Pathology of vascular diseases
Lecture 3&4

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Inflammatory diseases of blood vessels

Vasculitis is a general term for vessel wall inflammation with variable manifestations depending on the organ affected.

Besides the findings referable to the specific tissues involved, the clinical manifestations typically include constitutional signs and symptoms associated with systemic inflammation, such as fever, myalgia, arthralgia, and malaise.

Vasculitis can affect any vessels of any type in any organ.

Etiology of vasculitis

The main pathogenic mechanisms of vasculitis are:

1. **Infectious:** Direct invasion of the vascular walls by microorganisms e.g. bacteria Neisseria), Spirochetal (syphilis), fungi and viruses.

2. Immunologic:

Systemic lupus erythematosus and rheumatoid arthritis. Drug-induced Vasculitis

Kawasaki disease.

3. Unknown:

Giant cell (temporal) arteritis

It is a chronic, classically granulomatous inflammation of large- to small-sized arteries that principally affects arteries in the head.

It is the most common form of vasculitis among elderly adults over 50 yrs.

The temporal arteries, vertebral and ophthalmic arteries, as well as the aorta (giant cell aortitis), can be involved.

Because ophthalmic artery involvement can lead to sudden and permanent blindness, affected persons must be diagnosed and treated properly

Morphology of Giant cell Arteritis: commonest pattern characterized by:

- Nodular thickenings of affected segment of arteries with reduction of the lumen and may become thrombosed.

↙Granulomatous inflammation of the inner half of the media
↙Fragmentation of the internal elastic lamina.

Clinical Features

- Temporal arteritis is rare before age 50, symptoms may be only constitutional: fever, fatigue or may involve facial pain or headache, most intense along the course of the superficial temporal artery, which can be painful to palpation.
- Ocular symptoms (due to involvement of the ophthalmic artery) abruptly appear in about 50% of patients; these range from diplopia to complete vision loss.
- Diagnosis depends on biopsy and histologic confirmation, however, because giant cell arteritis can be focal within an artery, a negative biopsy result does not exclude the diagnosis.

The ESR is often markedly elevated (over 100 mm/hr).

- Corticosteroids or anti-TNF therapies are typically effective

Takayasu arteritis

- This is granulomatous vasculitis that classically involves the **aortic arch.**
- In half the cases, it affects also the pulmonary arteries.
- It is characterized principally by **ocular disturbances and marked weakening** of the pulses in the upper extremities (pulseless disease). It is seen predominantly in females younger than age 40.
- Autoimmune mechanisms are suspected.
- **Microscopically**: there is chronic inflammation of the adventitia and the media, sometimes with granulomatous inflammation.
- Thus, the disease may be indistinguishable from giant cell (temporal) arteritis.
- In fact, distinctions among giant cell lesions of the aorta are based largely on the age of the patient, and most giant cell lesions of the aorta in young patients are Takayasu arteritis.
- Involvement of the root of the aorta may cause dilation

of the aortic valve ring, producing aortic valve insufficiency.

Polyarteritis nodosa:

PAN is a systemic vasculitis of small- or medium-sized muscular arteries that typically affects renal and visceral vessels but spares the pulmonary circulation.

The cause remains unknown in the majority of cases.

Pathological features:

PAN is associated with segmental transmural necrotizing inflammation of small- to medium-sized arteries, often with superimposed aneurysms and/or thrombosis with fibrinoid necrosis

Kidney, heart, liver, and gastrointestinal tract vessels are involved.

Clinical Features

PAN is primarily a disease of young adults but can occur in all age groups, the course is frequently remitting and episodic.

Typical presentation includes rapidly accelerating hypertension due to renal artery involvement; abdominal pain and bloody stools caused by vascular gastrointestinal lesions

Renal involvement is often a major cause of mortality.

Untreated, PAN is typically fatal, but immunosuppression can result in remissions or cure in 90% of cases.

Kawasaki disease

This is an acute, febrile, usually self-limited illness of infancy and childhood associated with large- to medium-sized vessel arteritis.

80% of the patients are younger than 4 years of age.

