ZAPOROZHZHIAN STATE MEDICAL UNIVERSITY

The department of pathological anatomy and forensic medicine with basis of law

Tuberculosis:

- classification
- morphology
- clinical features

Lecture on pathological anatomy for the 3-rd year students

Tuberculosis is a chronic communicable disease caused by a variety of tubercle bacilli, especially:

- *Micobacterium tuberculosis hominis*
- *Micobacterium tuberculosis bovis.*

Lungs are the prime targets, but any organ may be infected. The characteristic lesion is a specific granuloma with central caseous necrosis.

Main features:

The micobacterium tuberculosis can invade organism as:

1. by inhalation into the respiratory tract
2. through ingestion into GI tract
3. the other portals of entry are:
   a) trans-placental
   b) mucous membranes of mouth and throat
   c) skin

Further, evolution of the infection depends upon various factors such as:

1. Nutritional
2. Immunological status

Clinical-morphological manifestations of disease

1. Primary tuberculosis: an initial infection, usually in children. The focus of infection is a small subpleural granuloma accompanied by granulomatous hilar lymph node infection with feather calcification - Ghon complex.
2. Secondary tuberculosis: seen mostly in adults as a reactivation of previous infection, particularly when health status declines. The granulomatous inflammation is much more florid and widespread. Typically, the upper lung lobes are most affected and cavitation can occur.
3. Hematogenous tuberculosis: when resistance to infection is particularly poor, a "miliary" pattern of spreading can occur in which there are a myriad of small millet seed (1-3 mm) granulomas, either in lung

Primary tuberculosis

The first infection with the tubercle bacilli is known as *primary disease or primary complex or primary tuberculosis* includes involvement of draining lymph nodes in addition to the initial lesion.

Primary tuberculosis is characterized by:

1) development of disease at the first getting of the MT into the organism;
2) sensibilisation and allergy of Hypersensitivity of Immediate Type;
3) prevalence of exudative-necrotic changes;
4) tendency to generalization;
5) non-specific reactions.

Pathogenesis

1. The organism gains entry into the body. The most common portal of entry is the respiratory tract (by inhalation).

The inhaled organism enters the alveolus and is ingested by the alveolar macrophage. The M. tuberculosis can either be killed by the macrophage; its growth inhibited or multiplies inside the macrophage, where it behaves like a parasite and lives in symbiosis with the cell.

Pathogenesis

2. During the next 4 - 6 weeks both cell-mediated hypersensitivity (or hypersensitivity type IV) and immunity develop in the host and these after the host response to the infection and result in the formation of the classic tubercle.

With the multiplication of the organism, the macrophage dies and released bacteria enter other macrophages. The cellular debris, the multiplying tuberculosis organisms, and the macrophages release many types of chemotactic factors and attract other

Pathogenesis

3. The interaction between cells and the organism is responsible for the formation of the tubercle, which contains a central necrotic area surrounded by granulation tissue consisting of macrophages, lymphocytes and other types of cells. The macrophages assume the form of the epithelioid cells and giant cells

(Langhan's cells), which form the most single characteristic features of tuberculous infection. Later, the central area of the tubercle undergoes necrosis leading to caseation, mainly due to hypersensitivity.

4. The activated macrophages either completely destroy the bacilli causing regression of the lesion or

Pathogenesis

5. In case of healing, the infiltrate is engulfed by fibrous tissue but may contain viable tubercle bacilli which lie dormant and get reactivated under more favorable circumstances.

The central area of caseation expands and undergoes liquefaction, by the action of hydrolytic enzymes of the macrophages and granulocytes. The liquefied caseum forms an ideal medium for the tubercle bacillus to grow and leads to its rapid multiplication. These organisms can either enter the blood stream and get disseminated or get discharged into the contiguous areas of the lung and airways and spread the disease locally.

Pathogenesis

6. Along with the development of the parenchymal lesion or caseous pneumonia, there is a lymphatic spread with lymphangitis and involvement of the regional lymph nodes.

The focus of caseous pneumonia, the lymphangitisand theregional lymphadenitis is the hallmark of the primary infection and is named, the primary tubercular complex

Morphology of the primary tubercular complex

The primary complex is located in the lower part of the right upper lobes or the upper part of the lower lobes in 3, 8,9,10 segments of the lung. The initial infection produces only slight abnormalities and may cause only slight malaise and mild fever.

