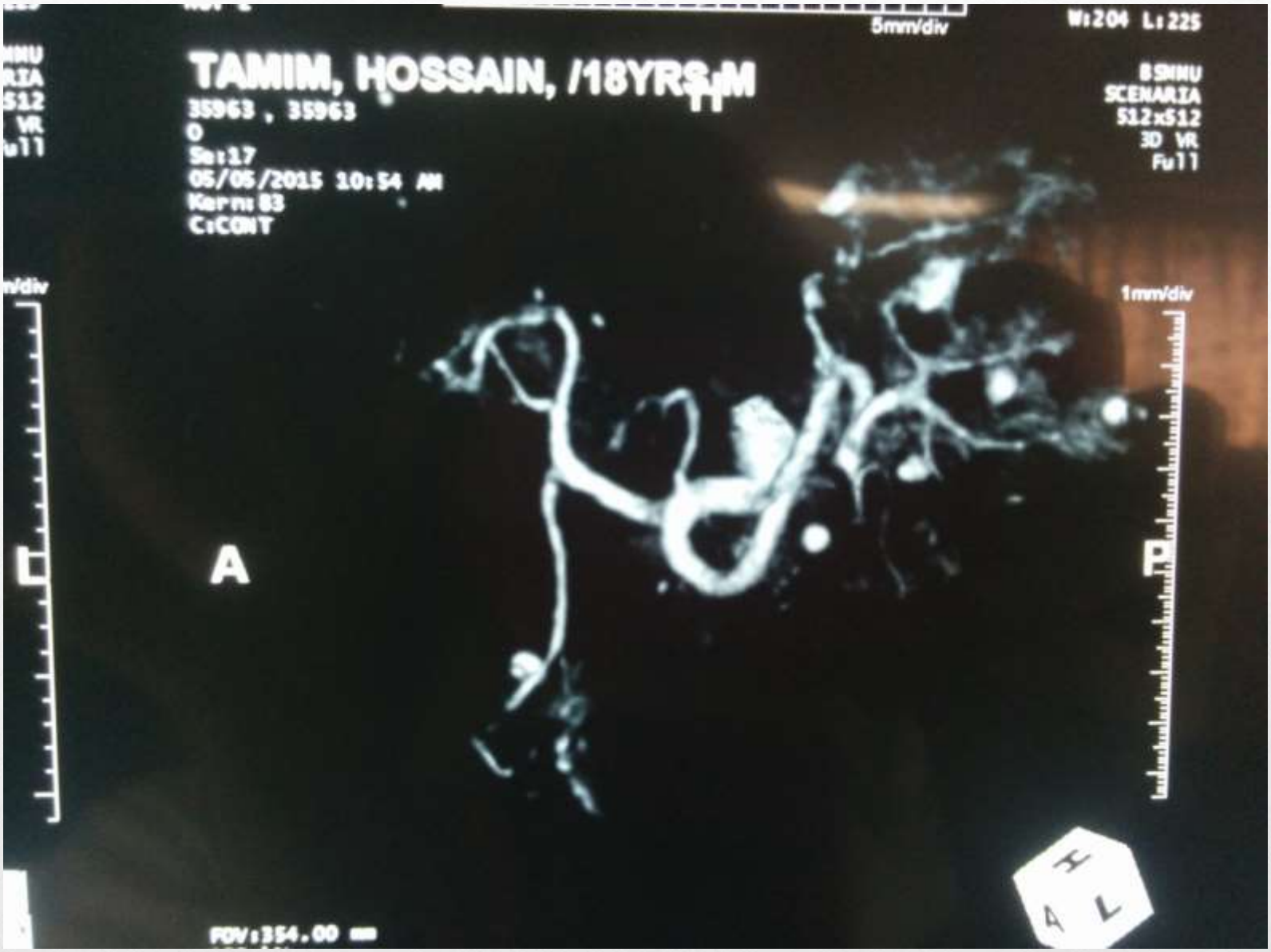
Poly Arteritis Nodosa

- Renal arteries most commonly involved leading to renovascular hypertension
- Pulmonary vessels NEVER involved
- Association with patients of
  - Hepatitis B
  - Hairy cell leukemia

