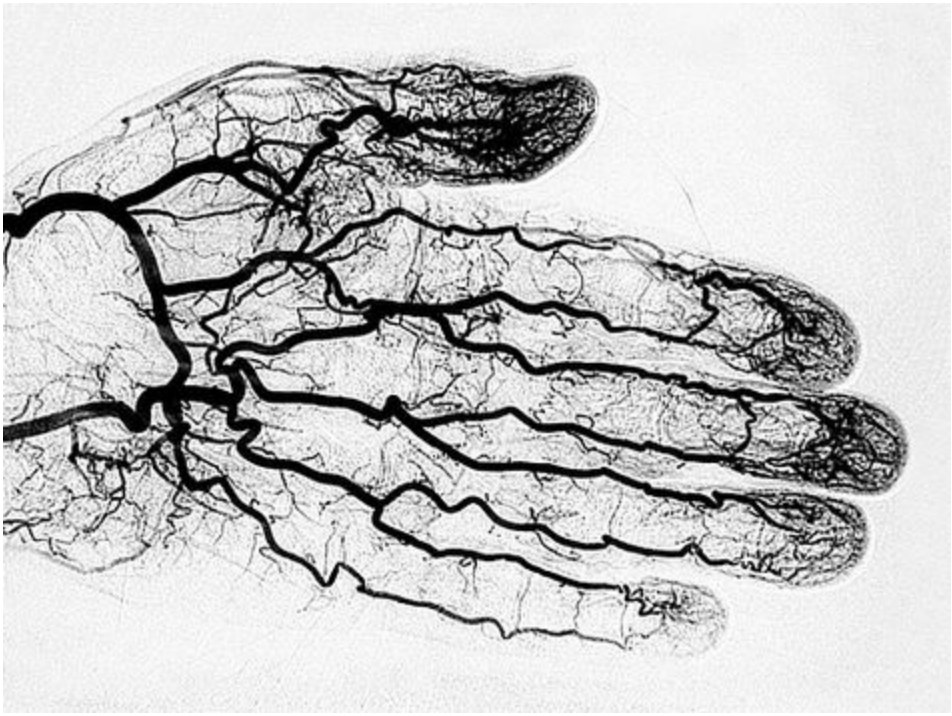
VASCULITIS

Robbins page 348



Objectives:

- Know the common causes of vasculitis with special emphasis on the clinicopathological features and mechanism of:
  - Giant cell arteritis.
  - Polyarteritis nodosa.
  - Wegener's granulomatosis.
  - Cutaneous hypersensitivity vasculitis.
- Thromboangiitis obliterans (Buerger's disease)
- Pathology of vasculitis: giant cell arteritis, polyarteritis nodosa, Wegener's granulomatosis and cutaneous hypersensitivity vasculitis.
- Henoch Schonlein purpura.

Important note: During the previous blocks, we noticed some mistakes just before the exam and we didn't have the time to edit the files. To make sure that all students are aware of any changes, please check out this link before viewing the file to know if there are any additions or changes. The same link will be used for all of our work: Pathology Edit

Vasculitis. Robbins page 348

[What's Vasculitis?](), [Vasculitis pathophysiology]().

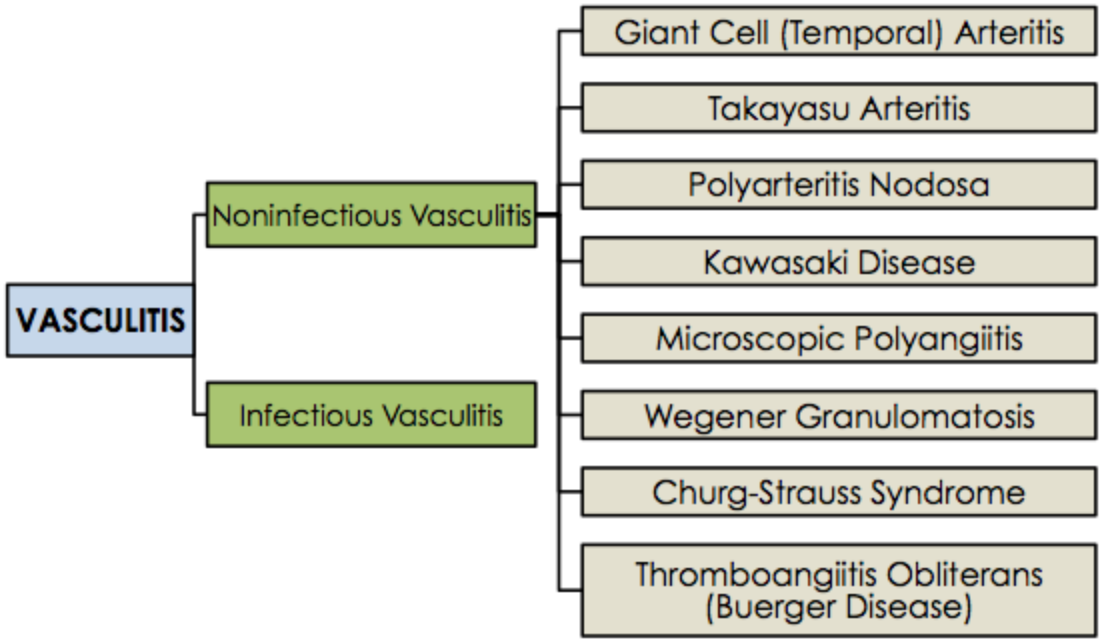
It is inflammation of vessel walls with many possible symptoms. **They are divided into two types:**

- **Non-infectious vasculitis.** Robbins page 348
  - Immune complex deposition. This form of vasculitis is seen in immunologic disorders such as systemic lupus erythematosus.
  - Anti-neutrophil cytoplasmic antibodies (ANCAs). ANCAs are autoantibodies that attack the inside (cytoplasm) of neutrophils. When ANCAs attack these neutrophils, they cause the white blood cells to attack the walls of small vessels in different tissues and organs of the body. This causes vasculitis. It has many types such as C-ANCAs or P-ANCA.
  - Anti-endothelial cell antibodies.
  - Autoreactive T cells.

- **Infectious vasculitis.** Robbins page 355

It can also be caused by infection, physical or chemical injury.

- The two most common pathogenic mechanisms of vasculitis are *immune-mediated inflammation* and *direct vascular invasion by infectious pathogens*.



