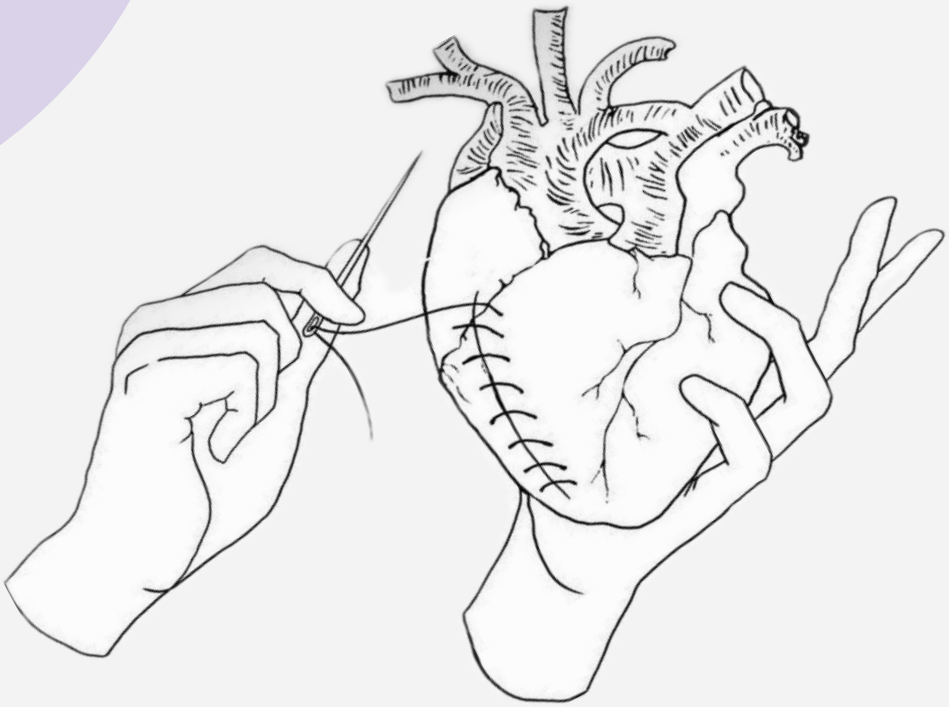
Pathology of Vasculitis



Editing file:

COLOR INDEX:

MAIN TEXT (BLACK)

FEMALE SLIDES (PINK)

MALE SLIDES (BLUE)

IMPORTANT (RED)

DR'S NOTE (GREEN)

EXTRA INFO (GREY)

Objective

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

- Giant cell arteritis
- Polyarteritis nodosa
- Wegener's granulomatosis
- Cutaneous hypersensitivity vasculitis and Henoch Schonlein purpura.
- purpura.
- Thromboangiitis obliterans (Burger's disease)

If you want to read the lecture from Robbins click here

Introduction: Vasculitis

Vasculitis

It is inflammation of vessel (arteries (more common) and veins) walls with many possible symptoms (depending on the vessel it's affecting) often with necrosis

Causes of Vasculitis

Immune-mediated (Most common)

Main immunological mechanisms:

- Immune complex deposition
- Antineutrophil cytoplasmic antibodies (ANCAs) (antibodies against cytoplasmic neutrophils)
- Anti-endothelial cell antibodies
- Autoreactive T cells

Invasion of vascular walls by

- Infectious pathogens
- Physical or chemical injury

Overview: Types of Vasculitis

They are grouped according to the size of blood vessels affected.

Vessel	Disease	Notes
Large	**Giant-cell arteritis**	>50yrs. Arteries of head.
	Takayasu arteritis	F <40yrs. “Pulseless disease
Medium	**Polyarteritis nodosa**	Young adults. Widespread.
	Kawasaki disease	<4yr. Coronary disease. Lymph nodes.
	Berger disease	35 y , smokers , extremities
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) Arteritis

Giant-Cell (Temporal) Arteritis

- Chronic, granulomatous inflammation of large to medium sized arteries (large to small-sized arteries)
- The involvement is segmental (not the whole artery is affected) ,acute and chronic.
- Principally Affects the arteries in the head-especially the temporal arteries

Affect the branches of the carotid artery in the head

- temporal artery
- branches of the ophthalmic artery

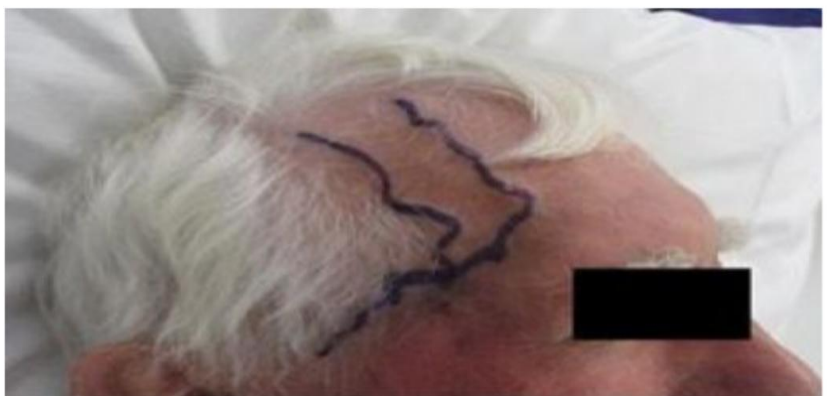
rarely affect the aorta (giant-cell aortitis).

