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Pathology

Lec.3

CHAPTER ONE
PATHOLOGY OF THE CARDIOVASCULAR SYSTEM

ANEURYSMS AND DISSECTION

An aneurysm by definition is a localized abnormal dilatation of any vessel including the heart. Aneurysms therefore may occur in arteries or veins but the aorta is the most commonly involved vessel. Left ventricular aneurysm may complicate myocardial infarction. Aneurysms are either true or false. A true aneurysm is bounded by the components of the blood vessel wall i.e. the blood is still within the confines of the circulatory system. In contrast, a false aneurysm (pseudoaneurysm, pulsating hematoma) is an extra-vascular collection of blood that communicates with the intravascular space. Its wall is derived from the outer layers of the arterial wall or peri-arterial tissue. False aneurysm is seen for e.g. as a result of a post-myocardial infarction rupture contained by pericardial adhesions or a leak at the anastomosis of a vascular graft. ***Arterial dissection****, usually of the aorta (the so called dissecting aneurysm), arises when blood enters the wall of the artery, dissecting between its layers and creating a blood-filled cavity (hematoma) within the wall itself.*

Classifications of aneurysms

Aneurysms are classified either morphologically (according to their gross appearance or etiologically (the underlying mechanism responsible for their development).

Morphological classification *(Fig. 3-1)*

This is based on the macroscopic shape and size

1. ***Berry aneurysm*** *is a small, spherical dilatation usually up to 1.5 cm in diameter. It is most frequently seen within the circle of Willis at the base of the brain.*

2. ***Saccular aneurysm*** *is a spherical bulge from a portion of the vessel wall that varies in size from 5 to 20 cm in diameter. A saccular aneurysm could be considered from the morphological point of view a giant berry aneurysm.*

3. ***Fusiform aneurysm*** *results from gradual, progressive dilatation of the whole circumference of a segment of the vessel and may reach up to 20 cm in diameter.*

Etiological classification

1. *Atherosclerosis*
2. *Cystic medial necrosis or degeneration*
3. *Syphilis*
4. *Vasculitides e.g. PAN .*
5. *Trauma leading to arterio-venous aneurysm*
6. *Congenital defects such as that producing berry aneurysms in the brain*
7. *Mycotic aneurysm produced as a result of infection of the arterial wall.*

The two most important causes of aortic aneurysms are atherosclerosis and cystic medial degeneration. However, any vessel may be affected by a wide variety of disorders that weaken the wall.

Atherosclerotic aneurysm

Atherosclerosis is the most frequent etiology of aneurysms. It causes arterial wall thinning through medial destruction secondary to intimal plaques. Atherosclerosis is a major cause of abdominal aneurysms.

Pathologic features (Fig. 3-2)

- *Atherosclerotic aneurysms usually occur in the abdominal aorta, mostly affecting the aortic segment between the levels of renal arteries and the iliac bifurcation. They may also be seen in the common iliac arteries as well as in the arch and descending portions of thoracic aorta.*
- *The aneurysms are usually fusiform, contains atheromatous ulcers covered by mural thrombi. The latter may be a source of emboli that may lodge in renal vessels or those to the lower limbs.*

Two Abdominal Aortic Aneurysm (AAA) variants merit special mention:

a. ***Inflammatory*** *AAAs are characterized by dense periaortic fibrosis containing abundant lymphoplasmacytic infiltrate with many macrophages and often giant cells. Their cause is uncertain.*
b. ***Mycotic*** *AAAs are atherosclerotic lesions infected by lodging of circulating microorganisms in the wall, particularly in the setting of bacteremia from a primary Salmonella gastroenteritis. In such cases, suppuration further destroys the media, potentiating rapid dilation and rupture.*

The clinical effects of aortic aneurysm include

1. ***Rupture*** *in to the peritoneal cavity or retroperitoneum with massive or fatal hemorrhage.*
2. ***Pressure on adjacent structures*** *leading for e.g. obstruction of a ureter or erosion of vertebrae.*
3. ***Occlusion of a*** *vessel either by direct pressure or through intramural thrombus formation e.g. vertebral branches supplying spinal cord.*
4. ***Embolism*** *from the atheroma or mural thrombus.*
5. ***Creation of abdominal mass*** *that may be confused with a tumor.*

Prosthetic grafts should replace large aneurysms (> 5 cm in diameter) to avoid the possibility of rupture.

