Pathology Lecture #32
Pulmonary Lecture #4
Obstructive Lung Disease (continued), Restrictive Lung Disease
Filename: Lecture32Desc.doc
Alex A. Pappas, MD

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. Alpha-1-antitrypsin deficiency is a relatively uncommon cause of emphysema, but serves as the model for the pathogenesis of the two common forms of emphysema, centriacinar and panacinar. Many of these patients develop symptomatic emphysema, particularly if they smoke. They also develop a characteristic chronic hepatitis and cirrhosis of the liver.

2. This is a patient who has marked cirrhosis due to alpha-1-antitrypsin deficiency.

3. The characteristic PAS cytoplasmic-positive globules in hepatoctyes reflect the mutant alpha-1-antitrypsin protein that cannot be secreted.

4. Chronic bronchitis is common among smokers and urban dwellers in smog-ridden cities. The forms of chronic bronchitis are listed.

5. The distinctive feature in the pathogenesis of chronic bronchitis is the hypersecretion of mucus in the large airways (bronchioles). Airway obstruction ultimately occurs because of inflammation, fibrosis, and resultant narrowing of the bronchioles ("small airway" disease). In patients with bronchitis, there is often coexisting emphysema.

6. In this microscopic section of chronic bronchitis (Robbins, Figure 13- 9), there is marked thickening of the mucus gland and squamous metaplasia that begins in the larger airways.

7. Clinical features of chronic bronchitis are summarized.

8. Bronchiectasis is a secondary disorder where the bronchi and bronchioles are permanently dilated.

9. Bronchiectasis begins with chronic persistent infection from various etiologies leading to bronchial wall damage.

10. Likewise, obstruction from a tumor or foreign body can lead to bronchial wall damage.

11. Bronchial obstruction due to various disorders is the usual cause of bronchiectasis. Cystic fibrosis (CF) is the most common lethal genetic disorder affecting white populations. CF is associated with a widespread defect in the secretary process of exocrine glands. The primary

defect is in the transport of chloride ions across epithelial cells. In the respiratory tract this defect leads to thick dehydrated mucus, obstruction, infection, abscess formation and bronchiectasis. In Kartagener's syndrome, an autosomal disorder, there is defective ciliary action leading to persistent infections and bronchiectasis.

12. Bronchiectatic involvement of the lungs usually affects the lower lobes bilaterally, particularly those airways that are most vertical. The most severe involvement is in the distal bronchi and bronchioles.

13. This microscopic section is from a child dying of bronchiectasis caused by cystic fibrosis. The alveoli are destroyed, the airspaces enlarged, and there is squamous metaplasia of the small bronchioles with peribronchial inflammation.

14. In this same case, there is marked squamous metaplasia of the bronchiole with a florid acute and chronic inflammation. Within the lumen of the airway is necrotic debris.

15. Clinical course of bronchiectasis.

16. Restrictive lung disease is characterized by reduced compliance and can be broadly categorized as acute or chronic.

17. The clinical symptoms of restrictive lung disease are summarized.

18. Damage to either the capillary endothelium or the alveolar epithelium can, in time, lead to changes in the interstitium (Robbins, Figure 13-11). Because of the prominent changes in the interstitium, these disorders are often referred to as interstitial lung disease.

19. Interstitial fluid or fibrosis produces a "stiff lung". Decreased compliance (stiff lung) leads to dyspnea. Damage to the alveolar epithelium and interstitial vasculature leads to hypoxia. With progression, there is respiratory failure, pulmonary hypertension, and cor pulmonale.

20. The major restrictive lung diseases (RLD) that will be discussed are tabulated. With chronic RLD, respiratory dysfunction develops insidiously and has variable amounts of chronic inflammation and fibrosis. Acute RLD develops abruptly.

21. Adult respiratory distress syndrome (ARDS) has been known in the past as shock lung. The clinical features of ARDS are summarized. The morphologic counterpart of ARDS is diffuse alveolar damage (DAD). The morphologic features of DAD/ARDS are summarized.

