Cardiovascular Lecture #2
Vasculitis, Venous Disease, Vascular Neoplasia
Heart: CHF, Ischemic Disease, Angina
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These descriptions to the slides are adjuncts to the lectures. These descriptions are not meant to replace either the lectures or the reading assignments, but to aid in your review of the images and text slides.

1. Vasculitis is any inflammatory disorder (e.g. infectious, autoimmune, etc.) of blood vessels. Arteries, veins, or lymphatics can be affected. Arterial vasculitis is dominant in its potential for morbidity and mortality. Venous vasculitis is more common and the potential for thromboembolism makes it a very serious disorder.

2. There are three broad categories of arterial vasculitis: Hypersensitivity, autoimmune associated (SLE, RA), and a group of distinct clinicopathologic syndromes causing a widespread arterial vasculitis known as systemic necrotizing vasculitis.

3. The systemic arterial vasculitides have associated with them antineutrophilic cytoplasmic autoantibodies (ANCA). ANCAs are useful diagnostic indicators of arterial vasculitis; their presence and titers correlate with disease activity. Perinuclear antineutrophilic cytoplasmic autoantibodies, or P-ANCA, are directed against myeloperoxidase in neutrophil primary granules and are frequently observed in patients with polyarteritis nodosa and primary glomerular disease. Cytoplasmic antineutrophilic cytoplasmic autoantibodies, or C-ANCA, are directed against leukocyte proteinase-3 and are found in patients with Wegener's granulomatosis.

4. Polyarteritis nodosa. The essential features of polyarteritis nodosa are summarized. The symptoms vary with the organ involved. Interestingly, the aorta and pulmonary vasculature are spared.

5. Polyarteritis nodosa (Robbins, Figure 10-13): Medium muscular artery. There is central segmental necrosis (central pink zone) with marked inflammation of the arterial wall. There is a segment of normal vessel wall at the arrow. The lesions are segmental (skip lesions) and can lead to aneurysmal dilatation and to nodularity as older lesions become fibrotic. In suspected cases, biopsies are taken from either skeletal muscle or kidney. Renal failure is a common cause of death.

6. Wegener's granulomatosis. The essential features are summarized.

7. Wegener's granulomatosis (Robbins, Figure 10-14). There is marked inflammation of this artery. Adjacent to the artery is granulomatous inflammation, in which epitheloid and giant cells are seen (arrows).

8. Temporal (giant cell, cranial) arteritis. The essential features are summarized. Blindness is a major complication and the disease responds well to steroids. A biopsy may require a one-inch segment of artery.

9. Temporal arteritis (Robbins, Figure 10-15). There is granulomatous inflammation of the internal portion of the media centered on the internal elastic membrane. A mononuclear cell infiltrate with multinucleate giant cells, and some loss of the internal elastic membrane is present. The vessel becomes nodular and can be painful on palpation.

10. Buerger's disease. A remitting, relapsing, inflammatory disorder that often leads to thrombosis.

11. Buerger's disease: Essential features. Cessation of smoking early in the disease can bring relief. Vascular insufficiency (claudication, color, and temperature changes) will develop.

12. Buerger's disease (Robbins, Figure 10-15). This vessel shows acute and chronic inflammation of the vessel wall. The lumen is occluded with thrombus, which shows two abscesses (arrows). This inflammatory process will spread to adjacent nerves and veins.

13. This patient did not stop smoking.

14. Aneurysms are caused by abnormal dilatation of arteries or veins. Arterial aneurysms, particularly of the aorta, are most often due to atherosclerosis (AS) in concert with hypertension. Any process that causes weakening of the arterial wall (e.g. trauma, fungal infections, etc.) can lead to an aneurysm.

15. Aortic aneurysms are by far most likely caused by AS and hypertension. Advanced AS coupled with hypertension weakens the media, leading to aneurysmal dilatation. Aortic abdominal aneurysm (AAA) is most often seen in middle-aged males.

16. Atherosclerotic abdominal aortic aneurysm (Robbins, Figure 10-17-A). The dilatation above the iliac bifurcation is obvious. Not seen are the renal arteries, but the aneurysm is below the renal arteries, the most common location. Above the aneurysm notice the severe atherosclerotic lesions that are irregularly shaped, showing ulceration and hemorrhage. The opened aneurysm is filled with thrombus (Robbins, Figure 10-17-B).