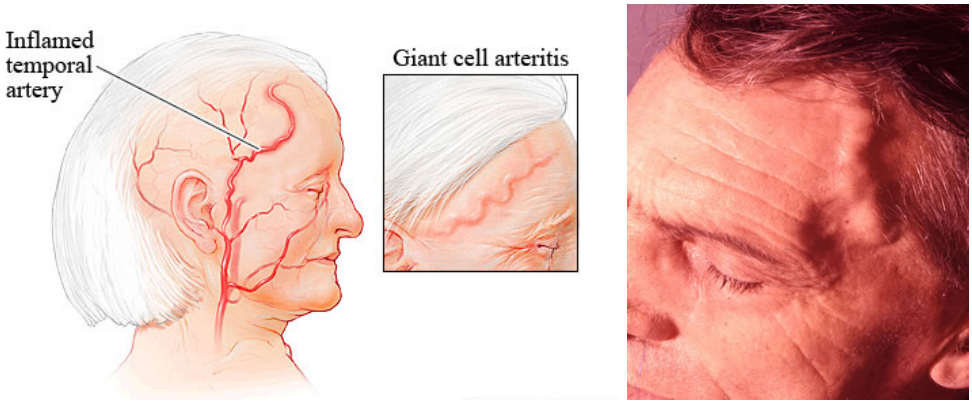
[Vasculitis (Signs & Symptoms).]()

Signs & Symptoms of systemic inflammation: fever, myalgia[1], arthralgias[2], and malaise. Besides a specific findings for each case depending on the type of the B. V that is attacked (small, medium, large).

[1] ألم عضلي
[2] ألم في المفاصل

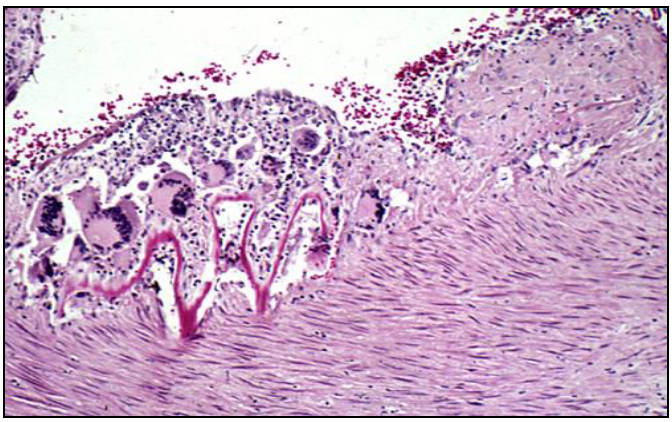
GIANT-CELL (TEMPORAL) ARTERITIS. Robbins page 350

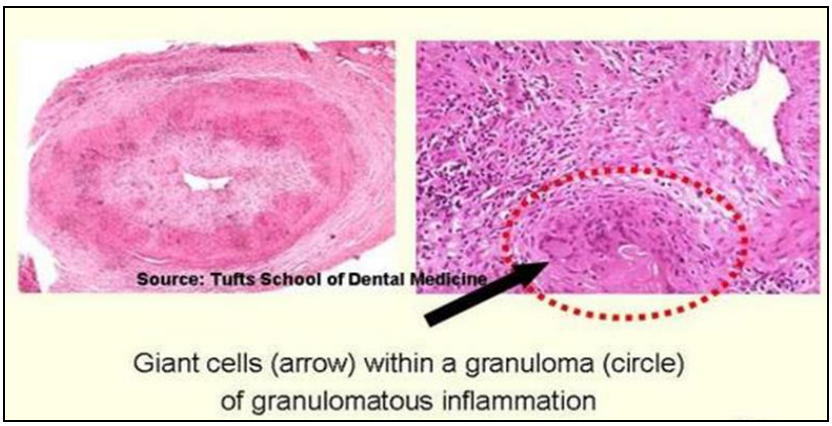
DISORDER	VASCULITIS	EPIDEMIOLOGY	CLINICAL LABORATORY FINDING & TREATMENT
GIANT-CELL (Temporal) arteritis	Chronic, granulomatous inflammation of large to small arteries, especially in head particularly the branches of the carotid artery (**temporal** a. and branches of the **ophthalmic** a.) Involvement is segmental, acute and chronic.	**Adult > 50 years of age** Etiology: T cell–mediated immune response to an as-yet uncharacterized vessel wall antigen.	1. Fever. 2. facial pain or headache often most intense along the course of the superficial temporal artery. 3. Thickened and painful temporal artery. 4. Jaw pain. 5. Visual problems and acute vision loss. The diagnosis depends on biopsy and histologic confirmation. **Treatment:** corticosteroids.



MORPHOLOGY.

- Granulomatous inflammation of the blood vessel wall.
- Giant cells.
- Disruption and fragmentation of internal elastic lamina.
- Proliferation of the intima with associated occlusion of the lumen.
- The healed stage reveals collagenous thickening of the vessel wall and the artery is transformed into a fibrous cord.





Giant cells (arrow) within a granuloma (circle) of granulomatous inflammation

POLYARTERITIS NODOSA. Robbins page 352

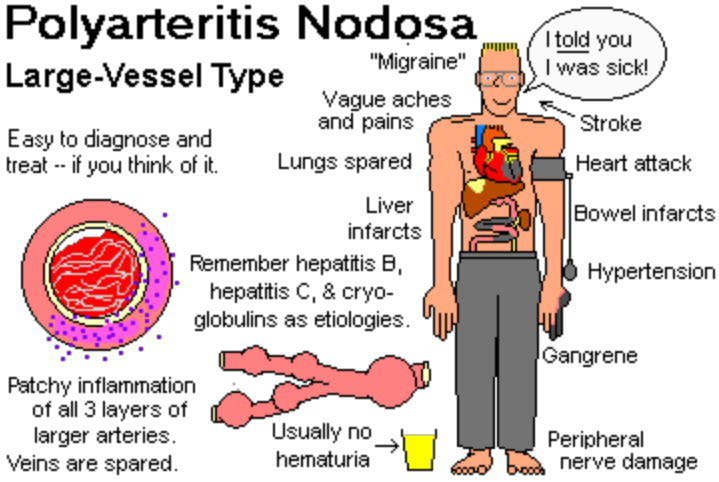
[PAN - Polyarteritis Nodosa.]