22. The most common conditions associated with the development of ARDS are sepsis, pulmonary infections, gastric aspiration, and trauma. As you can see in Table 13-1 of Robbins, there are a host of other associated etiologies. These four account for more than 50% of ARDS.

23. Robbins, Figure 13-12. A simplified model for DAD in endotoxemia which leads to sticking and activation of neutrophils. Activation of neutrophils results in release of oxidants, proteases, and prostaglandins. The end result is interstitial fibrosis and necrosis.

24. Diffuse alveolar damage in the early exudative stage has intraalveolar and interstitial edemas and capillary congestion present. The lungs grossly resemble liver; they are dark red, firm, airless, and heavy.

25. ARDS/DAD with hyaline membrane formation lining distended alveolar ducts. Some alveoli are distended; others are collapsed. Many alveoli contain desquamated cells and proteinaceous debris (Robbins, Figure 13-13).

26. The prognosis with ARDS is grim, however, survival continues to improve. If an individual with ARDS survives, then pulmonary function is usually restored.

27. Acute pulmonary edema presents with acute respiratory distress. The most common cause is left-sided congestive heart failure causing increased hydrostatic pressure. The lungs are wet and heavy.

28. Microscopically the alveoli are filled with pale pink edema fluid containing few cells. The alveolar capillaries are engorged.

29. CXRAY with Acute Pulmonary Edema. The heart is enlarged and bilateral. Fluffy infiltrates are seen primarily in the lower lobes.

30. Chronic RLD, or interstitial lung disease, is a heterogeneous group of disorders affecting the interstitium of the lung parenchyma.

31. In RLD, the FVC is reduced proportionately to the FEV_1, and thus the ratio or percentage of FEV_1 to FVC is normal, as illustrated in spirogram C of this figure.

32. The most common causes of RLD or interstitial lung disease are listed.

33. The major chronic interstitial lung diseases that are associated with alveolitis and fibrosis are listed.

34. The major chronic interstitial lung diseases associated with fibrosis and granulomas are listed.

35. The essential clinical features of idiopathic pulmonary fibrosis (IPF).

36. A simplified sequence in the pathogenesis of IPF.

37. Possible schema of the pathogenesis of IPF (Robbins, Figure 13-14).

38. In this microscopic picture of IPF (Robbins, Figure 13-15), the alveolar walls are thickened by fibrosis and there is an interstitial infiltrate of mononuclear cells. There are irregular dilated airspaces. Alternating areas of fibrosis and dilation give the lungs a gross "honeycombed" appearance.

39. Honeycombed lung of IPF.

40. Honeycombed lung of IPF with emphysema on the right, with a normal lung on the left for comparison.

41. Blank

42. CXRAY of IPF. Radiodense linear streaking is readily apparent in the lower lung fields.

43. MRI of IPF on the left with normal on the right.

44. Sarcoidosis is a systemic granulomatous disease of unknown etiology in which the lungs are a common site of involvement. Since so many other diseases can cause noncaseating granulomas, the histopathologic diagnosis of sarcoidosis is an exclusionary factor.

45. The essential features of the etiology and pathogenesis of sarcoidosis are summarized. It is a cell-mediated immunity to an unidentified antigen.

46. Virtually any organ can be affected. The noncaseating granulomas have a predilection for lymph nodes, the lungs, and the other organs listed.

47. This CXRAY shows the characteristic bilateral hilar adenopathy ("potato nodes") of sarcoidosis.

48. The noncaseating granulomas of sarcoidosis show aggregates of tightly clustered epithelial cells with Langerhans' or foreign-body type giant cells (Robbins, Figure 13-16). In the lung, there may be a rim of lymphocytes, as in this case, or fibrosis.

49. The asteroid bodies found in sarcoidosis are stellate inclusions within giant cells. Asteroid bodies may be found in other granulomatous diseases.

50. The Schaumann bodies are laminated concretions of calcium and protein.

51. In many patients, sarcoidosis is asypmtomatic, discovered on routine chest films as bilateral hilar adenopathy. The clinical outcome in sarcoidosis is summarized.