Types of progression of primary tubercular complex:

healing of primary complex;

generalization of process - lead to disseminated of the disease. This can occur at both the sites: the lung and the lymph nodes;

Progression of the primary tubercular complex

The healed lesion in the parenchyma can be seen as a speck of calcification on routine X-ray or seen post-mortem.

Healing of primary complex begins at initial affect:

- perifocal inflammation resolute,
- exudative inflammation is replaced by productive;
- capsule is formed around focus of necrosis.

Progression of the primary tubercular complex

Caseous masses are being dehydrated and petrificated, and then ossificated. Such healed initial centre is named **Ghon's focus**. Ghon focus's, in the lung is typically a 1-cm, grayish, circumscribed nodule. At the place of tubercular lymphangitis a fibrinous row will be formed. Healing in lymphatic nodes is similar to pulmonary centre.

Most of the organisms die, but a few remain viable for years. Later, if immune mechanisms wane or fail, the resting bacilli may break out and cause serious tubercular infection.

Progressive primary tuberculosis

Growth of primary parenchymal injury

Progressive primary tuberculosis is a rarer alternative course, in which the immune response fails to control multiplication of the tubercle bacilli. It occur in patients with suppressed or defective immunity.

The primary Ghon's focus in the lung enlarges rapidly, erodes the bronchial tree, and spreads, a sequence that results in adjacent "satellite" lesions:

)tuberculous bronchopneumonia

2) pleuritis followed by pleural effusion

3) endobronchial ulceration and stenosis, which can produce either a complete or partial obstruction

)segmental lung collapse, with compensatory emphysema or an obstructive emphysema

Progressive primary tuberculosis

Lymphogenous spreadingis characterized by involvement the new groups of lymph nodes, such as: paratracheal, supraclavicular, subclavian, cervical and development of tuberculous mezadenitis. The enlargement of the lymph nodes may produce a wheeze by compressing the bronchus.

Hematogenous spreading

The most serious immediate complication is ***miliary tuberculosis***, in which there is invasion of the bloodstream by *M. tuberculosis* and dissemination throughout the body. This occurs when the parenchymal part of the Ghon's complex involves a pulmonary artery or vein and discharges its infected contents into the blood.

Morphology of miliary tuberculosis

Macroscopically: multiple granulomas develop in many organs of the body. The lesions are classically 1-3mm in diameter, yellowish white, and evenly distributed through the affected organ. An area of necrosis may be seen in the center.

Microscopically, the lesions of miliary tuberculosis consist of small granulomas, usually with a central necrosis, where numerous organisms are seen.

Few organs are spared; those most often involved are the lungs, spleen, liver, kidney, meningeas, and bone marrow. Miliary tuberculosis used to be found most often in children, but in industrialized countries it has become more common in the elderly.

Hematogenous Tuberculosis

Hematogenous tuberculosis appears after primary tuberculosis under following conditions:

1. the presence of sensibilization to tuberculin,
2. strongly pronounced immunity
3. the presence of healed foci, after hematogenous generalization of primary tuberculosis

Hematogenous tuberculosis is characterized by

1. proliferative reaction or formation of the granulomas
2. hematogenous spreading

Hematogenous tuberculosis has three forms:

1. Generalized hematogenous tuberculosis is more serious form with dissemination of granulomas
2. Hematogenous pulmonare tuberculosis
3. Hematogenous tuberculosis with un-pulmonary

Generalized hematogenous tuberculosis is more serious form with dissemination of granulomas

Classification:

a) Acute tubercular sepsis;

b) Acute general miliary tuberculosis;

c) Acute general large-focal tuberculosis

d) Chronic miliary tuberculosis.

Hematogenous pulmonare tuberculosis

Classification:

a) Acute miliary tuberculosis;

b)Chronic miliary tuberculosis;

c)Chronic large-focal tuberculosis or hematogenous-disseminative.