(PAN) is a systemic vasculitis of small or medium-sized muscular arteries. Affect young adults but can occur in all age groups. The clinical course may range from acute to chronic but typically is episodic disease with long symptom-free intervals. Affect all organs especially the kidney and spares[3] the lung. Most frequent sites are *kidneys*, *heart*, *liver*, and *gastrointestinal* tract. It's found that in one third of the patients that polyarteritis nodosa has been associated with **hepatitis B** or **hepatitis C**. Due to the formation of immune-complex that deposit in the blood vessel. While the main cause is unknown.

Clinical manifestations:

1. Fever.
2. Weight loss.
3. Abdominal pain and melena (bloody stool).
4. Muscular pain and neuritis.

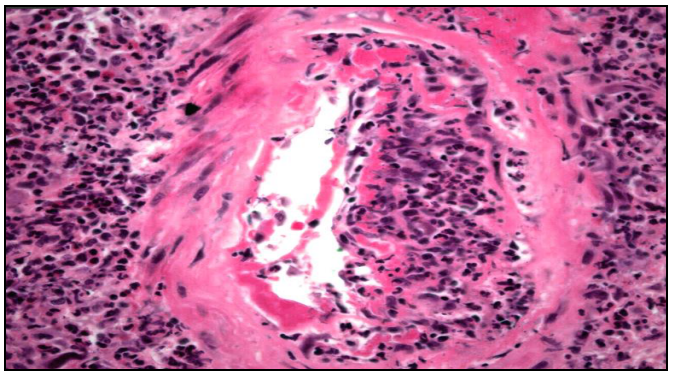
The Clinical manifestations are a result from ischemia and infarction of affected tissues and organs.



Complications:

- Weakening of the arterial wall due to the inflammatory process may cause aneurysmal dilation or localized rupture.
- *Renal arterial involvement* is often prominent and is a major cause of death.
- Fatal if untreated, but **steroids** and **cyclophosphamide** are curative.

MORPHOLOGY.



Classic PAN is a segmental necrotizing inflammation of arteries of medium to small size often with overlapping thrombosis. Lesions usually involve only part of the vessel.

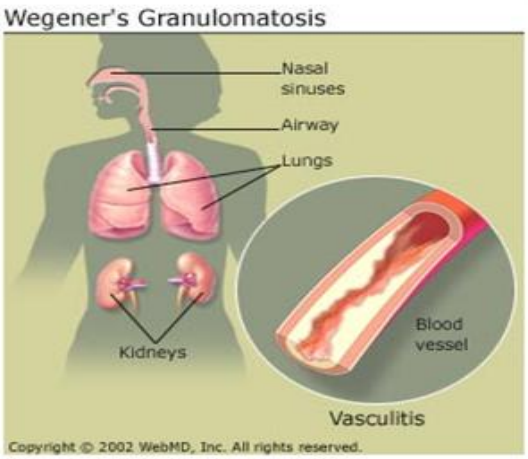
In the ***acute phase***, there is transmural mixed inflammatory infiltrate composed of neutrophils and mononuclear cells, frequently accompanied by fibrinoid necrosis and luminal thrombosis. Older lesions show fibrous thickening of the vessel wall extending into the adventitia. Particularly characteristic of PAN is that all the different stages of activity (i.e. active and chronic stages) may coexist in same artery or in different vessels at the same time.

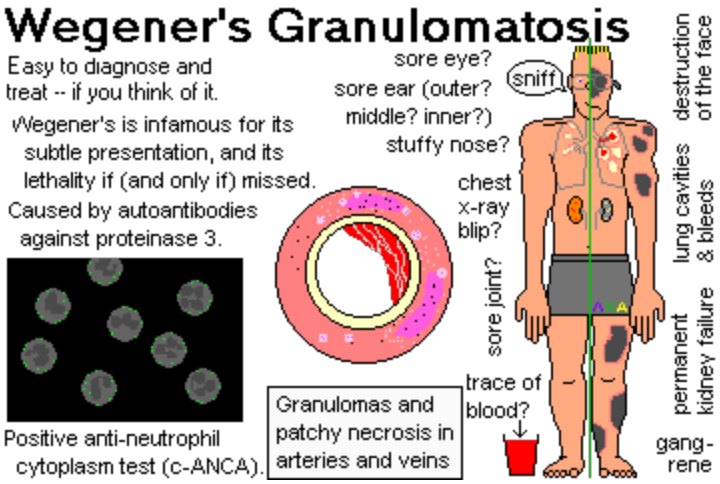
Polyarteritis nodosa with segmental inflammation and **fibrinoid necrosis** and occlusion of the lumen of this artery. Note that part of the vessel wall at the left side is uninvolved.

[3] Doesn't affect.

WEGENER GRANULOMATOSIS. Robbins page 353

[Wegener Granulomatosis.](), [Wegener's granulomatosis and microscopic polyangiitis.]()





Is a necrotizing vasculitis characterized by the triad of:

1) Necrotizing granulomas of the *lung* and/or *upper respiratory tract*. ex: ear,nose, sinus, throat.
2) Necrotizing or granulomatous vasculitis of *small to medium-sized vessels.* ex: capillary, venules, artery.
3) Glomerulo*nephritis*. renal disease in the form of necrotizing, crescentic.

Characteristics of WG :

- Males are affected more often than females, at an average age of about 40 years
- It is likely to be initiated as a cell-mediated hypersensitivity response directed against inhaled infectious or environmental antigens.
- Persistent pneumonitis, chronic sinusitis, mucosal ulcerations of the nasopharynx, and evidence of renal disease (hematuria, proteinuria).

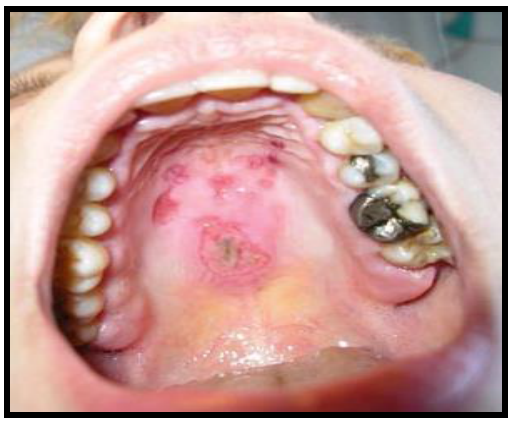
Diagnosis:

- Biopsy.
- **C-ANCAs** (anti-neutrophilic cytoplasmic antibodies) (another name is PR3-ANCA) is positive in serum of more than 95% of patients. (probably derived from subsequent tissue injury, it's a useful markers of disease activity to follow up)

Untreated: fatal - mortality rate at 1 year 80% if not treated.