Its clinical significance related to **involvement of coronary arteries** which result in aneurysms that rupture or thrombose, causing MI and death.

In genetically susceptible persons, a variety of infectious agents (mostly viral) have been regard as triggering of this disease.

Clinical features: (Mucocutenous LN syndrome) 1- High fever

2- Skin rash

3- Erythema of the conjunctiva, oral mucosa, palms and feet. 4- Cervical lymphadenopathy.

5- Vasculitis **characteristically involves the coronaries**.

Henoch-Schonlein purpura

It is a **small vessel vasculitis** most commonly seen in children. It is characterized by abdominal pain, acute arthritis, glomerulonephritis (hematuria) and non-thrombocytopenic purpura that is distributed over the extensor aspects of the limbs and buttocks.

These skin lesions consist of subepidermal necrotizing vasculitis involving small blood vessels.

Deposition of IgA is present in the glomeuli and affected small blood vessels

It is a distinctive disease characterized by segmental vasculitis with thrombosis of medium sized and small arteries especially the tibial and radial arteries that often leads to vascular insufficiency, typically of the extremities.

It occurs almost exclusively in heavy cigarette smokers, usually before the age of 35, the relationship to cigarette smoking is a consistent feature of this disease which explained by endothelial injury either directly or through **hypersensitivity to some tobacco products.**

Morphology: Affected vessels show acute and chronic inflammation, accompanied by luminal thrombosis with small microabscesses composed of neutrophils surrounded by granulomatous inflammation

Clinical features begin with features of vascular insufficiency e.g.pain on exercise and intermittent claudication.

Eventually gangrene of the extremities occurs that may be treated by amputation.

Remission and relapses correlate with cessation and resumption of smoking.

Raynaud's phenomenon

Raynaud phenomenon results from exaggerated vasoconstriction of arteries and arterioles in responses to cold or emotion. It most commonly affects the extremities, particularly the fingers and toes, but also occasionally the nose, earlobes, or lips.

The restricted blood flow induces paroxysmal pallor and even cyanosis in severe cases; involved digits classically show "red, white, and blue" color changes from most proximal to most distal, correlating with proximal vasodilation, central vasoconstriction, and more distal cyanosis

Raynaud phenomenon may be

a **primary disease** with no underlying cause or
secondary to a variety of conditions

Primary Raynaud phenomenon

It affects 3% to 5% of the general population and shows a predilection for young women. Structural changes in the arterial walls are absent except late in the course, when intimal thickening can appear, It tends to symmetrically affect the extremities

The course of Raynaud phenomenon is usually benign, but when long-standing can result in atrophy of the skin, subcutaneous tissues, and muscles. Ulceration and ischemic gangrene are rare.

In contrast, **secondary Raynaud phenomenon** refers to vascular insufficiency of the extremities secondary to arterial disease including SLE, scleroderma, Buerger disease, or even atherosclerosis.

Clinically, secondary Raynaud phenomenon tends to have asymmetric involvement of the extremities and progressively worsens over time.

The significance of Raynaud phenomenon that it may be the first manifestation of immune-mediated vasculitis so any

patient with new symptoms should be evaluated, of these patients 10% will manifest an underlying disorder.

Venous diseases

Varicose veins and phlebothrombosis/thrombophlebitis together account for at least 90% of clinical venous disease.

Varicose Veins

Varicose veins are abnormally dilated, tortuous veins produced by prolonged, increased intraluminal pressure with vessel dilation and incompetence of the venous valves.

The superficial veins of the upper and lower leg are commonly involved because venous pressures in these sites can be markedly elevated (up to 10 times normal) by prolonged dependent posture.

About 20% of men and a third of women develop lower extremity varicose veins, higher incidence in women probably reflects the prolonged elevation in venous pressure caused by compression of the inferior vena cava by the gravid uterus during pregnancy.

Clinical Features: congestion, edema, pain, and thrombosis, secondary tissue ischemia results from chronic venous congestion and poor vessel drainage leading to stasis dermatitis and ulcerations.