17. The clinical consequences of aortic aneurysms are summarized. Rupture of an aortic aneurysm is the most feared consequence. The mortality is quite high.

18. Syphilitic aortitis/aneurysm is seen in the tertiary stage of syphilis, causing obliterative arteritis of the vaso vasorum, the nutrient plexus of the aorta. The subsequent ischemia and destruction of the media leads to dilatation of the aortic root, aortic valve insufficiency, and intimal changes known as tree barking.

19. Histologic section of aorta with syphilis. Note the chronic lymphocytic inflammation, which is the hallmark of the lesion.

20. Heart and aorta from root to bifurcation of the iliac arteries showing marked aneurysmal dilation of the aortic root.

21. Since the development of a syphilitic aortic aneurysm occurs gradually, symptoms such as cough, dsyphagia, and referred pain can occur. Death usually occurs due to congestive heart failure (CHF) secondary to aortic valve insufficiency.

22. In aortic dissection (dissecting hematoma), blood dissects along laminar planes of the aortic media, forming blood-filled channels that often rupture and result in death. Most dissections originate with an intimal tear within 10 cm of the aortic valve. In contrast to AS and syphilitic aneurysms, dissecting aneurysms have minimal dilation.

23. The most common cause of aortic dissection by far is hypertension complicated by atherosclerosis. Patients with Marfan's syndrome, a defect in elastic tissue formation, are also at risk. A particularly uncommon but real complication during pregnancy.

24. Aortic dissection demonstrating a small oblique intimal tear (probe) in an area free of atheromatous plaque. Blood has entered the media, creating an intramural hematoma (narrow arrows). The hematoma is arrested at the distal site where atherosclerosis is present.

25. Microscopic view of dissecting aneurysm demonstrating an aortic intramural hematoma (asterisk). Elastic fibers stain black and blood stains red in this special stain.

26. Microscopic of cystic medial degeneration of Marfan's syndrome (Robbins, Figure 10-18-A). Elastic fibers stain black. There is disruption and fragmentation of the aortic media elastic lamella, with formation of areas devoid of elastin (asterisk). Normal media for comparison shows the regular layered pattern of elastic tissue.

27. Aortic dissection presents with excruciating, through-and-through chest pain. If the patient survives the initial presentation, then treatment to lower blood pressure and surgery may salvage the patient.

28. Venous disorders, primarily varicose veins of the legs, cause a great deal of discomfort and morbidity, but are rarely life-threatening unless phlebothrombosis with subsequent thromboembolism occurs. Varicose veins are abnormally dilated, tortuous veins caused by increased intraluminal pressure and loss of support of the vessel wall. Varicose veins most often affect the superficial veins of the leg and are seen most often in women who have been pregnant. Varicose veins have a familial predilection and tend to be seen in older women.

29. Varicosity of the perforating vein of the popliteal area. Note the smaller veins showing arborization.

30. In the USA, varicosities of the venous plexus in the esophagus are attributed to increased portal pressure from cirrhosis of the liver. Hemorrhoids are varicose dilatation of the veins of the anorectal junction, caused by increased pressure, and most often associated with prolonged reading while in the executive washroom.

31. Esophagus (white tissue) and stomach (reddish tissue with folds) with ruptured esophageal varicose veins (dark red areas) on the esophageal surface near the esophageal junction. The liver is underlying the esophagus in this specimen and shows cirrhosis. The mortality of ruptured esophageal varicies is between 50-75% on initial presentation. With recurrent rupture, death is almost assured.

32. Histologic section of the gastroesophogeal junction. There are dilated veins within the submucosa, which is what is seen in esophageal varicies.

33. Phlebothrombosis/thrombophlebitis is thrombus formation in veins. Thrombus formation, which is often clinically silent, with embolization to the lungs, is a leading cause of morbidity and death. Pulmonary thromboembolism will be discussed in detail in the pulmonary lecture series.

34. This is venous thrombus of the innominate vein of the leg.

35. Lymphatic disorders are most often secondary to inflammation (infection) or cancer. Primary disorders (e.g. Milroy's disease) are extremely rare. The hallmark clinical finding of lymphatic obstruction is "peau d' orange", where the skin takes on the texture of an orange peel. Often this is seen in the female breast with lymphatic dissemination of a primary cancer.