Treatment: **(additional info from robbins)** Steroids, immunosuppressive therapy, anti-B cell antibody.

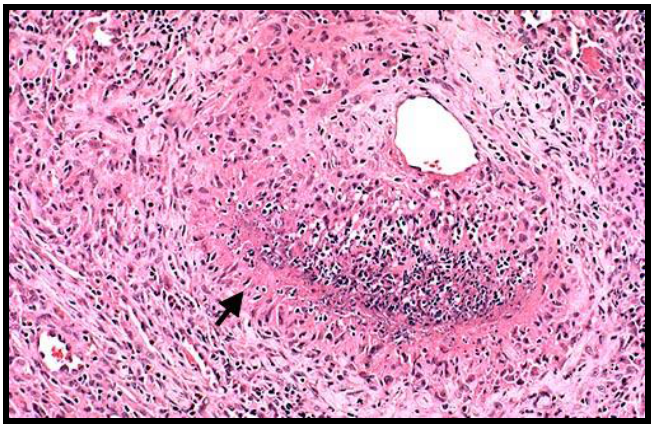
- most patients survive, but remain at high risk for relapses that can ultimately lead to renal failure.

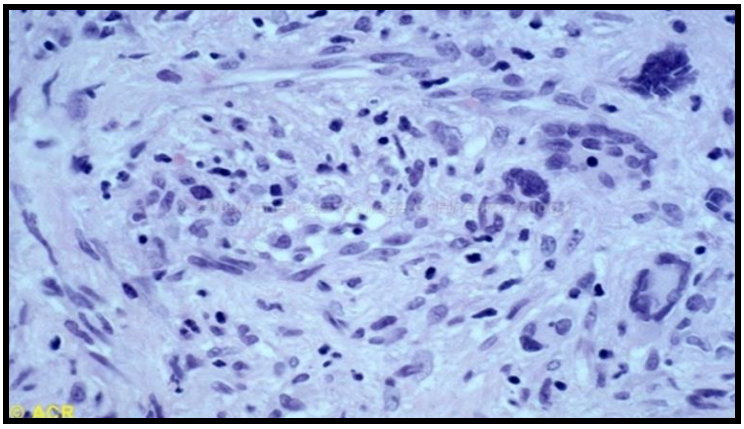


Wegener granulomatosis: palatal ulceration

- mucosal ulceration 75 %

Wegener granulomatosis: palatal destruction





Granuloma findings:

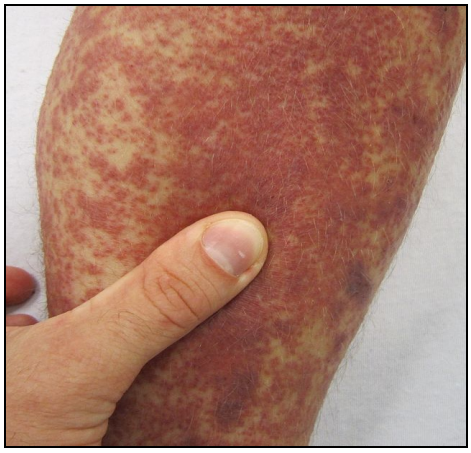
- inflammatory cells.
- Giant cells.
- lymphocytes.

MICROSCOPIC POLYANGIITIS[4] [POLYARTERITIS]. Robbins page 352

Also is called (CUTANEOUS LEUKOCYTOCLASTIC OR HYPERSENSITIVITY VASCULITIS ANGIITIS).

It is a systemic necrotizing small vessel vasculitis (Rarely, larger arteries may be involved) associated with **glomerulonephritis**.

- **P-ANCA** is characteristically present.



In many cases, an antibody response to antigens such as drugs (e.g., penicillin), microorganisms (e.g., streptococci), heterologous proteins, or tumor proteins is the presumed cause. This can result in immune complex deposition, or it may trigger secondary immune responses.

It is characterized by acute inflammation of small blood vessels (usually postcapillary venules in the dermis). It affects many organs *e.g. skin (most common), mucous membranes, lungs , brain, heart, GI , kidneys and muscle.*

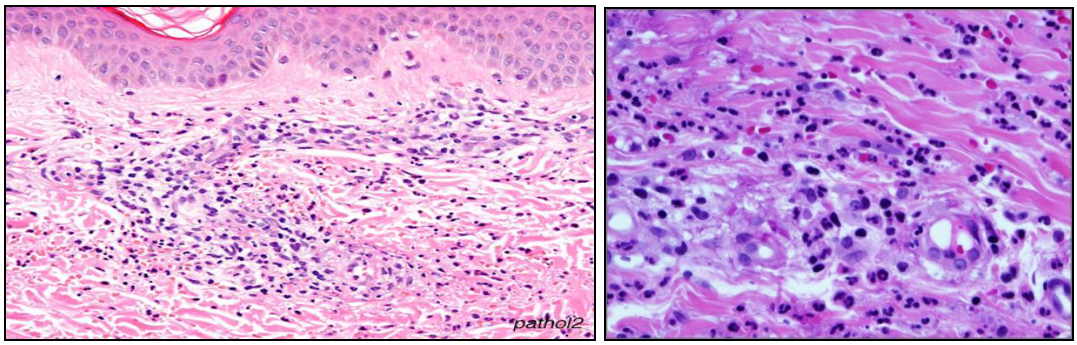
- It is manifest by palpable purpura[5] when the skin is involved.

Leukocytoclasis: refers to the damage caused by nuclear debris from infiltrating neutrophils in and around the vessels.

- **It may be a part of a systemic diseases:**
  - collagen vascular diseases (lupus erythematosus, rheumatoid arthritis),
  - Henoch-Schonlein purpura (next page).

Diagnosis: Skin biopsy, P-ANCA levels in blood.