Giant-Cell (Temporal) Arteritis

Females Dr said:age and gender is your key word

Epidemiology

- Most common type of vasculitis
- More common in females (F:M, 2:1)
- Above 50 years old
- Unknown cause, But it is probably an autoimmune condition. T cell-mediated



Giant-Cell (Temporal) Arteritis

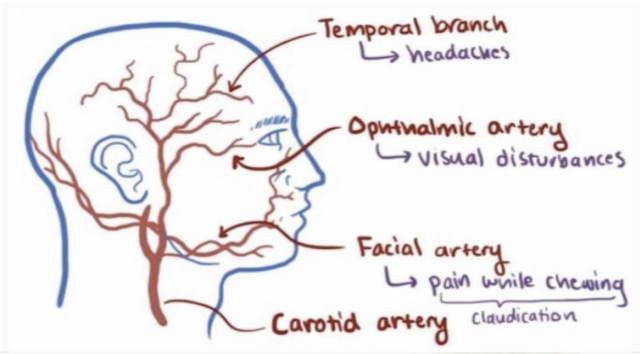
Symptoms (Clinical features)

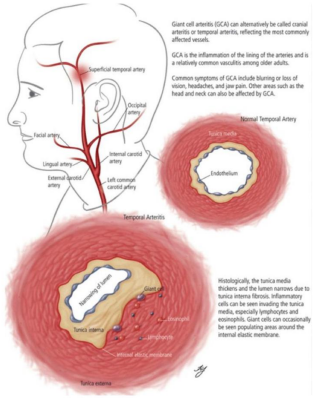
1. Visual problems and acute vision loss
2. Thickened and painful temporal artery.
3. Facial pain or headache, often most intense along the course of the superficial temporal artery. which is painful to palpation
4. Jaw pain.
5. Vague symptoms: Fever, fatigue and weight loss

Females Dr key word:65 years elderly sufferers from headache

Diagnosis — The diagnosis depends on biopsy and histologic confirm

Treatment — corticosteroids (weakens immune response)

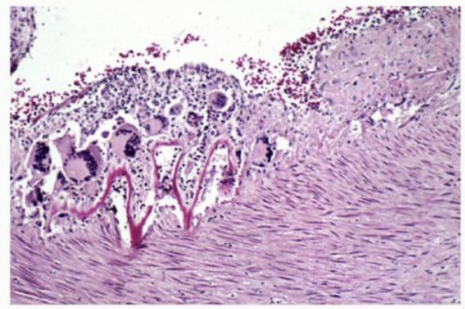


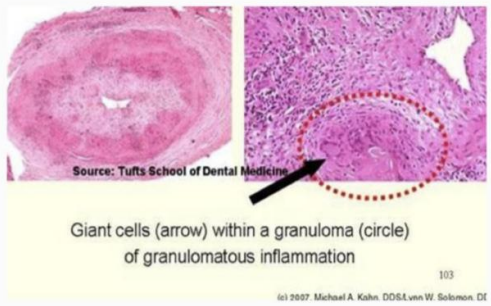


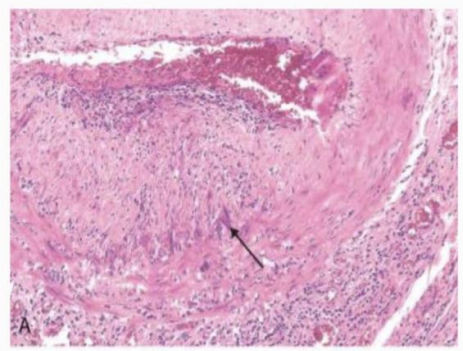
Giant-Cell (Temporal) Arteritis

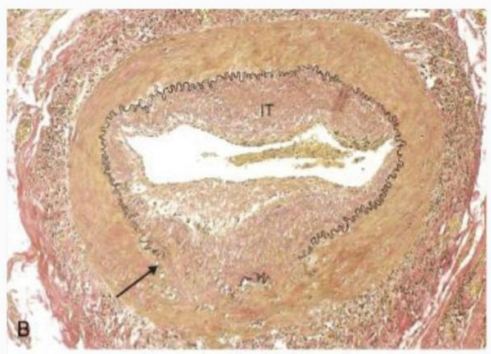
Morphology

- Granulomatous inflammation of the blood vessel wall.
- Giant cells. Necrotizing granuloma
- 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.





