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