Histologically: There is infiltration of vessel wall with neutrophils, which become fragmented called as leukocytoclasia or nuclear dust.



Leukocytoclastic vasculitis in a skin biopsy showing fragmentation of neutrophil nuclei in and around vessel walls.

- It is the most common vasculitis seen in clinical practice.

How to differentiate from wegener granulomatosis?

Microscopic polyangiitis doesn't affect the nasopharynx, microscopic findings DOESN'T show granulomas.

---

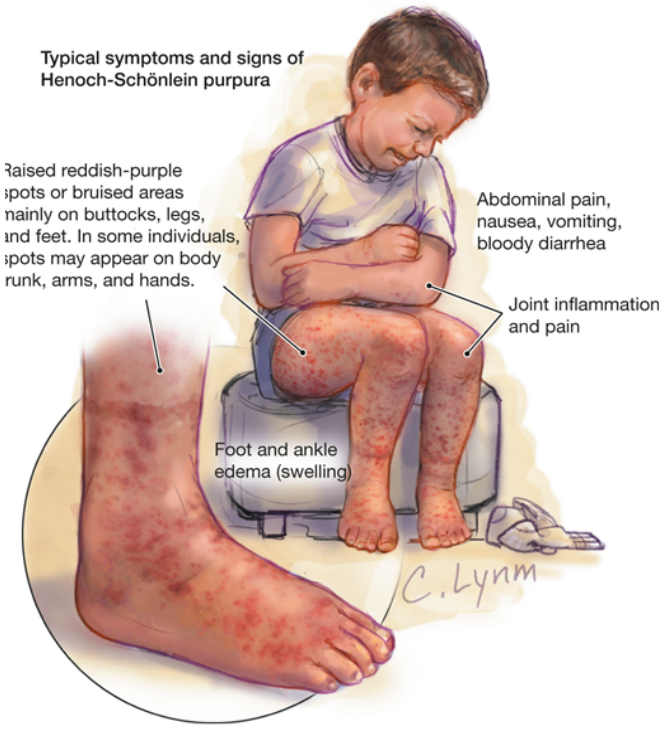
[4] التهاب الأوعية المجهرية

[5] a rash of purple spots on the skin caused by internal bleeding from small blood vessels.

HENOCH-SCHONLEIN PURPURA (HSP).

HSP is an **IgA-mediated**, autoimmune systemic small vessel hypersensitivity vasculitis of childhood. It causes skin purpura, arthritis, abdominal pain, gastrointestinal bleeding, orchitis[6] and nephritis.

- The aetiology remains **unknown**.
- **Immunoglobulin A (IgA)** and complement component 3 (C3) are deposited on arterioles, capillaries, and venules.
- Serum levels of IgA are high in HSP.



Churg-Strauss syndrome. (Allergic Granulomatosis and Angiitis) (Robbins page 354)

Churg-Strauss Syndrome. **(Very usefull video)**

A small vessel necrotizing vasculitis classically associated with asthma, allergic rhinitis, lung infiltrates, peripheral eosinophilia, extravascular necrotizing granulomas and a striking infiltration of vessels. It's a rare disease affecting 1 in a million.

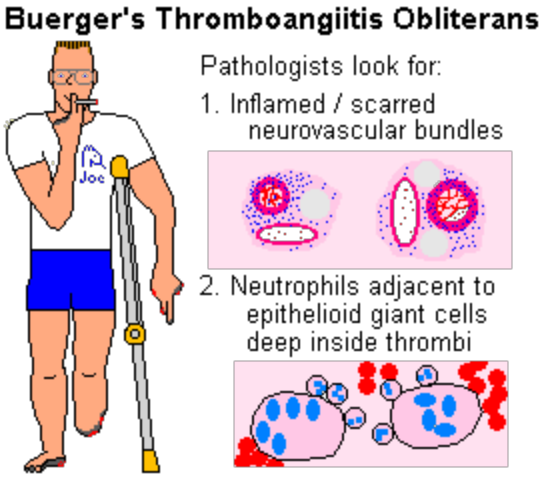
- It differs from other types of vasculitis by the presence of granulomas and eosinophils (***eosinophilia***).
- Eosinophil-rich and granulomatous inflammation involving the respiratory tract and necrotizing vasculitis affecting small vessels.
- Associated with **p-ANCA** **(Perinuclear Anti-Neutrophil Cytoplasmic Antibodies).**

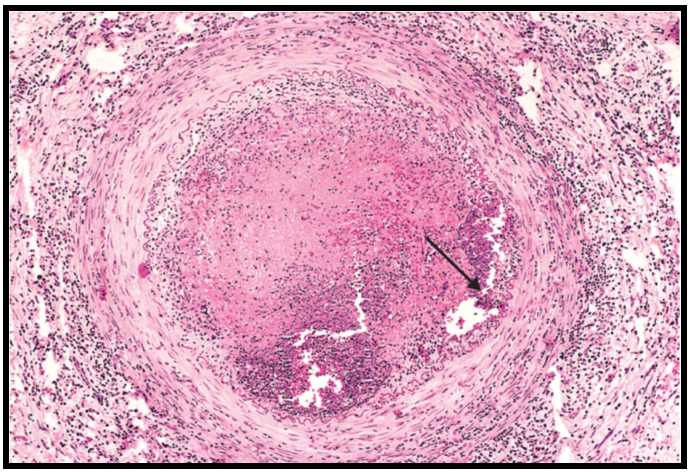
[6] inflammation of one or both of the testicles.

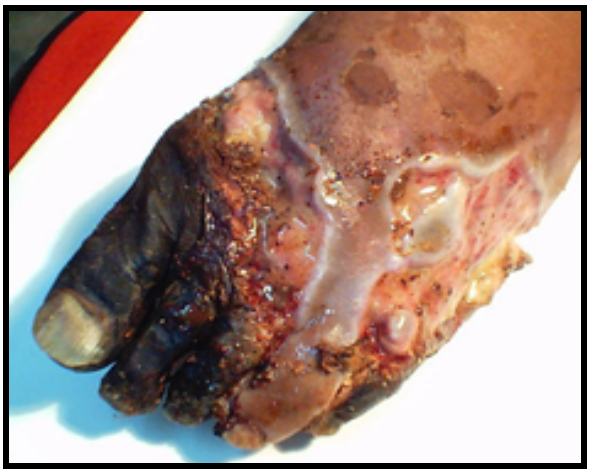
Thromboangiitis Obliterans (Buerger Disease). Robbins page 354

Unknown etiology (Direct endothelial cell toxicity caused by some component of tobacco is suspected)

- Results in severe vascular insufficiency and **gangrene** of the extremities.
- Focal sharply segmental acute and chronic inflammation of medium-sized and small arteries, especially the tibial and radial arteries, associated with thrombosis.
- Almost exclusively in heavy tobacco smokers and usually develops before age 35.
- The inflammation often extends into contiguous veins and nerves (a feature that is rare in other forms of vasculitis).
- In early stages, mixed inflammatory infiltrates are accompanied by luminal thrombosis; small microabscesses, occasionally rimmed by granulomatous inflammation.