Clinical Presentation

- **Systemic:** fever, fatigue, wt loss
- **Abdominal pain** due to mesenteric angina/ischemia
- **Mononeuritis multiplex**
- **Myalgias/arthalgias/mild arthritis**
- **Renal:** uremia, Hypertension
- **Skin:** livedo reticularis, fingertip ulceration, subcutaneous nodules
- **Testicular** pain or tenderness

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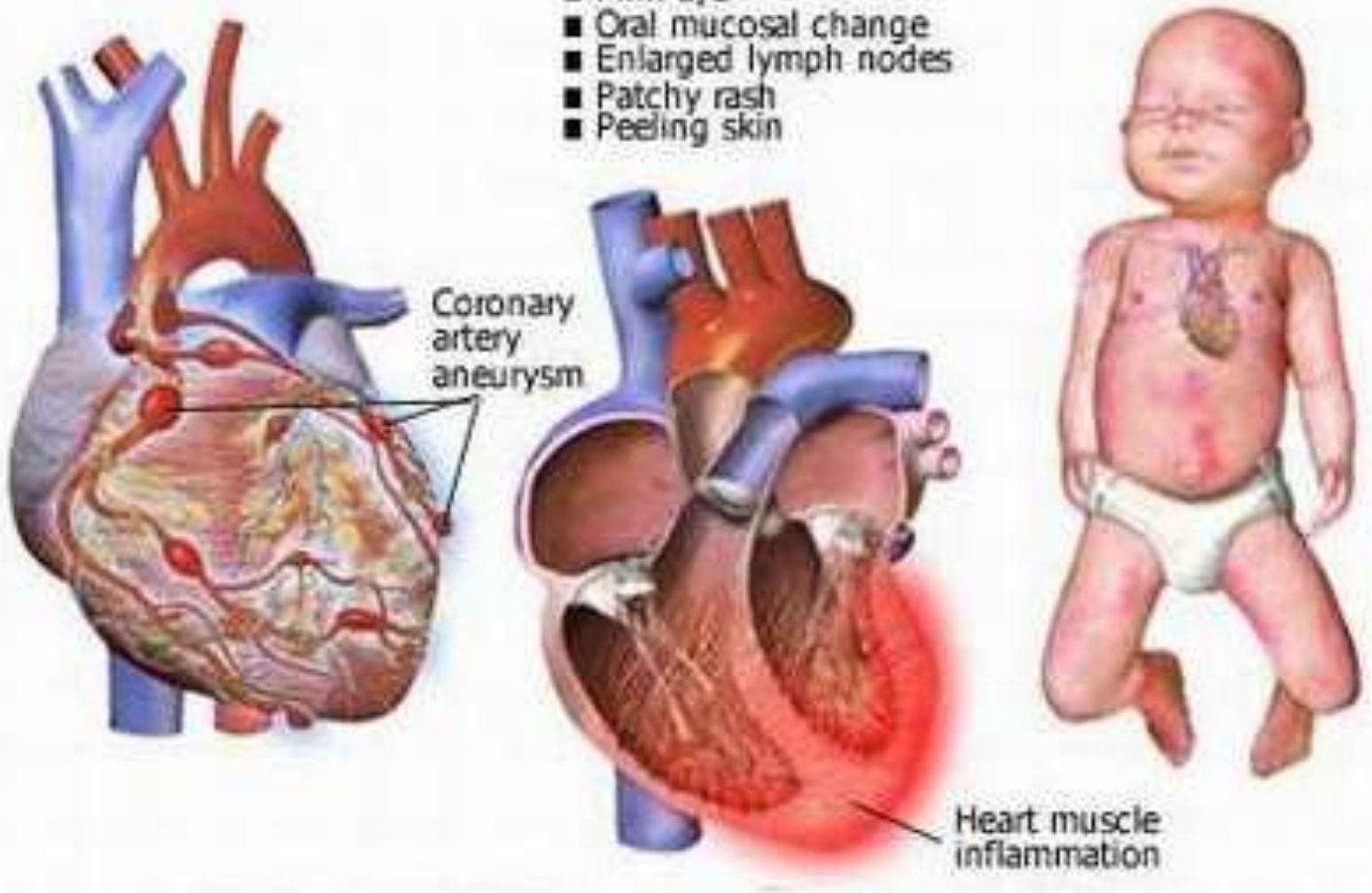
Kawasaki Disease