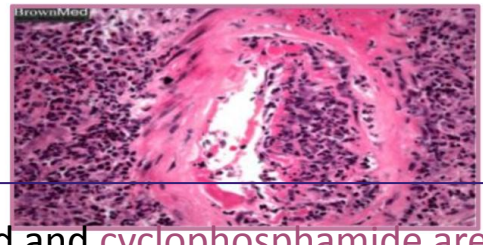




Polyarteritis nodosa (PAN)

Polyarteritis nodosa (PAN)

There is (systemic) segmental necrotizing inflammation of arteries of medium to small size (Small or medium-sized muscular arteries, But not arterioles,capillaries,or venules) , in any organ except the lungs (sparing the pulmonary circulation).

Epidemiology	Largely in young adults
Morphology	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.  
Treatment	Fatal if untreated, but steroid and cyclophosphamide are curative. other immunosuppressive therapy results in remissions or cures in 90% .

Polyarteritis nodosa (PAN)

Characteristics

Females Dr key word:20 years old man suffering from Hepatitis

1. Most frequently kidneys (most common, so renal manifestations are seen), heart, liver, and gastrointestinal tract.
2. Renal arterial involvement is often prominent and is a major cause of death.
3. PAN been associated with hepatitis B or hepatitis C virus infection. Some 30% of patients with PAN have hepatitis B antigenemia.
4. Weakening of the arterial wall due to the inflammatory process may cause aneurysmal dilation or localized rupture.
5. Particularly characteristic of PAN is that all the different stages of activity from early to late (i.e. active and chronic stages) may coexist in same artery or in different artery at the same time.
6. No association with ANCA (antineutrophil cytoplasmic antibodies)
7. Typically episodic, with long symptom-free intervals

Polyarteritis nodosa (PAN)

Symptoms (Clinical features)

Because the vascular involvement is widely scattered, the clinical findings may be varied and puzzling

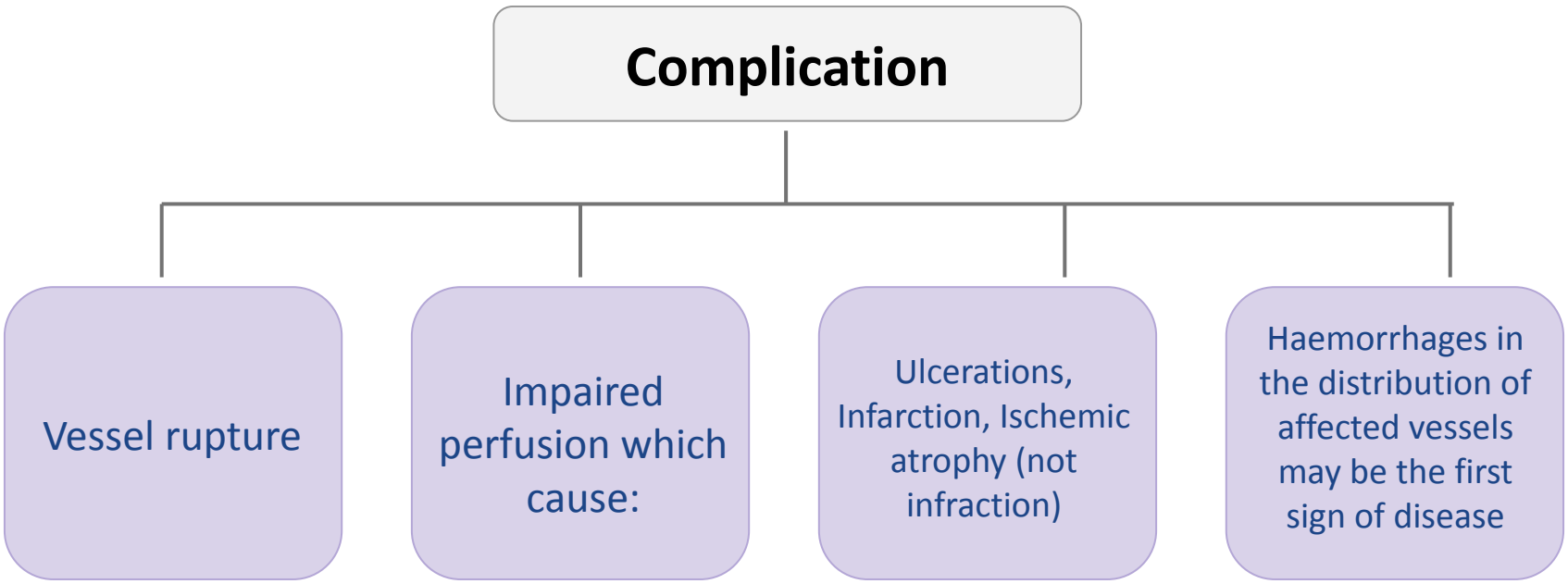
Some clinical manifestations are due to ischemia and infarction of affected tissues/ organs.

