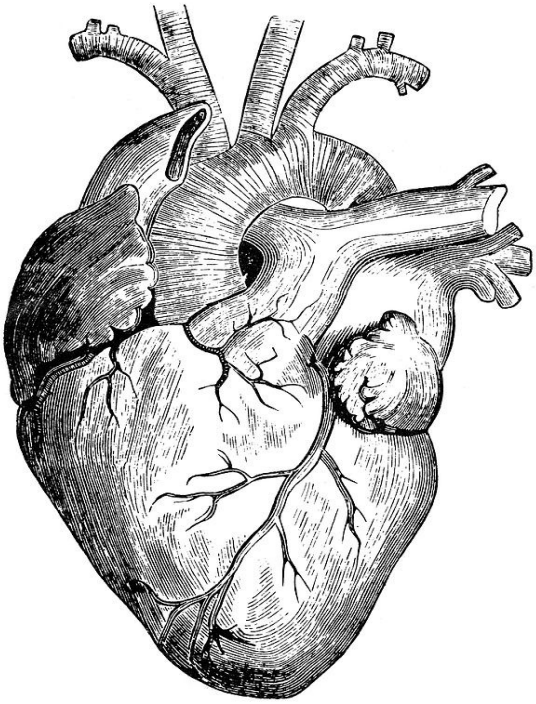
MED437
KING SAUD UNIVERSITY

PATHOLOGY
TEAM 437



Pathology

teamwork

Lecture (6) :

Vasculitis

Editing File

Color Index :-

- VERY IMPORTANT
- Extra explanation
- Examples
- Diseases names: Underlined
- Definitions

*It always seems impossible, until it's done..

Objectives :

- Know the common causes of vasculitis with special emphasis on the clinic-pathological features and mechanism of :

1. Giant cell arteritis.
2. Polyarteritis nodosa.
3. Wegener's granulomatosis.
4. Leukocytoclastic vasculitis.

* Try to focus on the **red** text, all of it is important.

INTRODUCTION

Vasculitis : It is the inflammation of vessel walls with many possible symptoms.

Causes:

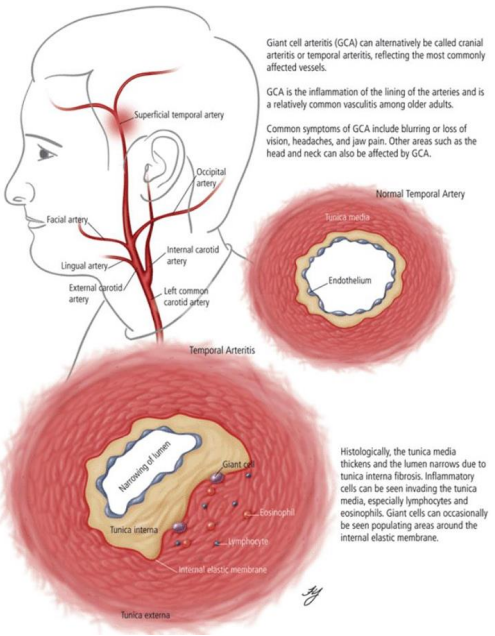
1. It is usually immune-mediated :
   - Immune complex deposition
   - Antineutrophil cytoplasmic antibodies (ANCAs)
   - Anti-endothelial cell antibodies
   - Autoreactive T cells
2. It also can be caused by infection, physical or chemical injury.

Quick look on Vasculitis:

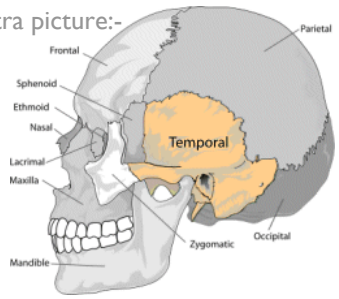
Vessel	Disease	Features
Large	Giant-cell arteritis	>50 years. Arteries of the head.
	Takayasu arteritis	Female <40. "Pulseless disease"
Medium	Polyarteritis nodosa	Young adults. Widespread.
	Kawasaki disease	<4. Coronary disease. Lymph nodes.
Small	Wegener granulomatosis	Lung, kidney, c-ANCA.
	Churg-Strauss syndrome	Lung, Eosinophils, Asthma, p-ANCA.
	Microscopic polyangiitis	Lung, kidney, p-ANCA.
	Cutaneous Leukocytoclastic vasculitis	Idiopathic, infectious, drugs, chemicals, cancer and systemic disease like HNP.

