Pathology of pulmonary tuberculosis

Dr: Salah Ahmed

Is a chronic granulomatous disease, caused by Mycobacterium
tuberculosis (hominis)
Usually it involves lungs but may affect any organ or tissue
Transmission: 1- direct inhalation of organisms in infectious
aerosols
2- contaminated milk drinking (M. bovis)
Factors increasing the risk include:
1- poverty 2- crowding 3- old people
4- malnutrition 5- alcoholism 6- chronic debilitating illness
7- D.M 8- Hodgkin 9- HIV infection
10- immunosuppression 11- chronic lungs diseases (silicosis)

Pathogenesis:

- based on development of cell-mediated immunity
- two stages:

1- 0 – 3 weeks:

- virulent mycobacteria enter into macrophage endosomes (mediated by receptors) they able to inhibit normal microbicidal response by:
    1- arrest endosomal maturation
    2- manipulation of endosomal pH
    3- ineffective phagolysosome formation
- this results in:
    1- bacterial proliferation within macrophages and airspaces
    2- bacteremia with seeding of multiple sites
- most patients at this stage are asymptomatic or have flulike illness

2- more than 3 weeks: (development of cell-mediated immunity)

- bacterial antigens reach draining lymph nodes and are presented to CD4+ T cells
- under influence of IL-12 T cells generated capable of secreting interferon gamma
- interferon gamma activates macrophages which in turn release mediators:
    1- TNF: stimulates recruitment of monocytes which differentiated into epithelioid
    2- NO: capable of oxidative destruction of mycobacteria
    3- free radicals: can have antibacterial activity

- defect in any of the steps of T cells response (IL-12, INF, TNF, NO) results in:

1- poorly formed granulomas

2- absence of resistance and disease progression

Pathogenesis of tuberculosis

Primary tuberculosis:

1- is the form of disease that develops in previously unexposed to infection individual

2- common in elderly, malnourished and immunosuppressed

3- the source of organism is exogenous

4- about 5% of those newly infected persons develop significant disease

5- **Morphology:**

- the inhaled bacilli implant in the lower part of the upper lobe or the upper part of the lower lobe, usually close to the pleura.

Grossly:

i- area of gray-white inflammatory consolidation develops (**Ghon focus**) with caseous necrosis

ii- The bacilli, either free or within phagocytes, drain to the regional nodes, which also caseate

iii-This combination of parenchymal lesion and nodal involvement is called (**Ghon complex**)

iv- In approximately 95% of cases, development of cell-mediated immunity controls the infection the Ghon complex undergoes fibrosis, often followed by calcification (**Ranke complex**)

Microscopically: caseating and noncaseating **granulomas (**tubercles) in Ghon focus and complex

Figure:

A, B: granuloma with necrosis

C: granuloma with no necrosis

D: in immunocompromised individuals no granuloma (sheets of histiocytes with mycobacteria)

6- **Fate of primary tuberculosis**: either

a- is controlled with no viable bacteria (**healed lesion)**

b- the foci of scarring may harbor viable bacteria for years which become source of reactivation when host defenses compromised with development of secondary tuberculosis (**Latent lesion**)

c- uncommonly the disease may develop into **progressive primary tuberculosis** (immunocompromised individuals, malnourished children, elderly) with lymphohematogenous dissemination and development of miliary TB

Secondary tuberculosis:

1- develops in previously exposed (sensitized) to infection individuals

2- it may arise from:

a- reactivation of dormant primary lesion (weakened resistance), more commonly

b- exogenous reinfection

3- **Morphology:**

a- secondary tuberculosis is classically located to apex of one or both upper lobes

b- apical lesion (**Localized secondary lesion)**:

Grossly: firm, gray-white with central caseation

Microscopically: caseating or noncaseating granuloma

4- **Fate of secondary pulmonary tuberculosis:**

a- it may heal by fibrosis (either spontaneously or after therapy)

b- or the disease may progress into:

Progressive pulmonary tuberculosis:

- The localized lesion enlarges with erosion into bronchi (cavity) and blood vessels (hemoptysis)
- If treatment is adequate, the process may be arrested (healing by fibrosis)
- If the treatment is inadequate, or if host defenses are impaired, the infection may spread: 1- by direct expansion

2- via airways

3- lymphatic channels
4- vascular system

- leading to:

1- **Miliary pulmonary disease:**

- occurs when organisms through lymphatics reach the right side of the heart and then into the pulmonary arteries and into lungs

- multiple small, visible foci scattered through the lung
- complications: pleural effusion, empyema, pluritis

2- **Endobronchial, endotracheal, laryngeal tuberculosis:**

- may develop when organisms spread either through lymphatic channels or from expectorated infectious material

3- **Systemic miliary tuberculosis**

- occurs when organisms through pulmonary veins reach the left heart and then to systemic arterial system
- every organ in the body may be seeded
- common in the liver, bone marrow, spleen, adrenals, meninges, kidneys, fallopian tubes, and epididymis

4- **Isolated-organ tuberculosis:**

- occurs in any organ or tissue hematogenously

Secondary pulmonary tuberculosis. The upper parts of both lungs with gray-white areas of caseation and areas of cavitation.

Miliary pulmonary tuberculosis
Adrenal tuberculosis
Testicular tuberculosis
Intestinal tuberculosis
Prostate tuberculosis

Vertebral tuberculosis (Pott disease)

Clinical course:

- malaise, anorexia, weight loss, fever (*low grade* and appearing late afternoon and then subsiding), and *night sweating*
- With progressive pulmonary involvement: purulent sputum, *hemoptysis*
- *Pleuritic pain*: results from extension of the infection to the pleura
- Extrapulmonary manifestations of tuberculosis depend on the organ involved
- The diagnosis:
    1- the history and physical examinations
    2- radiographic findings (*consolidation or cavitation)*
    3- finding of bacilli in sputum (AFB, culture, PCR)
    4- Mantoux test

Thank you