Fever, weight loss, abdominal pain and melena (bloody stool), muscular pain & aches and neuritis

Hypertension, usually developing rapidly

Biopsy is often necessary to confirm the diagnosis

Polyarteritis nodosa (PAN)

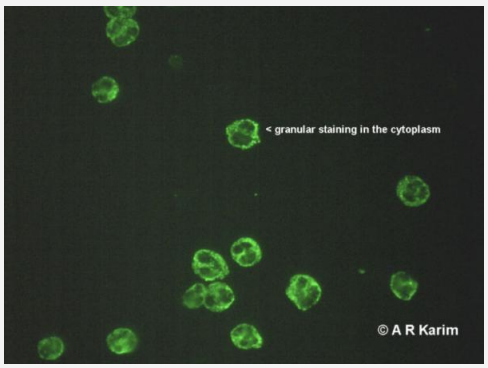


Antineutrophil cytoplasmic antibodies (ANCA)

Antineutrophil Cytoplasmic Antibodies

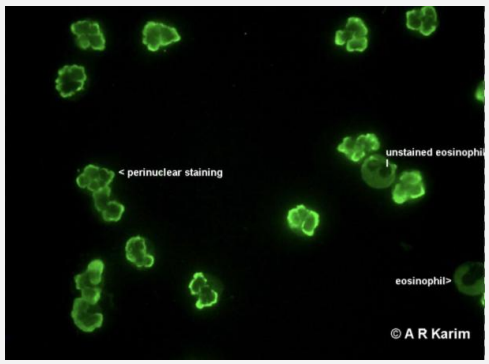
Cytoplasmic localization (c-ANCA)

the most common target antigen is proteinase-3 (PR3)
-typical of Wegener granulomatosis



Perinuclear localization (p-ANCA)

most of the autoantibodies are specific for myeloperoxidase (MPO) -microscopic polyangiitis and Churg-Strauss syndrome



ANCAs serve as useful diagnostic markers for the ANCA-associated vasculitides

Their levels can reflect the degree of inflammatory activity

Granulomatosis with Polyangiitis
(Previously: Wegener granulomatosis)

Definition

is a type of necrotizing vasculitis characterized by wegener's triad. The name highlights the two central pathologic features of the disease, granuloma formation and inflammation of blood vessels. (Uncommon disease)

Morphology

Females Dr key word:40 years old man with a positive C-ANCA

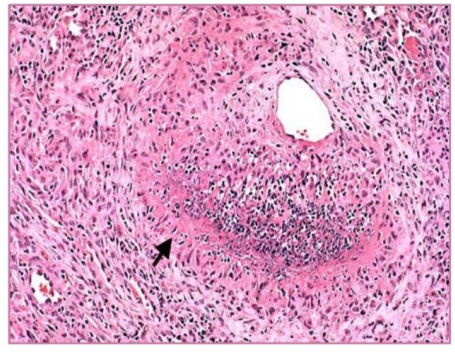
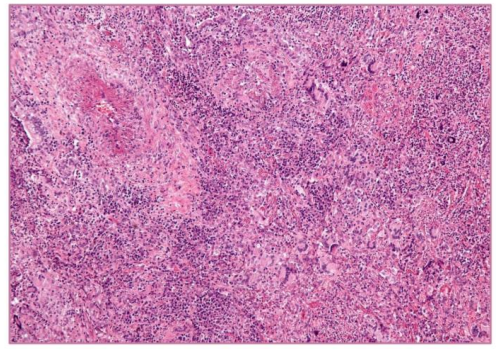
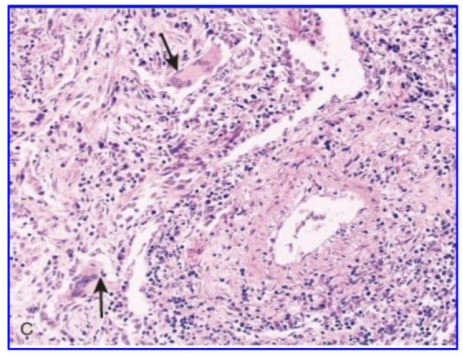
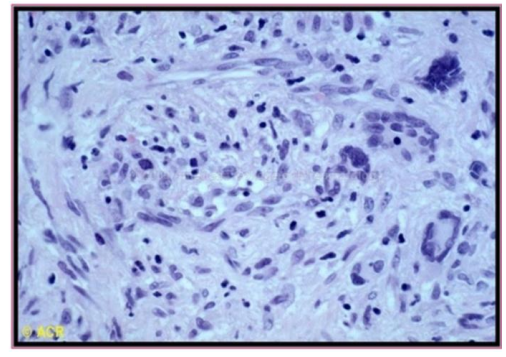
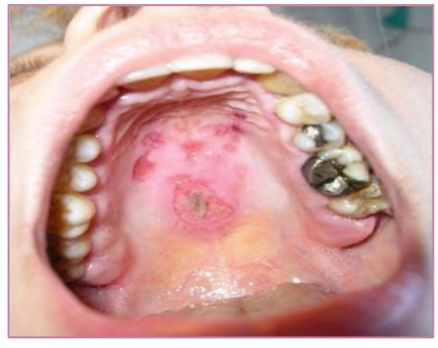
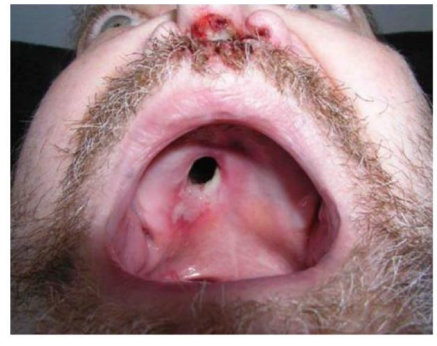
Acute necrotizing granulomas of the upper and lower respiratory tract (lung), or both