GIANT CELL (TEMPORAL) ARTERIES

- Most common type of vasculitis.
- Affect patients more than 50 years of age (only one occurs in elderly)
- Female to male ratio is 2:1 respectively.
- Chronic, granulomatous inflammation of **large** to small arteries, especially in the head, particularly the branches of the carotid artery (temporal artery (headache) and branches of the ophthalmic artery (blindness)).
- Involvement is segmental, acute and chronic. by segmental it means it only affects sections of the arteries rather than the whole artery



Extra picture:-



Clinical Features:

❖ Symptoms :

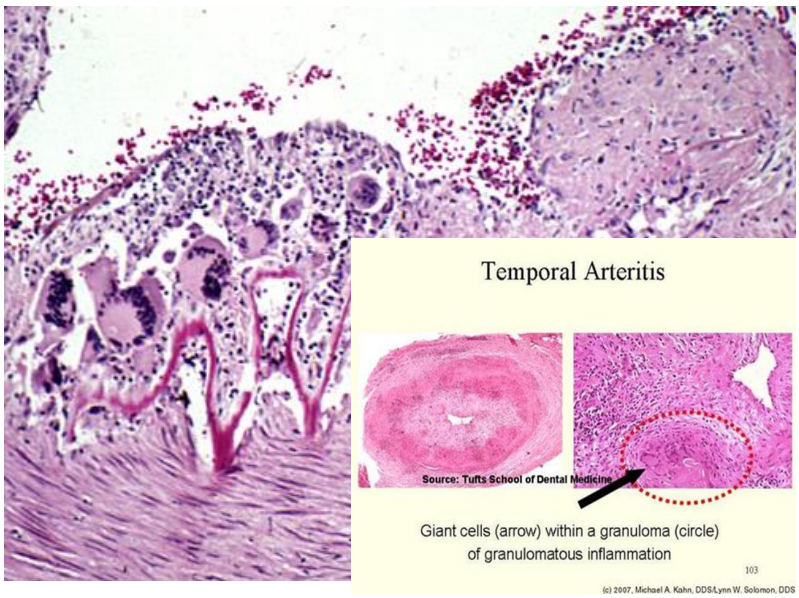
- Fever. general symptom from inflammatory response
- headache. often most intense along the course of the superficial temporal artery
- Thickened and painful temporal artery. thickened From the inflammation and painful from the inflammatory mediators which cause pain
- Facial pain or Jaw pain. when the facial artery is involved
- Visual problems and acute vision loss. when the ophthalmic artery is involved

- more specific symptoms occur when the organ supplied lacks blood supply due to the inflammation of the artery supplying the organ

❖ The diagnosis depends on biopsy and histologic confirmation.

❖ Treatment : corticosteroids. It weakens the Immune response that is causing the inflammation

Mnemonic: Giant old Head = affects Arteries in the head



Morphology:

❖ Granulmatous inflammation of the blood vessel wall.

❖ Giant cells.

❖ Disruption and fragmentation of internal elastic lamina.

❖ The healed stage reveals collagenous thickening of the vessel wall and the artery is transformed into a fibrous cord.

❖ Proliferation of the intima with associated occlusion of the lumen.

POLYARTERITIS NODOSA

- Cutaneous only or systemic (can affect any organ).
- Disease of young adults.
- There is segmental necrotizing inflammation of arteries of medium to small size, in any organ (especially the kidneys and skin) except the lung.
  Mnemonic: Polyarteritis Nodosa = Pulmonary Are Not damaged
- Polyarteritis nodosa has been associated with hepatitis B or hepatitis C.

Clinical Manifestations

Results from ischemia and infarction of affected tissues and organs.