Aortic dissection (dissecting hematoma, dissecting aneurysm)

This is characterized by dissection of blood along the plane of aortic media, with the formation of blood-filled channel within the aortic wall that often ruptures, causing massive hemorrhage. The dissection may or may not be associated with significant dilatation of the aorta

. This dissection of the aorta occur principally in two groups of patients

1. *Hypertensive men over 40 to 60 years of age (90 % of the cases)*
2. *In those with a systemic or localized abnormality of connective tissue that affects the aorta (e.g. Marfans syndrome) (10% of the cases), the patients are usually younger than the above group.*

Conditions associated with aortic dissection are

1. *Hypertension (80% of the cases)*
2. *Cystic medial necrosis or degeneration of the aortic wall*
3. *Previous surgery to the aorta e.g. coronary bypass or aortic valve replacement*
4. *Pregnancy usually third trimester*

Gross features (Fig. 3-3 A)

- *A tear in the aortic intima causes the dissection. This is usually transverse and located within the ascending portion of thoracic aorta.*
- *This tear exposes the diseased media to the blood at intra-aortic pressure. The media is cleaved into two layers, creating a false lumen in addition to the existing true lumen.*

Microscopic features

- *The blood dissects into the media of the wall creating a vessel with a double lumen.* ***(Fig. 3-3*** *B)*
- *In most patients with aortic dissection no specific underlying causative pathology is seen in the aortic wall.*
- *The most frequent histologically detectable abnormality is called cystic medial* ***degeneration*** *(CMD); this is presumably responsible weakening of the wall. The degenerative changes range from mild fragmentation of elastic fibers to focal separation of both elastic and fibro-muscular fibers by small clefts or cystic spaces (cystic medial degeneration).*

- ***Aortic dissection may have the following consequences***

1. ***Rupture*** *into any of the three body cavities i.e. pericardial, pleural or peritoneal. This is the most common cause of death.*
2. ***Extension of the dissection*** *into the great arteries of the neck, coronaries, renal, mesenteric, or iliac arteries. This leads to their obstruction with subsequent ischemic damage to the relevant organs or tissues*

e.g. myocardial infarction, renal infarction, and spinal cord ischemic injury (due to involvement of spinal arteries).

3. ***Retrograde dissection*** *into the aortic root that leads to disruption of the valvular apparatus with consequent aortic valve insufficiency.*
4. ***Rupture in the lumen of the aorta*** *through a second distal tear. This is thought to avert a fatal extra-aortic hemorrhage.*

Syphilitic (Luetic) aneurysm

This is a recognized complication of tertiary syphilis. With the decline in the incidence of tertiary syphilis, these types of aneurysms have become uncommon. The dilatation is confined to the thoracic aorta and usually involves the arch. To begin with, there is inflammation of the vasa vasorum within the aortic adventitia that eventuates in their luminal obliteration (oblitrative endarteritis). The inflamed small vessels (vasa) are surrounded by an infiltrate rich in plasma cells. This leads to ischemic injury of the media that terminates in medial scarring and hence weakening and aneurysmal dilatation. Contraction of the scarred media leads to intimal redundancy with subsequent wrinkling referred to as 'tree barking'. Syphilitic aortitis may also cause aortic valve ring dilatation resulting in aortic insufficiency. This is due to circumferential stretching of the cusps and widening of the commissures between the cusps. On the long run the Lt ventricular wall undergoes volume overload hypertrophy with subsequent dilatation. The resultant markedly cardiomegaly has been likened to a cow's heart .

The thoracic location of syphilitic aneurysm distinguishes it from typical atherosclerotic aneurysm, which rarely affects the aortic arch and never involves the root of the aorta.

Mycotic aneurysm

This refers to a dilatation of an artery as a result of weakness of its wall secondary to infection. Thrombosis and rupture are possible complications. The infection reaches the artery through one of three routes

1. *Lodgment of septic embolus in the artery, usually complicating infective endocarditis.*
2. *Extension of an adjacent Suppurative processes.*
3. *Circulating microorganisms (bacteremia, septicemia) that directly infect the arterial* ***wall.***

Berry aneurysm (saccular aneurysm-Congenital aneurysm)

This is the most frequent type of intracranial aneurysms and the one most frequently responsible for subarachnoid hemorrhage. It has an incidence of about 2% in the general population. An unruptured berry aneurysm is a thin-walled bright red out-pouching at arterial branch points along the circle of Willis or major vessels just beyond. The pathogenesis is thought to be due to congenital defect of the media especially at bifurcations. Ruptured berry aneurysm with clinically significant subarachnoid hemorrhage is most frequent in the age group of 40-50 years.

DISEASES OF VEINS AND LYMPHATICS

Varicose veins and phlebothrombosis/thrombophlebitis together constitute about 90% of venous diseases.