necrotizing or granulomatous vasculitis of small to medium - sized vessels (most prominent in the lungs and upper airways)

renal disease in the form of focal necrotizing, often crescentic, glomerulonephritis/glomerulitis

Epidemiology	Males are affected more often than females, at an average age of about 40-50 years
Symptoms	Persistent pneumonitis , chronic sinusitis , mucosal ulcerations of the nasopharynx ,and evidence of renal disease.
Diagnosis	C-ANCAs (antineutrophil cytoplasmic antibodies) is positive in serum of more than 95% of patients.

Granulomatosis with Polyangiitis
(Previously: Wegener granulomatosis)

Prognosis	• Without Rx -> 80% die • With Rx -> 90% live (not cured) • The Rx -> immunosuppression Untreated: fatal - may lead to death within 2 years if not treated.
Morphology	     Wegener granulomatosis: palatal ulceration  Wegener granulomatosis: palatal destruction

Microscopic polyangiitis/ polyarteritis

Definition

- It is a systemic small vessel vasculitis associated with glomerulonephritis (renal disease).

Characteristics

1. P-ANCA is characteristically present in more than 70% of patients
2. In the past it has been confused with leukocytoclastic vasculitis.
3. Necrotizing vasculitis that generally affects capillaries as well as arterioles and venules of a size smaller than those involved in PAN
4. Rarely, larger arteries may be involved
5. All lesions of microscopic polyangiitis tend to be ofthe same age in any given patient
6. Necrotizing glomerulonephritis (90% of patients) and pulmonary capillaritis are particularly common

MALE SLIDES

Microscopic polyangiitis/ polyarteritis

Epidemiology

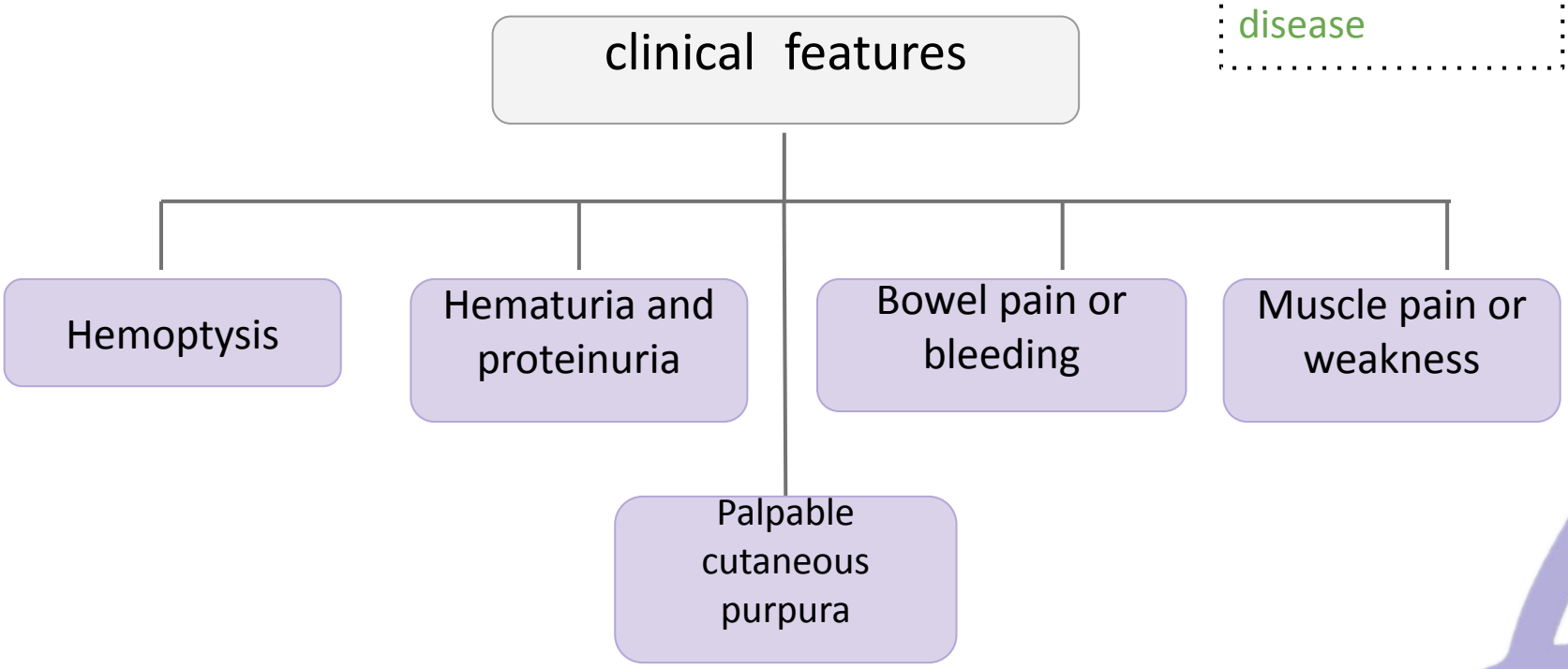
In many cases, an antibody response to antigens such as drugs (e.g., penicillin), microorganisms (e.g., streptococci), heterologous proteins, or tumor proteins is the presumed cause