Features of hematogenous-disseminative tuberculosis:

- in adults only;
- prevalence apex- plural localization;
- proliferative tissue reaction;
- development of the pneumosclerosis and emphysema of lungs;
- cor pulmonare (hypertrophy of right ventricle of heart);
- presence of un-pulmonary tubercular foci

Hematogenous tuberculosis with un-pulmonary lesions or organic tuberculosis

Classification

1) tuberculosis of bone and joints,
2) tuberculosis of kidneys,
3) tuberculosis of urinary- genital tract,
4) tuberculosis of skin,
5) tuberculosis of endocrine organs and others .

Organic tuberculosis is characterized by acute and chronic destruction and insufficiency of organs

Secondary tuberculosis

Secondary tuberculosis usually results from reactivation of dormant, endogenous tubercle bacilli in a sensitized patient who has had previous contact with the tubercle bacillus.

In some cases, the disease is caused by re-infection with exogenous bacilli.

Secondary tuberculosis develop after primary infection. Reactivation typically begins in the apical or posterior segments (often 1-st and 2-nd segments) of one or both upper lobes ***("Simon's foci"***), where the organisms were seeded during the primary infection.

Characteristics of Secondary Tuberculosis

1. May be in adults only as post primary disease (or re-infection);
2. Only Pulmonary localization (often 1-st and 2-nd segments);
3. Contact and intracanalicular spreading;
4. Shifts of the clinical-morphological forms.

The clinical symptoms of secondary tuberculosis:

1) begins with cough, which may be attributed to smoking or to a "cold"
2) low-grade fever, with general malaise, fatigue, anorexia, weight loss, and often night sweats
3) as the disease progresses, the cough worsens and the sputum may be streaked with blood
4) the rupture of a branch of the pulmonary artery in the

Forms (or stages) of the secondary tuberculosis

1. **Acute local tuberculosis** is characterized by specific endo-, meso--, and pan-bronchitis. During the treatment the exudative process is replaced by proliferative process. Foci of caseous necrosis are incapsulatedand petrificated.
2. **Fibrous-local tuberculosis** forms due to intensification of acute local tuberculosis with formation of fibrous capsule .
3. **Infiltrative tuberculosis** is characterized by extension of perifocal inflammation.
4. **Tuberculoma** consists of focus necrosis surrounded by fibrous capsule. Size of tuberculoma may be near 2-5cm. (It must be differentiated from tumor of the lungs).

Forms (or stages) of the secondary tuberculosis

5. **Caseous pneumonia** develops at progressing of infiltrative tuberculosis, when the caseous changes prevail over peri-focal.
6. **Acute cavernous tuberculosis** develops due to lysis of caseous necrosis and characterized by formation of the cavity. It must be differentiated from primary cavernous tuberculosis.
7. **Cirrhotic tuberculosis** is a progressive variant of fibrous-cavernous tuberculosis. Lungs are deformed due to development of the diffuse pneumosclerosis.

Forms (or stages) of the secondary tuberculosis

8. Fibrous-cavernous tuberculosis is most frequent form. Macroscopically, the lesions are spherical and cavitary lesions. A fibrous capsule surrounds a caseous, acellular center, which contains numerous tubercle bacilli. From these cavitary nodules the organisms can spread through the lungs and be discharged into the air during coughing.

Morphological features:

1) The wall of cavern has three membranes:

internal membrane occurs by necrotic

tissue,

medium membrane occurs by special granular tissue,

external membrane occurs by fibrous tissue

2) Internal surface can be connected with bronchus,

Complications of secondary tuberculosis (secondary effects):

1) scarring and calcification;
2) spreading into other areas;
3) pneumothorax due to rupture of caverns,
4) pleural fibrosis and adhesions, with associated pleurisy,
5) acute pleuritic pain, and shortness of breath;
6) rupture of a caseous lesion, which spills bacilli into the pleural cavity;

Complications of secondary tuberculosis (secondary effects):

7) erosion into a bronchus, which seeds the mucosa of bronchioles, bronchi, and trachea;

8) implantation of bacilli in the larynx, which causes laryngitis, hoarseness, and pain during swallowing.

9) Lesions of secondary tuberculosis acquired through the gastrointestinal tract (usually with *M. t. bovis)* can lead to entrapment of bacilli into lymphoid patches of small and large intestine.

Reasons of patient's death

- Chronic respiratory-cardiac insufficiency due to development cor pulmonare
- Acute hemorrhage due to erosions of vessels
- Chronic renal insufficiency due to development of amyloidosis of kidneys
- Intoxication