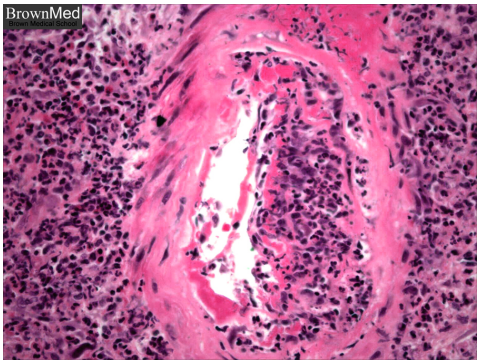
Fever general symptom from inflammatory response

weight loss, abdominal pain and melena (bloody stool), muscular pain and neuritis.
All result from the inflammation and necrosis of the arteries supplying the organ

Renal arterial involvement is often prominent and is a major cause of death.

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.

❖ Fatal if untreated, but steroids and cyclophosphamide are curative.
Steroids are used to inhibit wbc from migrating and causing necrosis
Cyclophosphamide is used to damage the dna of Immune cells that cause the damage



- 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.

WEGENER GRANULOMATOSIS (NEW NAME IS GRANULOMATOSIS WITH POLYANGITIS)

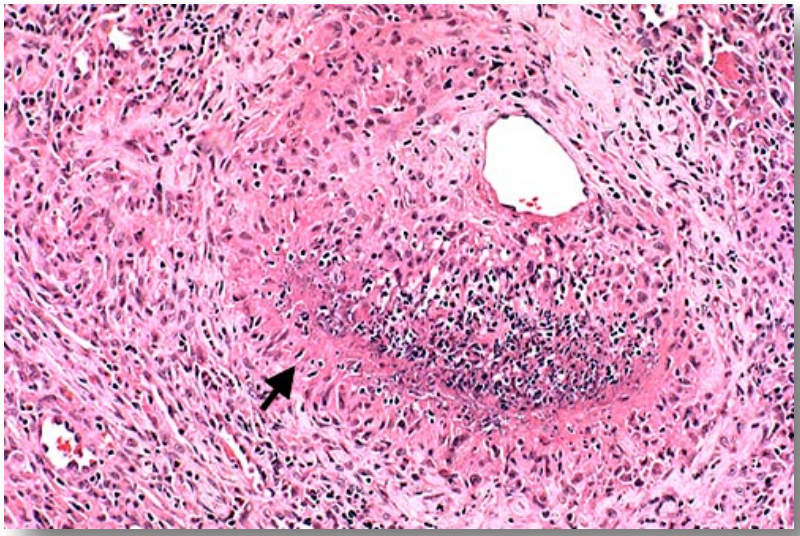
- Males are affected more often than females, at an average age of about 40 years
- C- ANCAs (antineutrophilic cytoplasmic antibodies) is positive in serum of more than 95% of patients.
- Persistent pneumonitis, chronic sinusitis, mucosal ulcerations of the nasopharynx , and evidence of renal disease. Wegener Granulomatosis involves damage to the Respiratory tract and Kidney only
- Untreated: fatal - may lead to death within 2 years if not treated.

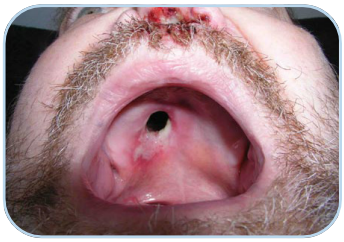
Necrotizing granulomas of the upper and lower respiratory tract. (respiratory syptoms)

WG is a necrotizing vasculitis characterized by the **triad** of:

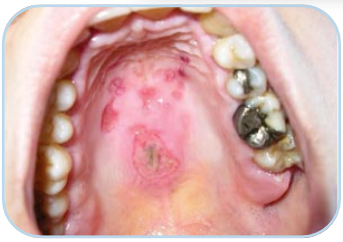
Renal disease in the form of necrotizing, crescentic, glomerulonephritis.

necrotizing or granulomatous vasculitis of small to medium-sized vessels.