This can result in immune complex deposition, or it may trigger secondary immune responses

clinical features

Females Dr key word: P-ANCA positive patient with renal disease

Depending on the organ involved, major clinical features include:

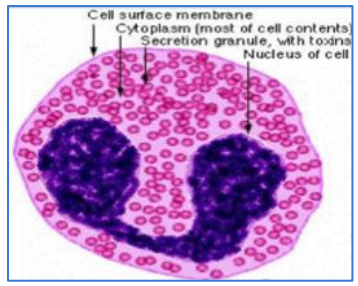


Churg-Strauss syndrome (additional reading)

Definition

- Eosinophil-rich and granulomatous inflammation involving the respiratory tract and necrotizing vasculitis affecting small vessels

Clinical features



Associated with asthma and blood Clinical eosinophilia

Associated with p-ANCAs

Cutaneous leukocytoclastic hypersensitivity vasculitis/ angiitis

Definition

- Necrotizing vasculitis of arterioles, capillaries, venules.
- It is inflammation of small blood vessels
- Leukocytoclasis refers to the nuclear debris of infiltrating neutrophils in and around the vessels.

Characteristics

1. It is the most common vasculitis seen in clinical practice.
2. commonly seen in the dermis of skin characterized by palpable purpura.
3. .All lesions tend to be of the same age. (All are acute or all are chronic)
4. It affects many organs
5. e.g. skin (most common), mucous membranes, lungs , brain, heart, GI , kidneys and muscle.

Cutaneous leukocytoclastic hypersensitivity vasculitis/ angiitis

Etiology

1. Idiopathic
2. Immunologic reaction to an antigen that may present as:
   - Drugs e.g. penicillin
   - Infectious microorganisms e.g. strept. and other infections, heterologous proteins,
   - food products and toxic chemicals
   - tumor antigens in various cancers.
3. It may be a part of a systemic diseases e.g:
   - Collagen vascular diseases (lupus erythematosus, rheumatoid arthritis)
   - Henoch-Schonlein purpura

Henoch-Schonlein purpura
HSP

FEMALE SLIDES

Definition

- HSP is an IgA-mediated, autoimmune systemic disease in which the small vessels show leukocytoclastic vasculitis.

Etiology

The etiology remains unknown

Clinical features

Females Dr key word:patient with a palpable skin lesions and a positive IgA

1. The immunofluorescence shows IgA immunoglobulin deposition in the wall the affected capillaries.
2. Skin biopsy will show necrotizing leukocytoclastic vasculitis of capillaries in the dermis.
3. Serum levels of IgA are high in HSP

Henoch-Schonlein purpura HSP

FEMALE SLIDES

Investigations

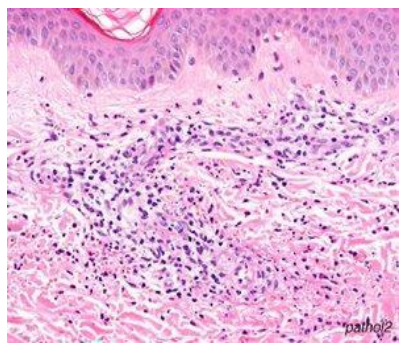
Investigations (Skin biopsy is often diagnostic.)

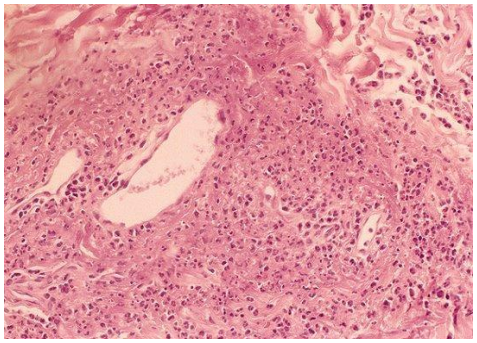
Direct immunofluorescence

will show deposits of IGA immunoglobulin in the wall the capillaries in Henoch-Schonlein purpura (HSP) .

Microscopically

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.

Thromboangiitis obliterans (Buerger disease)

Definition

- Buerger disease is a condition that occurs almost exclusively in heavy smokers of cigarettes.