36. Lymphangitis due to bacterial infection is most often associated with beta-hemolytic streptococcus.

37. Hemangiomas and vascular malformations are benign vascular processes that are often referred to respectively as "birthmarks" or "port wine" stains. The hemangioma usually presents shortly after birth (although 30% may be seen at birth), grows during the first year by hyperplasia, and usually involutes by puberty. Vascular malformations are always present at birth, although they may not be apparent, grow by hypertrophy, and never involute.

38. Clinical course of hemangioma. Growth by proliferation, followed by involution.

39. Child with hemangioma.

40. Same child treated with laser therapy.

41. Clinical course of vascular malformation. Hypertrophy without involution.

42. Patient with vascular malformation who had previous treatment with dermabrasion.

43. Same patient treated with laser therapy.

44. Vascular malformation treated with skin grafts.

45. Vascular malformation progressing without any treatment.

46. Kaposi's sarcoma (KS) is an undifferentiated tumor of spindle cells of either primitive mesenchymal or endothelial cells. KS has three distinct clinocopatholgic variants: Classic, endemic, and epidemic.

47. KS: Classic, endemic, and epidemic are compared and contrasted.

48. Schematic representation of the progressive gross and microscopic stages of KS (Robbins, Figure 10-23). The first stage shows patches consisting of pink to red to purple solitary or multiple macules confined to the lower extremities or feet. Microscopically, there are some dilated vessels and a rather nonspecific infiltrate of lymphocytes, plasma cells, and macrophages. In the second or plaque stage, raised plaques consisting of dermal, dilated, vascular channels lined by plump spindle cells are formed. In the third or nodular stage, spindle cells are found in the dermis and epidermis. In this stage, there may be involvement of lymph nodes and viscera in the epidemic (AIDS) and endemic (African) forms.

49. KS showing red-purple multiple macules and plaques on the leg.

50. KS showing purple plaques and nodular lesions of the toes.

51. KS showing plump spindle cells and vascular channels seen in the nodular stage. This lesion would be difficult to differentiate morphologically from an angiosarcoma.

52. KS showing plump spindle cells and vascular channels.

53. Our discussion will now turn to diseases of the heart. Heart disease is the number one killer in the USA. The most common cause of heart disease is ischemic heart disease (IHD) or obstructive coronary artery disease caused by atherosclerosis disease. Often complicating heart disease are its traveling companions, hypertension and diabetes. Hypertensive heart disease and cor pulmonale are less common secondary heart diseases but no less deadly. Systemic hypertension and increased pulmonary pressure ultimately leads to heart failure if untreated. We will first discuss congestive heart failure (CHF) since it is the common endpoint in many cardiac diseases.

54. Heart disease is the number one cause of death in the USA. The rate of morbidity and mortality due to heart disease has decreased in the past two decades, primarily due to improvements in lifestyle (decline in tobacco use, improved diet, and increased exercise), diagnosis, treatment, and follow-up. Currently 750,000 individuals die from heart disease annually, which is about twice the number of those dying from all forms of cancer.

55. Review of normal heart anatomy. The adult heart weighs about 250 to 300 gm in females and 300 to 350 gm in males. An increase in cardiac size is known as cardiomegaly. An increase in ventricular wall thickness along with an increase in weight is indicative of cardiac hypertrophy. Dilation refers to an enlarged heart chamber. A heart that is stressed or overworked first responds with hypertrophy, then dilation. When the heart can no longer compensate by these intrinsic physiologic responses, then heart failure supervenes. The coronary arteries originate from the aorta just distal to the aortic valve. The coronary arteries are 5 to 10 cm long, 2 to 4 mm in diameter and course along the epicardial surface. The three major coronary arteries are (1) the left anterior descending artery (LAD), (2) the left

circumflex artery (LCX), both of which arise from the left main coronary artery, and (3) the right coronary artery (RCA). The LAD supplies blood to the apex of the heart, the LCX supplies blood to the lateral wall of the left ventricle, and the RCA supplies blood to the right ventricular wall and the posterior third of the ventricular septum.

56. Congestive heart failure (CHF) is the common endpoint for many forms of heart disease (IHD, valve disease, hypertension, cardiomyopathy, conduction system, etc.). CHF has a poor prognosis of >50% mortality within five years. CHF is a multi-organ clinical syndrome in which cardiac function is insufficient to pump blood at the rate delivered by the venous system. There are a number of forms of heart failure. High output failure occurs when tissue demands can no longer be met, such as in hyperthyroidism or severe anemia. Forward failure occurs when there is inadequate cardiac output (CO). Backward failure occurs when there is venous system congestion. None of these descriptions are exclusive and often there is overlap.