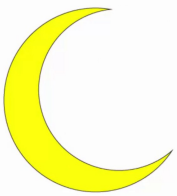


Palatal Destruction



Palatal Ulceration

Extra picture:- Crescentic

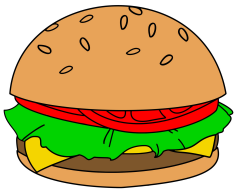


THROMBOANGIITIS OBLITERANS: (BUERGER'S DISEASE)

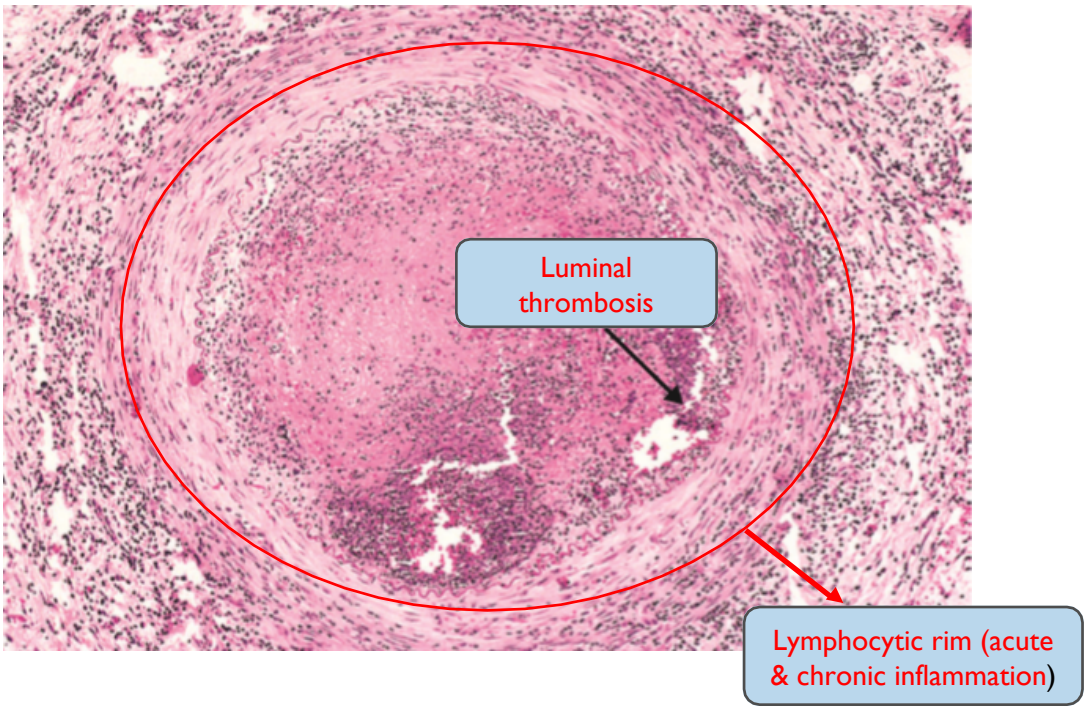
- Distinct disorder that results in severe vascular insufficiency and gangrene of extremities. It is characterized by areas of inflammation of medium and small sized arteries. It is associated with thrombosis and can extend to nearby veins as well as nerves.
- Abstinence of cigarette smoking in early stages of disease brings relief from further attacks

Features:

Extra picture:-
Buerger's sounds like Burgers



- Affects medium/small arteries
- Hands and legs
- Associated with heavy smokers. Before age of 35
- Pain at rest due to nerve damage
- Pain if affected part induced by exercise (instep claudication)
  claudication=العرج
- Chronic ulcerations in hand and foot can progress to gangrene



CUTANEOUS LEUKOCYTOCLASTIC OR HYPERSENSITIVITY VASCULITIS

❖ Necrotizing vasculitis that affects capillaries as well as small arterioles and venules. Vessels of the skin, mucous membranes, lungs, brain, heart, gastrointestinal tract, kidney and muscle can be involved.