Common varicosities in two other sites are :

- **Esophageal varices** which occur commonly due to liver cirrhosis due to portal hypertension. Esophageal varices may rupture and lead to massive

  (evenfatal) upper gastrointestinal hemorrhage.
- **Hemorrhoids** can also result from primary varicose dilation of the venous plexus at the anorectal junction (e.g., through prolonged pelvic vascular congestion due to pregnancy or straining to defecate).

Thrombophlebitis and phlebothrombosis are largely interchangeable terms for venous thrombosis and

inflammation; involving deep leg veins in more than 90% of cases.

Tumors of vascular system:

Benign tumor (Hemangioma)

Hemangiomas are very common benign tumors characterized by increased numbers of normal or abnormal vessels filled with blood.

Common in infancy and childhood and constitute 7% of all benign tumors of infancy and childhood.

The majority is superficial lesions, often of the head or neck, but they **may occur internally**, with nearly one third in the liver.

Malignant transformation occurs rarely (if at all).

There are several histologic and clinical variants

1. Capillary Hemangioma:
   - Juvenile hemangioma "strawberry type" of the skin of newborns is extremely common, and may be multiple.
   - It present from birth , grows rapidly in the first few months, begins to fade when the child is 1 to 3 years old, and regresses by age 7 in 75% to 90% of cases.
   - **Gross:** bright red to blue lesion of the skin or slightly elevated.
   - **Mic:** aggregates of **closely packed, thin-walled capillaries,** usually blood filled and lined by a flattened endothelium.
2. Cavernous hemangioma:

   Less common than the capillary hemangioma, characterized by the formation of large, dilated vascular channels, & frequently involve deep structures (liver)
3. Pyogenic granuloma :
   - It occurs in the gingiva of 1% of pregnant women and regresses after delivery.

- Red nodule attached by a stalk to the skin and gingival or oral mucosa, which bleeds easily and is often ulcerated.
- Approximately one third of lesions develop after trauma, resemblance to granulation tissue.
- The name of this lesion is misnomer it has no granuloma, not related to pyogenic infection.

Intermediate **Grade (Borderline) Tumors Kaposi Sarcoma**

Kaposi sarcoma (KS) is a vascular neoplasm caused by human herpesvirus 8 (HHV8, also known as Kaposi sarcoma herpesvirus). Although it occurs in a number of conditions, it is by far most common in patients with AIDS; also its presence is used as a criterion for diagnosis of AIDS.

Based on population demographics and risk factors, KS is categorized into four forms:

• **Classic KS** is a disorder of older men of Mediterranean, Middle Eastern, or Eastern European descent; it is uncommon in the United States. It can be associated with malignancy or altered immunity, but it is not associated with human immunodeficiency virus (HIV) infection.

• **Endemic African KS** typically occurs in HIV negative individuals younger than age 40 years and can follow an indolent or aggressive course.

• **Transplant-associated KS** occurs in solid-organ transplant recipients receiving T- cell immunosuppression; the risk can be 100-fold greater than for immunocompetent patients.

• **AIDS-associated KS** is an AIDS-defining illness, it

represents the most common HIV-related malignancy.

Morphology:

- Most common sites affected by kaposi sarcoma : leg ,face, feet.
- The cutaneous lesions progress through three stages: Patches then become larger, then become nodular. These lesions are composed of sheets of proliferating spindle cells, mostly in the dermis or subcutaneous tissues containing small vessels and slitlike spaces with red cells.
- **Malignant Tumors (angiosarcoma)**.
- Angiosarcomas are malignant endothelial neoplasms.
- They can be found anywhere in the body but most often in the skin, soft tissue, breast, and liver.
- They occur in both sexes and more often affect older adults.
- Hepatic angiosarcomas are associated with distinct carcinogens, (arsenic, Thorotras, and vinyl chloride).
- Gross: either small multiple red nodules; OR large, fleshy masses with central necrosis.
- Mic: all degrees of differentiation of these tumors may present (from well differentiated angiosarcoma (hemangiom like), to anaplastic angiosarcoma.
- Immunohistochemical staining for the endothelial cell marker CD31 demonstrating the endothelial nature of the tumor cells.

References:
Robbins Basic Pathology 11th edition