Characteristics	It is characterized by **segmental**, thrombosing, Focal sharply segmental **acute and chronic inflammation of medium-sized and small arteries**, principally of the leg and hands (tibial and radial arteries, associated with thrombosis) with secondary extension into adjacent veins and nerves.
epidemiology	• Unknown etiology • Patients are usually under 35 years of age. • Tobacco either leads to direct toxicity to endothelium, or induces an immune response • Almost exclusively in heavy tobacco smokers.

Thromboangiitis obliterans (Buerger disease)

Clinical features

Females Dr key word:25 years old man who is a chronic smoker

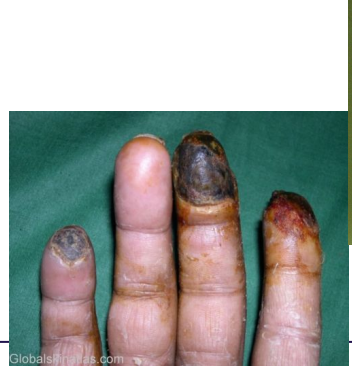
1. Patients can have pain even at rest, due to the neural involvement.
2. pain in the affected hand or foot induced by exercise (called instep claudication)
3. Chronic ulcerations of the toes, or fingers (extremities) may appear, followed in time by frank gangrene.
4. Abstinence from cigarette smoking in the early stages of the disease brings relief (ameliorate) from further attacks however, once established, the vascular lesions do not respond to smoking abstinence.
5. Results in severe vascular insufficiency and gangrene of the extremities
6. cold-induced Raynaud phenomenon
7. a superficial nodular phlebitis (venous inflammation)

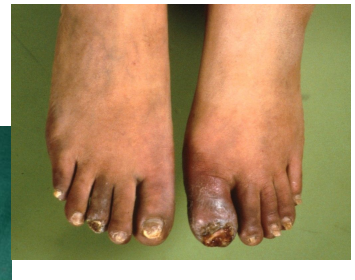
Thromboangiitis obliterans (Buerger disease)

Morphology

Macro

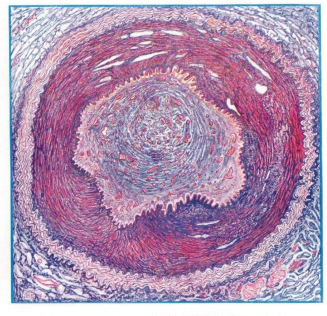
1. Distal limb ischemia, characterized by pain and discoloration of the affected limb due to reduced blood flow.
2. Ulcers and necrosis, resulting from severe tissue damage caused by occlusion of the vessels.
3. Superficial thrombophlebitis, which may be visible as reddish, tender, and cord-like structures under the skin.
4. Collateral circulation, which can develop as a compensatory mechanism to improve blood flow in areas where the vessels are occluded.
5. Segmental involvement of the vessels, with multiple affected areas separated by normal or less severely affected vessels.

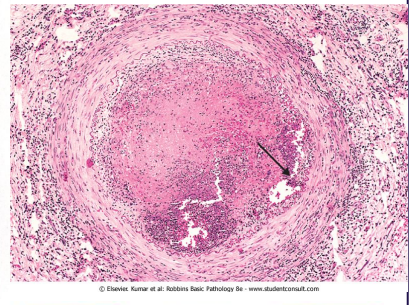


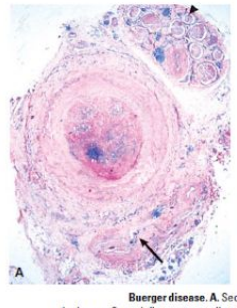


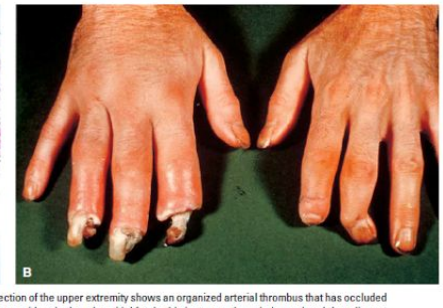
Micro

- Microscopically: there is acute and chronic inflammation, mixed inflammatory infiltrate are accompanied by luminal thrombosis; small microabscesses, occasionally rimmed by granulomatous inflammation.
- The inflammatory process extends into adjacent veins and nerves (rare with other forms of vasculitis), and in time all three structures become encased in fibrous tissue

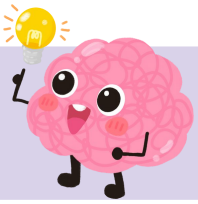






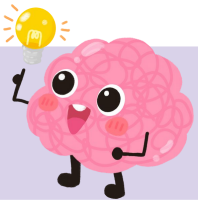


Buerger disease. A. Section of the upper extremity shows an organized arterial thrombus that has occluded the lumen. Some inflammatory cells are evident in the adventitial fat. In this instance, the vein (*arrow*) and the adjacent nerve (*arrowhead*) show foci of chronic inflammation. **B.** The hand shows necrosis of the tips of the fingers.