Features:

- Most common vasculitis seen in clinical practice
- Inflammation of small blood vessels (usually, post capillary venules in the dermis)
- Palpable purpura (purple discolored spots cause by bleeding under skin)
- Can be cutaneous or systemic disease
- Effects many organs, most notably the skin
- Characterized by Leukocytoclasis: karyorrhexis (fragmentation) of neutrophils in and around the vessels. (leading to purpura)

❖ Causes:

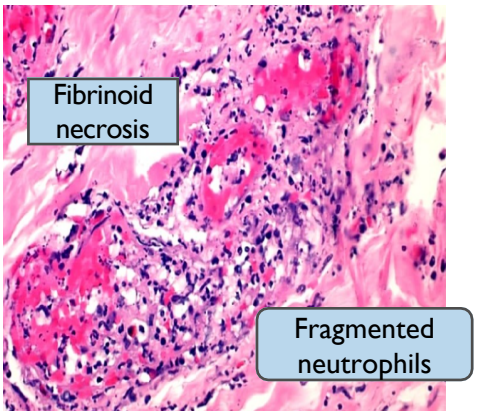
➢ Idiopathic
➢ Immune response towards:
- Drugs: Penicillin
- Infections : streptococcal
- Food products/ toxic chemicals
- Tumor antigens in cancer cells

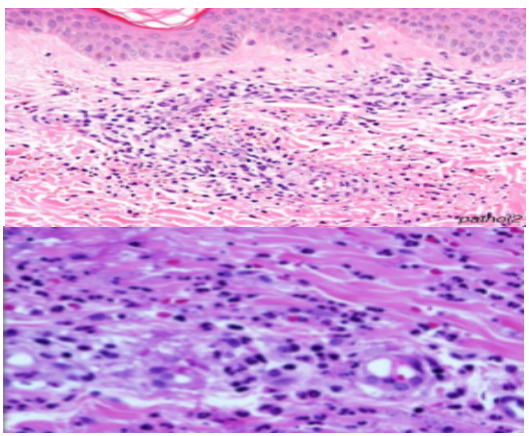
➢ Part of systemic disease:
- collagen vascular diseases:

✓ Lupus erythematosus
✓ Rheumatoid arthritis
- Henoch-Schönlein purpura

❖ Diagnosis:
skin biopsy

❖ Features:
Infiltration of vessel wall with neutrophils which then become fragmented resulting in leukocytoclasia or nuclear dust





HENOCH-SCHONLEIN PURPURA (HSP)

- HSP is an IgA-mediated, autoimmune systemic small vessel leukocytoclastic hypersensitivity vasculitis of childhood. It causes skin purpura, arthritis, abdominal pain, gastrointestinal bleeding, orchitis 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.
- Skin biopsy will show necrotizing leukocytoclastic vasculitis of capillaries in the dermis.

Summary Important!

	Vessels size	epidemiology	Tissues/organs affected	Clinical features	Microscopical features
Giant-Cell Arteritis	large to small vessels.	Patients >50, F:M = 2:1	Branches of the carotid artery (temporal and ophthalmic arteries)	- fever, facial pain or headache. -Thickened and painful temporal artery. -Visual loss if untreated.	-Granulomatous inflammation of the blood vessels. -Giant cells. -Disruption and fragmentation of the internal elastic lamina.
Polyarteritis Nodosa	medium to small vessels.	young adults.	-May be cutaneous only or systemic. -Affects any organ especially the kidneys and skin, not the lungs.	-Fever, weight loss, abdominal pain and melena (bloody stool), muscular pain and neuritis. -associated with hepatitis B and C	-inflammation. -fibrinoid necrosis.
Wegener granulomatosis	medium to small vessels.	Average of 40 years old. M>F.	-upper and lower respiratory tract→necrotizing granuloma. -renal disease→necrotizing, crescentic glomerular-nephritis.	-Persistent pneumonitis, chronic sinusitis, mucosal ulcerations of the nasopharynx, and evidence of renal disease. -C-ANCAs→is positive in serum of more than 95% of patients.	-necrotizing granulomas. -epithelioid histiocytes and neutrophils.
Thromboangiitis obliterans (Buerger disease)	medium to small vessels.	-Young adults, before age 35. -heavy smokers.	The periphery of the limbs.	- pain in the affect hand or foot induced by exercise (called *instep claudication*) -some patients have pain at rest. - if severe may lead to gangrene.	-acute and chronic inflammation -luminal thrombosis.
Leukocytoclastic vasculitis. *	small blood vessels (usually post-capillary venules in the dermis)	Pediatric patient.	-May be cutaneous only or systemic. (etiology: Idiopathic, antigenic reaction, systemic disease)	-If cutaneous→palpable purpura. -if systemic→may affect mucous membranes, lungs, brain, heart, GI, kidneys and muscle.	-Skin biopsy often reveals, inflammatory infiltration of neutrophils which become fragmented (karyorrhexis). -fibrinoid necrosis

*Henoch-Schonlein purpura(HSP): is a type of *Leukocytoclastic vasculitis* which is Ig-A mediated.