Clinical features.

- cold-induced Raynaud phenomenon[7]
- instep foot pain induced by exercise (instep claudication).
- A superficial nodular phlebitis (venous inflammation).
- Chronic extremity ulcerations can develop, progressing over time to frank gangrene.
- Abstinence[8] from cigarette smoking in the early stages of the disease brings relief from further attacks, however, once established, the vascular lesions do not respond to smoking abstinence.
- Patients tend to have pain even at rest, due to the neural involvement.

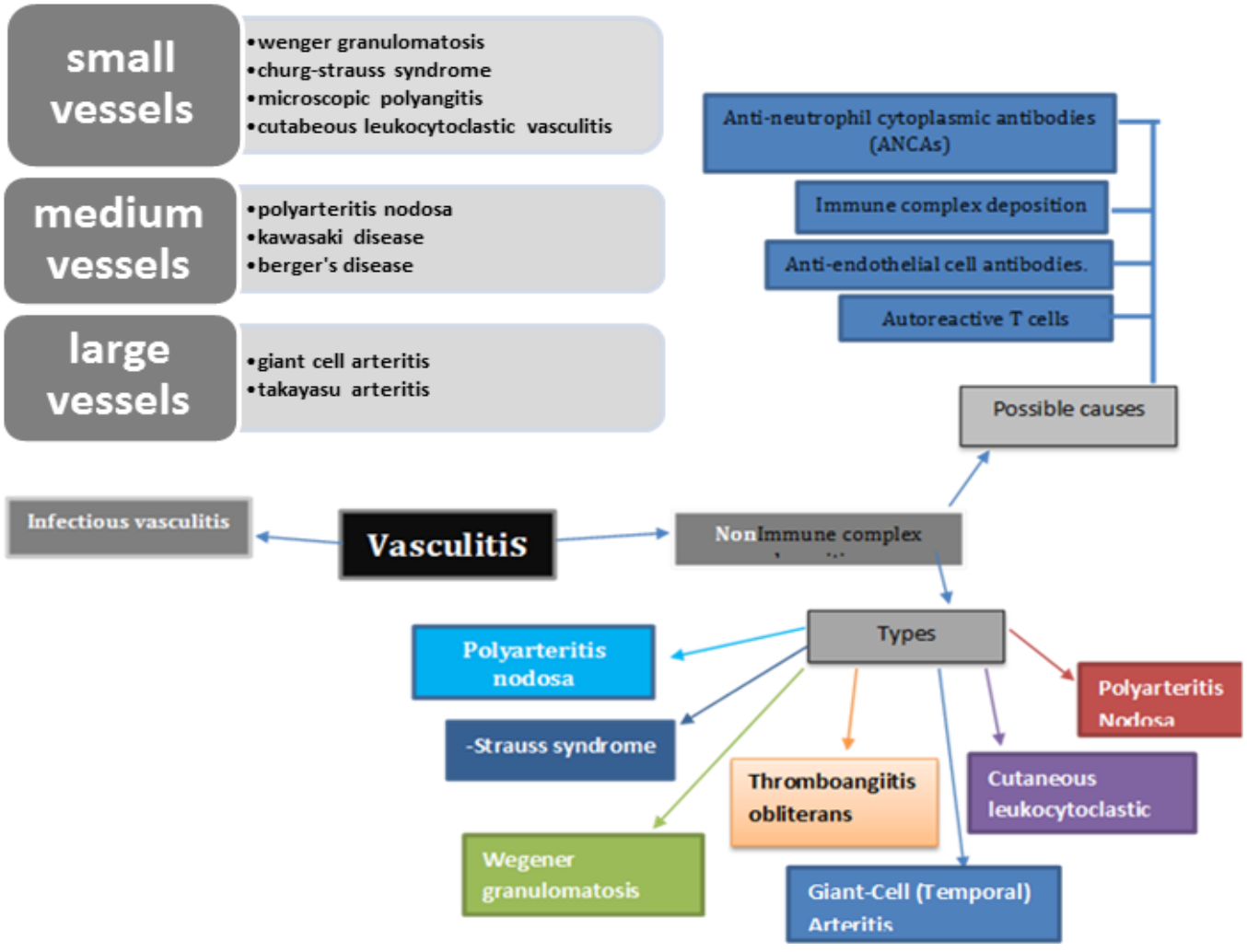
[7] A condition in which some areas of the body feel numb and cool in certain circumstance.
[8] The fact or practice of restraining oneself from indulging in something.

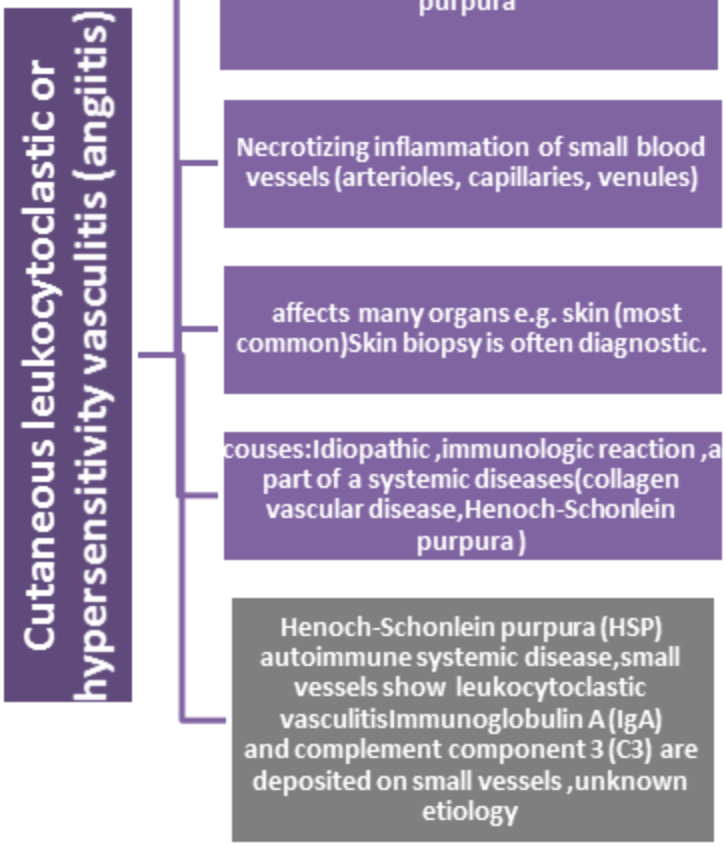
Summary.