A type of disease that primarily affects young children and believed to be caused by a non-contagious infection. Symptoms include:

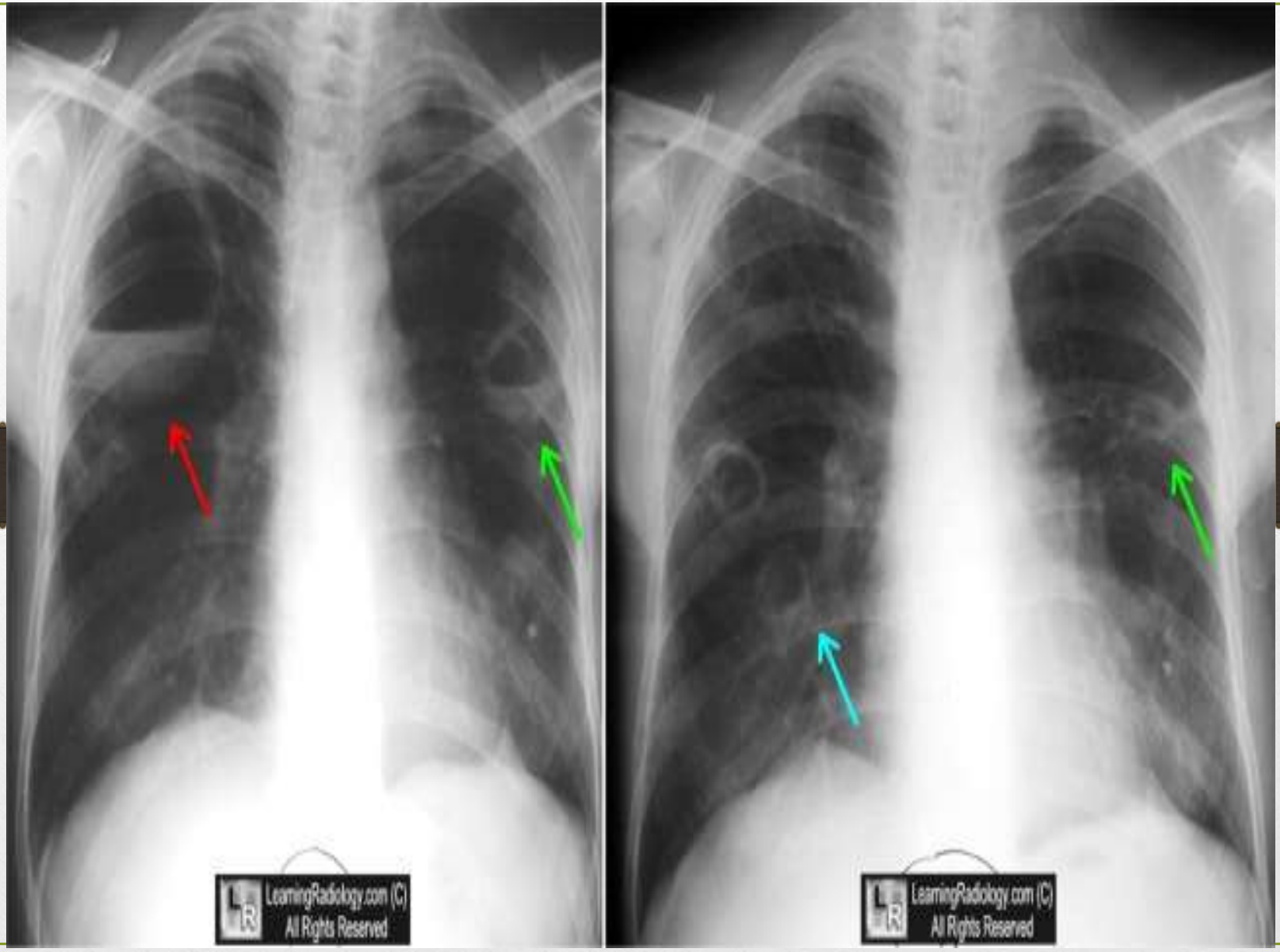
- Pink eye
- Oral mucosal change
- Enlarged lymph nodes
- Patchy rash
- Peeling skin