Cases from Dr. Alhumeidi:

Case 1:
Elderly patient with headache and visual disturbances.
Diagnosis: Giant-cell (temporal) vasculitis
Giant cell vasculitis is almost the only vasculitis that affects the elderly (old age is a hint)

Case 2:
A young adult that is a heavy smoker presents with pain in his feet while playing soccer
Diagnosis: thromboangiitis obliterans: buerger's disease
Smoking and exercise induced pain are hints

Case 3:
A pediatric patient presents with skin lesions, abdominal pain, hematuria, and blood in stool
Diagnosis: Leukocytoclastic vasculitis
The age of the patient and these clinical manifestations like skin lesions (pupura) are hints

Q1) What is the most common cause of vasculitis?

A. Immune-mediated
B. Infections
C. Congenital defect
D. Drugs

Q2) Patient came to the hospital having fever and headache, what artery is most likely thickened or painful?

A. Carotid artery
B. Ophthalmic artery
C. Brachiocephalic artery
D. Temporal artery

Q3) Regarding (Q2), what can be found in the patient's biopsy?

A. Disruption and fragmentation of internal elastic lamina
B. Segmental inflammation and fibrinoid necrosis
C. Crescentic inflammation of the arteries
D. Leukocytoclasia

Q4) A Patient came to the hospital and the doctor noticed an inflammation in a medium sized vessels. The patient has fever lost some weight, and he has a bloody stool. Which of the following organs **cannot** be affected?

A. Kidney
B. Heart
C. Lung
D. Liver

Q5) A 34 year old man came to the clinic with ulceration of the palate, what is the most likely diagnosis in this case?

A. Polyarteritis Nodosa
B. Wegener granulomatosis
C. Burger disease
D. Cutaneous leukocytoclastic

Q6) Regarding (Q5), what is the best test to confirm your diagnosis?

A. C-ANCA
B. ECR
C. Blood culture
D. X ray

Q7) Increased neutrophils infiltration and the presence of karyorrhexis of the neutrophils indicates?

A. Polyarteritis Nodosa
B. Wegener granulomatosis
C. Burger disease
D. Hypersensitivity vasculitis

Q8) In case of Thromboangiitis obliterans, which statement can be true?

A. Smoking is a risk factor
B. Pain without any activity
C. Gangrene
D. All of the above

Answers :

Q1 – A
Q2 – D
Q3 – A
Q4 – C
Q5 – B
Q6 – A
Q7 – D
Q8 – D

Males:

-Leader : منصور العبرة

خالد العقيلي

عبدالجبار اليماني

بندر الجماز

محمد المحيميد

راكان الغنيم

سليمان الزميع

طارق العلوان

أحمد الصبي

أنس السيف

تركي آل بنهار

خالد المطيري

سعد الفوزان

سعود الأحمري

سيف المشاري

عبدالعزيز العبدالكريم

عبدالله العبيدان

عبدالله السرجاني

فهد الفايز

محمد الأصقه

محمد بن معيوف

Females:

-Leader : فاطمة بالشرف

ريناد الغريبي

منيرة المسعد

شوق القحطاني

رزان الزهراني

بتول الرحيمي

فاطمة الديحان

الجوهرة الشنيفي

نورة القاضي

غادة الحيدري

مها العمري

غرام الجليدان

آلاء الصويغ

ال فهدة السليم

شيرين حمادي

رناد الفرم

نورة الحربي

ميعاد النفيعي

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Kindly contact us if you have any questions/comments and suggestions:

* EMAIL: pathology437@gmail.com
* TWITTER : @pathology437

GOOD LUCK ! ☺

*references:
- Robbins Basic Pathology
- Slides

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