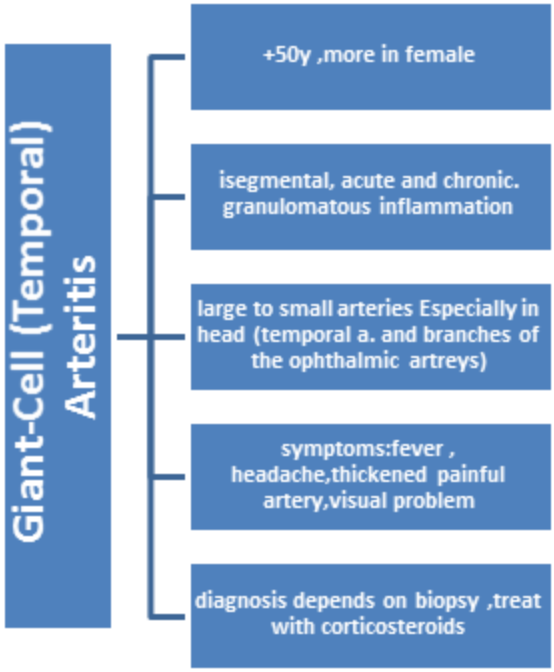
SUMMARY

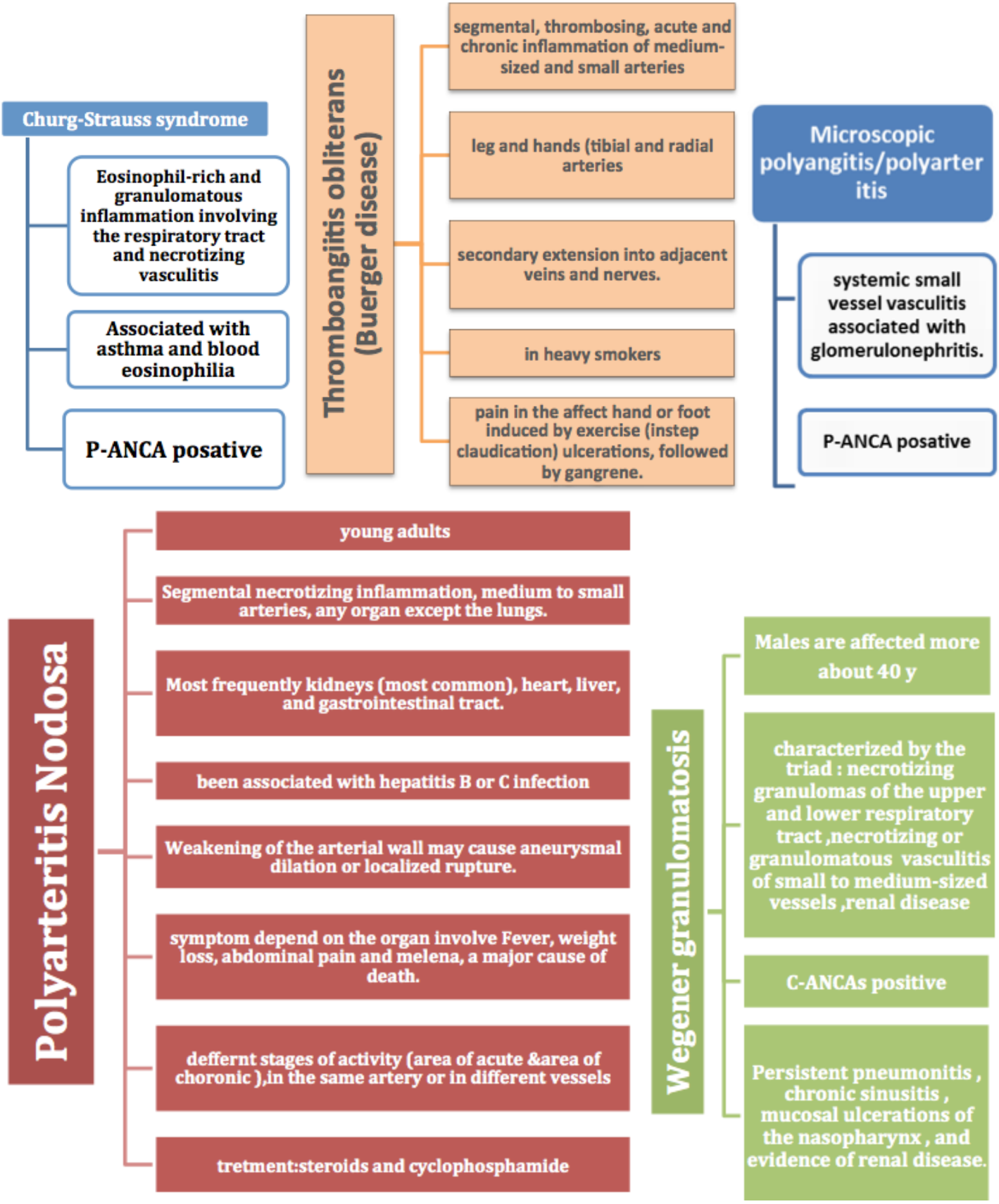
Vasculitis

- Vasculitis is defined as inflammation of vessel walls; it frequently is associated with systemic manifestations (including fever, malaise, myalgias, and arthralgias) and organ dysfunction that depends on the pattern of vascular involvement.
- Vasculitis can result from infections but more commonly has an immunologic basis such as immune complex deposition, anti-neutrophil antibodies (ANCAs), or anti–endothelial cell antibodies.
- Different forms of vasculitis tend to specifically affect vessels of a particular caliber and location (see Fig. 9–22).