Diagnostic features
of Kawasaki disease
Fever (for more
than 5 days)
Red eyes
Red, dry, cracked lips
and inflamed tongue
Swollen
lymph nodes
Widespread rash
Changes in hands and feet
Swelling and redness
Peeling of skin around
fingernails and toenails
(after 1-2 weeks)
S. KASTURIA

Wegener's Granulomatosis

- Classical triad → URT + LRT + renal
- Chronis sinusitis, Pulmonary nodules, Pulmonary cavities, Rapidly Progressive Glomerulonephritis
- Cutaneous vasculitis, Eye lesions may be present
- Non specific symptoms may predominate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Churg Strauss syndrome

- Also known as Allergic Granulomatosis
- Site: Blood vessels of the lungs
  GI Tract
  Peripheral nerves
  Heart, skin, and kidneys
- Presence of 4 or more criteria:-

(1) H/O Bronchial asthma

(2) Eosinophilia >10% in Peripheral Blood

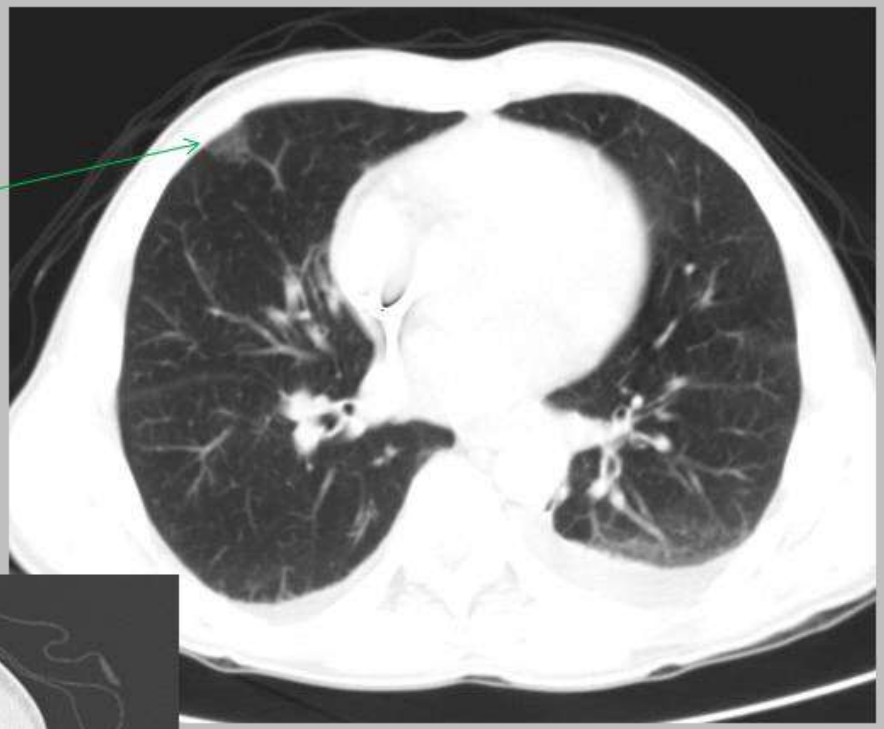
(3) Paranasal sinusitis

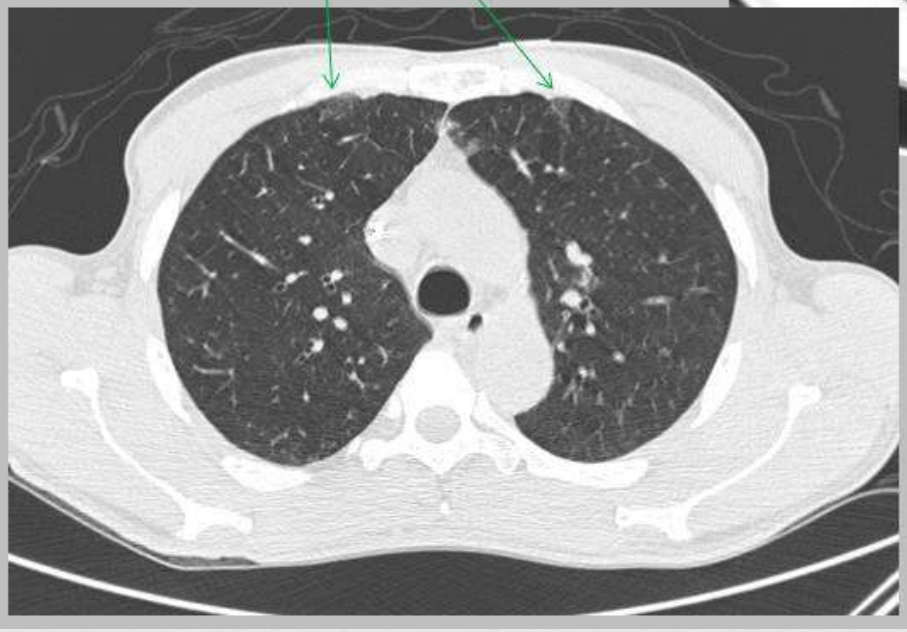
(4) Pulmonary infiltrates (Transient)

(5) Histology: vasculitis with extravascular eosinophils

(6) Mononeuritis multiplex or Polyneuropathy

Multifocal peripheral ground glass opacities that wax and wane … in a patient with asthma… is one of the most common presentations of Churg-Strauss Syndrome, although a very nonspecific one.