KEYWORDS

Giant-cell (temporal)arteritis	• large to medium/small-sized arteries • In ophthalmic artery • In temporal artery • Above 50 years old • Fever • Facial pain • Throbbing headache • blindness / visual problems • Jaw pain. • palpable temporal artery • Necrotizing granuloma
Polyarteritis nodosa (PAN)	• Segmental & necrotizing • medium to small size vessels • Doesn't involve the lungs • young adults. • Most frequently kidneys • associated with hepatitis B or hepatitis C virus • Ulcerations • fibrinoid necrosis • Fever & Weight loss • Abdominal pain & muscular pain
Granulomatosis with. Polyangiitis (Wegener granulomatosis)	• necrotizing vasculitis • upper and lower respiratory tract • average age of about 40-50 years • pneumonitis & chronic sinusitis • C-ANCAs Positive
Cutaneous leukocytoclastic (hypersensitivity vasculitis/ angiitis)	• Necrotizing vasculitis • small blood vessels • infiltrating neutrophils • palpable purpura. • All lesions tend to be of the same age. • Henoch-Schonlein purpura
Henoch-Schonlein purpura (HSP)	• IgA-mediated, • deposits of IGA



KEYWORDS

Churg-Strauss syndrome	• multiple purpuric skin lesions. • late onset asthma • mild hypertension. • increase in the number of eosinophils • P-ANCAs positive
Thromboangiitis obliterans (Buerger disease)	• heavy smokers of cigarettes. • segmental, thrombosing • medium-sized and small arteries • usually under 35 years of age. • pain in the affected hand or foot induced by exercise • Thrombosis with microabscesses

Answers:
1- A 2- C 3- D 4-C 5-C

MCQ

1- Which one of the following is a histological findings in leukocytoclastic vasculitis?			
A)Neutrophils infiltration	B)Fibrinoid necrosis	C)Activated macrophages with plasma cells	D)Giant cells with chronic inflammation
2- Which of the following vasculitis is associated with necrotizing granulomas of pulmonary and upper respiratory tract and glomerulonephritis?			
A)Henoch. schonlein purpura	B)Giant cell arteritis	C)Wegener's granulomatosis	D)Polyarteritis Nodosa
3- **Which of the following is an IgA vasculitis?**			
A)Giant cell arteritis	B)-Thromboangiitis obliterans	C)Granulomatosis with polyangiitis	D)Henoch-Schonlein purpura
4- which one of the following is not true about Polyarteritis nodosa (PAN)?			
A) Associated with Hepatitis C	B) Associated with Hepatitis B	C) Associated with ANCA	D) Active and chronic stages may coexist
5- A patient came with visual problem, biopsy was done and showed granulomatous inflammation what's the diagnosis?			
A) polyarteritis nodosa	B) cutaneous leukocytoclastic	C) giant cell arteritis	D) buerger disease

Answers:
1- A 2- D 3- C. 4-C 5-C

Cases

1- A 38-year-old female presents with the new onset of multiple purpuric skin lesions. Two years ago she developed late onset asthma and mild hypertension. Laboratory examination reveals an increase in the number of eosinophils in the peripheral blood (peripheral eosinophilia), and a biopsy from one of the purpuric skin lesions reveals leukocytoclastic vasculitis. No perivascular IgA deposits are found, and no antineutrophil cytoplasmic autoantibodies are present. Which one of the listed disorders is the best diagnosis for this individual?			
A)Churg-Strauss syndrome	B)Henoch-Schonlein purpura	C)Macroscopic polyarteritis nodosa	D)Microscopic polyangiitis
2- A 30-year-old male smoker presents with gangrene of his extremities. Which one of the following histologic findings from a biopsy of the blood vessels supplying this area would be most suggestive of the diagnosis of Burger's disease?			
A)Granulomatous inflammation with giant cells	B)Fibrinoid necrosis with overlying thrombosis	C)Focal aneurysmal dilation	D)Thrombosis with microabscesses
3- 30-year-old woman presents with a widespread skin rash that she has had for 5 days. She is taking sulfa medication for recurrent cystitis. A skin biopsy shows leukocytoclastic vasculitis involving dermal venues. What is the appropriate diagnosis?			
A).Buerger disease	B)Henoch-Schonlei purpura	C)Hypersensitivity Angitis	D)Polyarteritis nodosa
4- 5- a 56 year old female came to the hospital with: Face pain , 38c Temperature After examination the doctor told her that there is a damage in her ophthalmic artery and that she will be blind within 48 hours. Which one of the following is true about this disease?			
A) Affect both arteries and veins	B) Affect only large arteries	C) It could affect the aorta	D) Affect male more than female
5- 30-year-old smoker patient came to the hospital suffering from pain in his toes associated with chronic ulceration what's the diagnosis?			
A) Cutaneous leukocytoclastic	B) polyarteritis nodosa	C) Thromboangiitis obliterans	D) Giant-Cell (Temporal) Arteritis

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