Cutaneous leukocytoclastic or hypersensitivity vasculitis (angiitis)
the most common vasculitis (seen in the dermis of skin)characterized by palpable purpura
Necrotizing inflammation of small blood vessels (arterioles, capillaries, venules)
affects many organs e.g. skin (most common)Skin biopsy is often diagnostic.
couses:Idiopathic ,immunologic reaction ,a part of a systemic diseases(collagen vascular disease,Henoch-Schonlein purpura)
Henoch-Schonlein purpura (HSP) autoimmune systemic disease,small vessels show leukocytoclastic vasculitisImmunoglobulin A (IgA) and complement component 3 (C3) are deposited on small vessels ,unknown etiology


Giant-Cell (Temporal) Arteritis
+50y ,more in female
isegmental, acute and chronic. granulomatous inflammation
large to small arteries Especially in head (temporal a. and branches of the ophthalmic artreys)
symptoms:fever , headache,thickened painful artery,visual problem
diagnosis depends on biopsy ,treat with corticosteroids


Churg-Strauss syndrome
Eosinophil-rich and granulomatous inflammation involving the respiratory tract and necrotizing vasculitis
Associated with asthma and blood eosinophilia
P-ANCA posative
Thromboangiitis obliterans (Buerger disease)
segmental, thrombosing, acute and chronic inflammation of medium-sized and small arteries
leg and hands (tibial and radial arteries
secondary extension into adjacent veins and nerves.
in heavy smokers
pain in the affect hand or foot induced by exercise (instep claudication) ulcerations, followed by gangrene.
Microscopic polyangitis/polyarteritis
systemic small vessel vasculitis associated with glomerulonephritis.
P-ANCA posative
Polyarteritis Nodosa
young adults
Segmental necrotizing inflammation, medium to small arteries, any organ except the lungs.
Most frequently kidneys (most common), heart, liver, and gastrointestinal tract.
been associated with hepatitis B or C infection
Weakening of the arterial wall may cause aneurysmal dilation or localized rupture.
symptom depend on the organ involve Fever, weight loss, abdominal pain and melena, a major cause of death.
deffernt stages of activity (area of acute &area of choronic),in the same artery or in different vessels
tretment:steroids and cyclophosphamide
Wegener granulomatosis
Males are affected more about 40 y
characterized by the triad : necrotizing granulomas of the upper and lower respiratory tract ,necrotizing or granulomatous vasculitis of small to medium-sized vessels ,renal disease
C-ANCAs positive
Persistent pneumonitis , chronic sinusitis , mucosal ulcerations of the nasopharynx , and evidence of renal disease.

MCQ's.

1. **A 7-year-old child has had abdominal pain and dark urine for 10 days. Physical examination shows purpuric skin lesions on the trunk and extremities. Urinalysis shows hematuria and proteinuria. Serologic test results are negative for P-ANCAs and C-ANCAs. A skin biopsy specimen shows necrotizing vasculitis of small dermal vessels. A renal biopsy specimen shows immune complex deposition in glomeruli, with some IgA-rich immune complexes. Which of the following is the most likely diagnosis?**

A. Giant cell arteritis
B. Henoch-Schönlein purpura
C. Polyarteritis nodosa
D. Wegener granulomatosis

Ans: B, An IGA-mediated, autoimmune disease in which you see leukocytoclastic vasculitis and these symptoms.

2. **A 30-year-old woman has had coldness and numbness in her arms and decreased vision in the right eye for the past 5 months. On physical examination, Radial pulses are not palpable, but femoral pulses are strong. She has decreased sensation and cyanosis in her arms, but no warmth or swelling. A chest radiograph shows a prominent border on the right side of the heart and prominence of the pulmonary arteries. Laboratory studies show negative ANA test result. Her condition remains stable for the next year. Which of the following is the most likely diagnosis?**
    a. Aortic dissection
    b. Takayasu arteritis
    c. Microscopic polyangiitis
    d. Kawasaki disease

Ans: D, same symptoms of giant cell but pulseless.

3. **A 50-year-old man complains of a chronic cough that has persisted for the past 18 months. Physical examination shows nasopharyngeal ulcers, and the lungs have diffuse crackles bilaterally on auscultation. His serologic titer for C-ANCA is elevated. A chest radiograph shows multiple, small, bilateral pulmonary nodules. A nasal biopsy specimen shows mucosal and submucosal necrosis and necrotizing granulomatous inflammation. A transbronchial lung biopsy specimen shows a vasculitis involving the small peripheral pulmonary arteries and arterioles. Granulomatous inflammation is seen within and adjacent to small arterioles. Which of the following is the most likely diagnosis?**
    a. Polyarteritis nodosa
    b. microscopic polyangiitis
    c. Wegener granulomatosis
    d. atherosclerosis

Ans: C, Wegener granulomatosis is a form of hypersensitivity reaction to an unknown antigen characterized by necrotizing granulomatous inflammation that typically involves the respiratory tract, small to medium-sized vessels, and glomeruli.

4. **A female 70 years old came to hospital with fever, headache , jaw pain, pain intense along the course of the superficial temporal artery. What is the most likely diagnosis?**
   A. cutaneous leukocytoclastic
   B. Giant cell arteritis
   C. polyarteritis nodosa
   D. Wegener's granulomatosis

Ans: B

5. **Polyarteritis Nodosa Associated with all of the following except:**
   a. Hepatitis B
   b. Young adult
   c. fibrinoid necrosis.
   d. SLE

Ans: D

6. **Which blood vessels are inflamed in cutaneous leukocytoclastic?**
   a. Medium blood vessel
   b. Small blood vessel
   c. Large blood vessel
   d. Deep veins

Ans: A

Contact us on: Pathology434@gmail.com

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Good Luck!

عمر الرهبيني
مشهور الزارعي
عبدالرحمن المزعل
فيصل أبو نهية

مها الربيعة
ريما الرشيد
أمل سعد
هديل السلمي
ريم لبني
مشاعل حسين
ريما الناصر