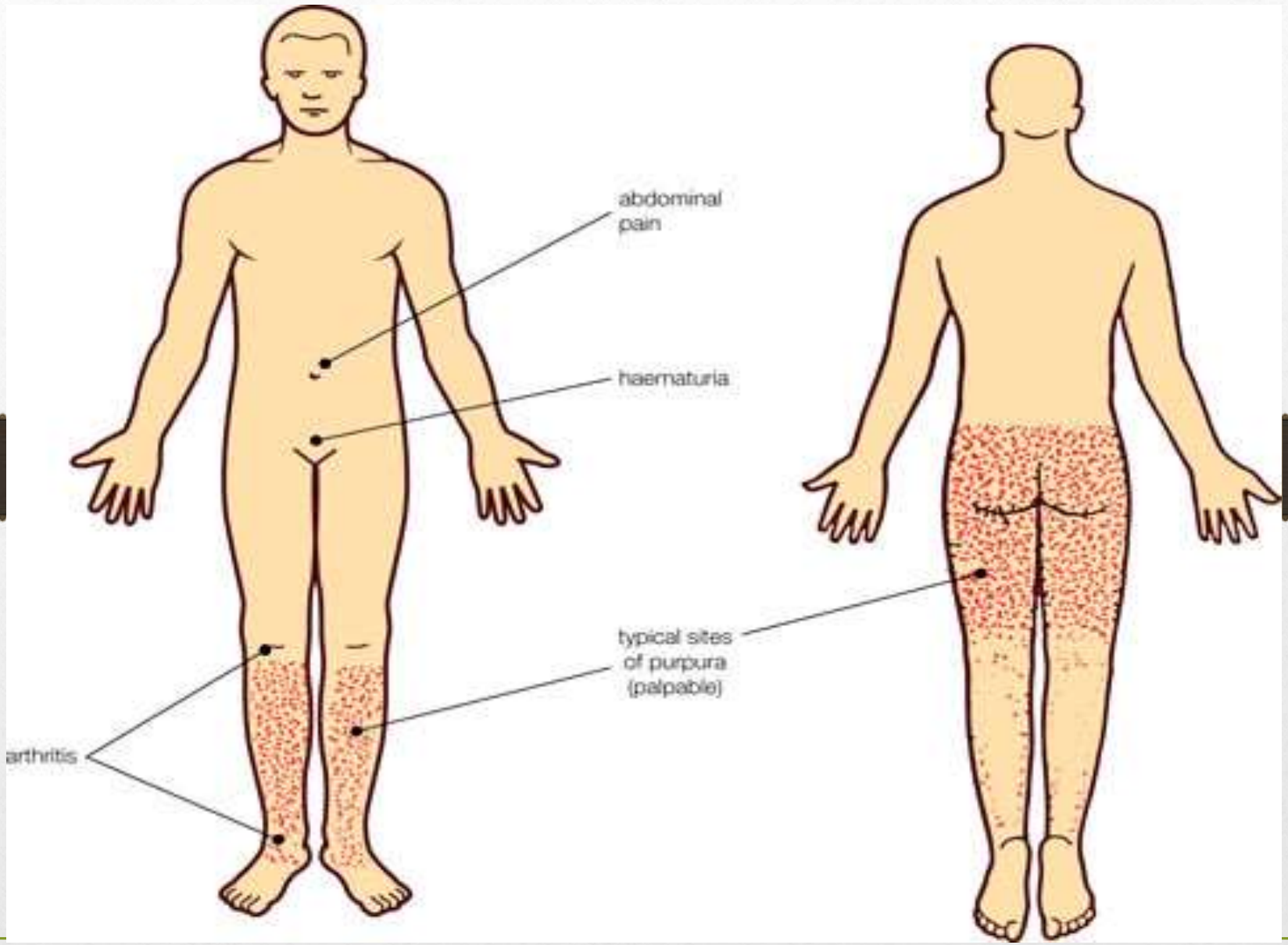




Henoch-Schönlein Purpura

Also referred to as **anaphylactoid purpura**

- Age at onset ≤20 years
  - palpable purpura (most commonly distributed over the buttocks and lower extremities)
  - Arthralgias
  - Bowel angina
  - Gastrointestinal bleeding
  - Haematuria
  - No new medication


abdominal pain
haematuria
typical sites of purpura (palpable)
arthritis

Essential Mixed Cryoglobulinemia

- 5 % of Chronic Hepatits C pts
- Cryoglobulins formed agianst HCV RNA
- Pulmonary, renal (MPGN), cutaneous vasculitis

Thromb Angiitis Obliterans

- Chronic heavy Smokers
- Inflammation of arteries, veins, nerves
- Upper and lower limb gangrene, claudication pain, rest pain

Step 5

How to diagnose vasculitis???

- To exclude vasculitis “mimics” and secondary causes
  - Blood cultures
  - Echocardiogram
  - Hepatitis screen (B and C)
  - HIV test
  - Antiglomerular basement membrane antibody
  - Antiphospholipid antibodies
  - Antinuclear antibody

- To assess extent of vasculitis
  - Urine dipstick and microscopy (all patients)
  - Chest radiography (all patients)
  - Nerve conduction studies/electromyography/CK
- To confirm diagnosis of vasculitis
  - Biopsy and/or angiogram

- To identify the specific type of vasculitis
  - ANCA
  - Cryoglobulin
  - Complement levels
  - Eosinophil counts/IgE levels