52. Hypersensitivity pneumonitis is an allergic alveolitis, unlike asthma, where the bronchioles are the focus. In allergic alveolitis there is decreased compliance, diffusion capacity, and total lung volume. Thus, allergic alveolitis is best classified as an RLD.

53. Selected causes of hypersensitivity pneumonitis (Robbins, Table 13-3).

54. Selected causes of hypersensitivity pneumonitis (Robbins, Table 13-3).

55. Clinical features of hypersensitivity pneumonitis.

56. The so-called diffuse pulmonary hemorrhage syndromes are summarized.

57. The lungs show fibrous thickening of the septa and intraalveolar hemorrhage. There are dark-staining, hemosiderin-laden macrophages indicating prior bleeding. Plasma pheresis to

remove the anti-basement membrane antibody and immunosuppression may be helpful in improving the prognosis in this once dismal disease.

58. The lungs are often the victims of environmental pollution (begins on page 222 of Robbins).

59. Naturally occurring pollutants cause disease by being present in abnormal quantities.

60. The proximal or acute toxicity of a pollutant occurs when it produces inflammation, necrosis, or hypersensitivity in a sensitized individual. The distal or chronic effects of a pollutant are difficult to study and evaluate. Chronic effects may take the form of chronic inflammation, fibrosis, degeneration, and cancer.

61. The lungs usually bear the brunt of environmental pollution and are particularly vulnerable when there is underlying pulmonary disease, especially COPD. The incidence of all lung disease is increasing as we continue to increasingly pollute the environment.

62. The various forms of air pollution are tabulated.

63. The reducing form of smog has clearly been linked with increased morbidity and mortality, especially in those patients with pre-existing lung disease. The photooxidant form of smog is increasingly being linked with pulmonary disease.

64. Air pollution can cause effects ranging from minor irritation to malignancy.

65. The factors determining whether an air pollutant can cause lung injury are summarized.

66. The patterns of lung injury related to air pollution are summarized (Robbins, Table 8-1).

67. Tobacco smoke is the number one disease-causing air pollutant.

68. The effects of the various tobacco constituents are summarized (Robbins, Table 8-2). Nicotine is more addictive than cocaine.

69. The amount of tobacco is "quantified" using the pack-year. Cigarette smoking is the most common cause of lung cancer.

70. The most common cause of chronic bronchitis is cigarette smoking.

71. The most common cause of emphysema is cigarette smoking.

72. Cigarette smoking is a major risk factor for atherosclerosis and acute myocardial infarction.

73. Sidestream, or second-hand smoke, can cause significant morbidity and mortality.

74. Cigarette smoking, or "cancer man" (Robbins, Figure 8-1).

75. Microscopic section of normal lung. There is a bronchiole in the upper left-hand corner and in the middle is a respiratory bronchiole. It is at the level of the respiratory bronchiole that the mineral dust impacts and begins the inflammatory process.

76. Although the definitions of the pneumoconioses have been broadened, we will discuss the mineral dust pneumoconioses that arise from workplace exposure.

77. The industries related to workplace exposure to mineral dusts are tabulated (Robbins, Table 8-3). Asbestos has been expanded to include family members and others exposed to asbestos outside the workplace. Coal dust is relatively inert, requiring large amounts before clinical disease occurs. The others are more fibrotic at lower concentrations and require less exposure. Asbestos is a known carcinogen. All of the pneumoconioses are exacerbated by cigarette smoking, asbestosis in particular.

78. A unifying concept for the development of lesions is depicted in Figure 8-2 of Robbins.

79. Coal dust induced disease is also known as black lung. The disease can range from totally asypmtomatic (asypmtomatic anthracosis, simple CWP) to symptomatic fibrosis and progressive massive fibrosis (PMF).

80. It is not clear what makes the lesions of simple CWP progress to PMF. It is known that associated pulmonary disease can exacerbate the disease.