Varicose veins

These are ***abnormally dilated, tortuous veins produced by prolonged increase in intraluminal*** *venous* ***pressure.*** *The superficial veins of the legs are the usual sites of involvement. Much less common, but more significant are involvement of veins in the lower esophagus (esophageal varices) due to portal hypertension for e.g. secondary to liver cirrhosis. Hemorrhoids are another example of varicose veins.*

Varicose veins of leg superficial veins Predisposing factors

1. *Conditions associated with elevation of venous pressure in these veins*
    a. *Pregnancy; this explains the higher incidence in females*
    b. *Obesity*
    c. *Occupations requiring long periods of standing*

2. *Weakening of the walls of veins*

a. *Defective development of the vein wall; this possibly explains the familial tendency of varicose veins.*
b. *Age; the condition is much more common over the age of 50 years.*

The affected veins, which are visible through the skin of legs, are dilated, tortuous, elongated and scarred. ***(Fig. 3-4)*** *There is variation in the thickness of the wall. The above changes lead to deformity and incompetence of the vein valves. This aggravates the situation and a vicious circle is thus created.*

Varicose veins lead to local venous stasis, congestion, edema and thrombosis. Embolism is very rare (superficial veins).

Disabling complications include

1. *Persistent edema*
2. *Stasis dermatitis (due to stasis of blood and liberation of hemosiderine)*
3. *Varicose ulcers.*

Thrombophlebitis and phlebothrombosis

These are two designations for inflammation and venous thrombosis.

Predisposing factors include

1. *Cardiac failure*
2. *Neoplasia*
3. *Pregnancy*
4. *Obesity*
5. *Postoperative states*
6. *Prolonged bed rest and immobilization*

Site of occurrence include

1. *The deep veins of the leg are the most common sites of venous thrombosis.*
2. *Additional sites for deep vein thrombosis (DVT) include periprostatic plexus of veins in males and the pelvic veins in females.*
3. *Dural sinuses and skull veins in bacterial meningitis and otitis media.*
4. *Portal vein thrombosis may complicate intra-abdominal sepsis.*

DISEASES OF LYMPHATIC VESSELS

Lymphangitis *refers to inflammation of lymphatic vessels due to drainage of infective focus. Group A beta-hemolytic streptococci is the most frequent offending organism. The condition is characterized clinically by the occurrence of painful subcutaneous red streaks extending along the course of lymphatics with painful enlargement of regional lymph nodes (acute lymphadenitis). If not treated the condition may be complicated by*

1. *Spread to surrounding soft tissue leading to cellulites or multiple local abscesses.*
2. *When regional lymph nodes fail to stop the spread of bacteria, drainage occurs into the venous system with subsequent bacteremia or septicemia.*

Lymphedema

Occlusion of lymphatic vessels leads to abnormal accumulation of interstitial fluid in the affected part. This is referred to as ***obstructive lymphedema. Causes of lymphatic vessels Obstructions include***

1. *spread of malignant tumors to regional lymph nodes and lymphatic channels.*
2. *Radical surgical removal of regional lymph nodes e.g axillary lymph odes dissection of radical mastectomy*
3. *Post-radiation fibrosis*
4. *Filariasis*
5. *Post-inflammatory scarring of lymphatic vessels.*

Persistence of the edema leads to

1. *Interstitial fibrosis, which is most evident in the subcutaneous tissue. This is manifested as indurations of the edematous area.*
2. *Enlargement of the affected par' (e.g. elephantiasis of the lower limb)*
3. *Peau d' orange appearance of the overlying skin*

4. *Skin ulceration.*

VASCULAR TUMORS

This is a heterogeneous group of neoplasms and tumor like conditions. It is best divided according to their biological behavior into the following three groups

I. Benign: e.g. hemangiomas, pyogenic granulomas, glomus tumor, and vascular ectasias.

II. Intermediate: locally aggressive tumors that rarely metastasize e.g. Hemangioendothelioma and Kaposis's sarcoma.

III. Malignant: e.g. angiosarcoma, hemagiopcricytoma.

1. Benign vascular tumors & tumor-like lesions

Hemangiomas *are very common tumors, constituting more than 5% of all benign tumors. They are most common in infants and children. They are subdivided into:*

Capillary hemangiomas*, which represent focal proliferations.of capillary-sized blood vessels. They usually occur in the skin, subcutaneous tissues, lips, and oral mucous membranes. Strawberry type of capillary her.angioma is seen in the skin of newborns, but it usually regresses and disappear in the majority of the cases*

Cavernous hemangiomas *are characterized by focal proliferation of large (venous-sized) vascular channels. They arc seen most often in the skin, lips, and tongue but also encountered in the liver, spleen and pancreas. (Fig. 3-5) In most cases, the tumors are of little clinical significance however,*

1. There can be a cosmetic disturbance. (Fig. 3-6)

2. *Visceral hemagiomas detected by imaging studies may need to be distinguished from more malignant tumors.*

3. *Brain hemangiomas can cause pressure symptoms or rupture.*

4 Cavernous hemangiomas are component of von Hippel-Lindau disease; they involve the cerebellum or brain stem and eye grounds, along with similar lesions in the pancreas and liver.