  - Specific findings on biopsy (necrotising granulomatous inflammation, presence of IgA deposits, evidence of immune complex formation (or its absence))

ANCA

- Two types of ANCA staining patterns are seen on immunofluorescence (IF), namely cytoplasmic (c-ANCA) and perinuclear (p-ANCA).

- ELISA should then always be performed in patients with positive results on immunofluorescence (IF) to identify the specific antigen targeted by ANCA

- Presence of c-ANCA with anti-proteinase 3 (anti-PR3) is highly suggestive of Wegener's granulomatosis while p- ANCA with anti-myeloperoxidase (anti-MPO) is more often encountered in those Churg-Strauss syndrome and microscopic polyangiitis

- For a positive IF test alone, sensitivity for AAV is around 67% and specificity is around 93%.
- For combined IF and ELISA, sensitivity decreases to around 52%, but specificity increases to 99%.
- It is worth mentioning here that false positive ANCA results could be seen in a wide variety of conditions especially when positive IF results are not confirmed by ELISA

- Conversely, ANCA can be negative in a significant proportion of patients with AAV (10%–20% of active, untreated Wegener's granulomatosis, 30% of limited Wegener's granulomatosis, 30% of MPA, and 50% of Churg-Strauss syndrome patients in most series)
- Thus, ANCA test should not be requested unless there is clinical suspicion of vasculitis and its absence should not be taken as evidence against AAV.

THANK YOU