57. Review of the vasculature. The arterial side of the vasculture is the high-pressure side of the system, whereas the venous side is the low-pressure side. In this schematic you can easily see that with decreased cardiac output (CO) there is inadequate oxygenation of the vital organs, causing blood to back up into the venous system and leading to hepatosplenomegaly, dependent edema of the extremities, and ultimately, pulmonary congestion and edema.

58. Because the right (right atrium and ventricle) and left (left atrium and ventricle) sides of the heart seem to function almost independently, it is convenient to classify heart failure as either left-sided or right-sided. The common causes of left- and right-sided heart failure are listed on this slide. Pure right-sided heart failure occurs only with a few diseases. The most common cause of right-sided heart failure is left-sided failure.

59. CHF: Local compensatory mechanisms. With heart failure, the heart first compensates by a sympathetic nervous system response. Increased catecholamines cause a more forceful contraction (inotropic effect) and an increase in heart rate, leading to an increase in cardiac output (CO). Over time, there is hypertrophy and then dilation. Dilation and stretching of the cardiac fibers leads to a more forceful contraction, thereby increasing CO. Beyond a certain point, further dilation leads to a decline in contraction strength. At this point, the patient develops decompensated heart failure.

60. Frank-Starling Law (Robbins, Figure 11-1). The curve shows the relationship between resting myocardial fiber length and force of contraction. In early heart failure, dilation results in contraction that is more forceful. With more severe degrees of dilation, contractility begins to decline. Cardiac output is then decreased (forward failure), followed by increased left ventricular end-diastolic filling pressure and increased venous pressure (backward failure).

61. CHF: Systemic compensatory mechanisms. In decompensated heart failure, there is decreased perfusion of the kidneys, which in turn causes activation of the renin-angiotensin system. Subsequent aldosterone release causes the renal tubules to reabsorb both sodium (Na) and water, which leads to an increase in total plasma volume (blood volume) to maintain cardiac output (CO). Unless the heart can pump the increased intravascular volume, there is an increase in both systemic and venous congestion (pulmonary and soft tissue edema).

62. The heart on the right is normal and the heart on the left shows marked cardiomegaly with hypertrophy and dilation due to chronic hypertension.

63. Symptoms of left- (systemic) and right- (venous) sided CHF are summarized. Often symptoms of both left- and right-sided CHF are seen in the same patient.

64. Cross-section of heart with CHF. The transverse section of the heart in the middle is normal. The heart on the left shows cardiac hypertrophy (increased mass) with a markedly thickened left ventricular wall. The heart on the right shows hypertrophy but has diminished wall thickness.

65. CXRAY: Lateral. This x-ray (lateral view) of a normal chest shows sharp angles of the diaphragm. The heart and aorta are outlined in black.

66. CXRAY: AP and lateral. CHF with pulmonary edema. This chest x-ray, anterior on left and lateral on right, shows pulmonary edema. In the AP view, the lung fields are obliterated with a fluid line in the left chest. The heart is enlarged and the pulmonary vasculature is prominent. The lateral CXRAY again shows obliteration of the diaphragmatic angles with fluid buildup.

67. CXRAY: AP. Cardiomegaly. The heart is enlarged with mild pulmonary congestion.

68. CXRAY: AP with left ventricular hypertrophy.

69. Acute pulmonary edema: Microscopic. There is marked congestion of the alveolar septa and there is protein-poor (pale pink) edema fluid in the alveolus. This patient had cardiogenic shock secondary to an acute myocardial infarction (AMI).

70. Chronic passive congestion of the lungs due to long-standing CHF. The pulmonary alveoli are packed with hemosiderin-laden macrophages. The alveolar septa are thickened with fibrosis and packed with erythrocytes (congestion). This patient with untreated hypertension developed CHF.

71. Nutmeg liver due to long-standing CHF. Atrophy of hepatocytes around the central vein due to chronic CHF gives the nutmeg appearance on the cut surface of the liver.

72. Liver: Long-standing CHF. The microscopic section shows the central vein of the liver with marked venous congestion of the sinusoids.

73. CHF clinical symptoms. The clinical symptoms of CHF are summarized.

74. CHF clinical symptoms. The clinical symptoms of CHF are summarized.

75. CHF is the common endpoint of many cardiac diseases.