Pyogenic Granuloma *(see GIT; mouth)*

This form of capillary hemangioma is a rapidly growing red nodule on the skin, gingival, or oral mucosa; it bleeds easily and is often ulcerated. Roughly a one third of lesions develop after trauma. The proliferating capillaries are accompanied by edema and an acute and chronic inflammatory infiltrate, an appearance with striking similarity to exuberant granulation tissue.

Pregnancy tumor *(granuloma gravidarum) is a pyogenic granuloma that occurs in the gingival of 1% of pregnant women. These lesions can spontaneously regress (especially after pregnancy) or undergo fibrosis.*

Lymphangioma

1. Simple (Capillary) Lymphangioma are *slightly elevated or pedunculated, small lesions are composed of small lymphatic channels. They are mainly seen in the head, neck, and axillary subcutaneous tissues.*

2. Cavernous Lymphangioma *(Cystic* ***Hygroma)*** *are typically found in the neck or axilla of children. and may fill the axilla or produce gross deformities about the neck. Tumors are composed of massively dilated endothelial-lined lymphatic spaces separated by intervening connective tissue stroma containing lymphoid aggregates.*

Glomangioma (glomus tumor) *is* ***a*** *tumor that originates from glomus bodies (which normally control skin blood flow and temperature), especially in fingers and toes. It is seen as a very tender, bluish nodule, near the end of a finger or toe. It consists of vascular spaces surrounded by rounded cuboidal cells of smooth muscle derivation.*

II.. Intermediate-Grade (Low-Grade Malignant) Tumors*: e.g*

Kaposi Sarcoma *is used to be fairly common in patients with AIDS prior to the advent of effective antiretroviral therapy, and its presence is used as a criterion for diagnosing AIDS. Four forms of the disease are recognized, all of these share the same underlying viral pathogenesis:*

1. ***Chronic*** *KS (classic KS) characteristically occurs in older men. It is not associated with HIV. There multiple red to purple skin plaques or nodules, usually in the distal lower extremities.*

2. ***Lymphadenopathic*** *KS [African, endemic KS) is particularly prevalent among South African Bantu children; it is also not associated with HIV. Skin lesions are sparse, and patients present instead with lymphadenopathy due to KS involvement; the tumor occasionally involves the viscera and is extremely aggressive.*

3. ***Transplant-associated*** *KS occurs in the setting of solid-organ transplantation with its attendant long-term immunosuppression. It tends to be aggressive (even fatal) with nodal, mucosal, and visceral involvement; cutaneous lesions may be absent.*

4. ***AIDS-associated KS*** *(epidemicKS) was found in a third of AIDS patients, particularly male homosexuals. However, with current regimens of intensive antiretroviral therapy, KS incidence is now less than 1% (although it is still the most prevalent malignancy in AIDS patients in the United States). AIDS-associated KS can involve lymph nodes and viscera, with wide dissemination early in the course of disease. Most patients eventually die of opportunistic infectious rather than from KS.*

Pathogenesis

Regardless of the clinical subtype (described above), 95% of KS lesions have been shown to be due to human herpes-virus 8 [HHV-8] infection. The virus is transmitted sexually and by poorly understood nonsexual routes.

Pathological features (Fig. 3-6)

- *Three stages are recognized: patch, plaque, and nodular.*
- *Patches are solitary or multiple pink, red, or purple macules, typically confined to the distal lower extremities.*

They are difficult to distinguish from granulation tissue.

- *With time, lesions spread proximally and convert into larger, raised* ***plaques*** *composed of dermal accumulations of dilated, jagged vascular channels lined by plump spindle cells and perivascular aggregates of similar spindled cells. Scattered between the vascular channels are red blood cells, hemosiderin-laden macrophages, lymphocytes, and plasma cells.*
- *At a still later stage, lesions become nodular. These lesions are more sarcomatous than the above. The nodular stage is often accompanied by nodal and visceral involvement, particularly in the African and AIDS-associated variants.*

III. Malignant Tumors

A. Angiosarcomas *are malignant endothelial neoplasm's with histology varying from highly differentiated tumors that resemble hemangiomas to anaplastic lesions. Older adults are commonly affected. T*

. Angiosarcomas can also be induced by radiation. Clinically, Angiosarcomas are locally invasive and can metastasize readily. The current 5-year survival rates approach 30%.

B. Hemangiopericytomas *are rare tumors derived from pericytes-myofibroblast-like cells that are normally arranged around capillaries and venules. They are most common on the lower extremities (especially the thigh) and in the retroperitoneum. They consist of numerous branching capillary channels and gaping sinusoidal spaces enclosed within nests of spindle-shaped to round cells. The rumors may recur after excision, and roughly half metastasize, usually hematogenously to lungs, bone, or liver.*