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Review Article

Tuberculosis: A basic discourse

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ABSTRACT

Tuberculosis has been among the top health threats and killers in human history. Current reemergence of the disease in most difficult form in parallel with the HIV epidemic constitutes global emergency. The magnitude of tuberculosis challenge mandates continuing education of all providing healthcare in the human biology of tuberculosis and its control. The present article presents unified simple overview of otherwise specialized scientific perspects of tuberculosis.

Mycobacterium tuberculosis infects every third human being. Around 9 million people globally contract tuberculosis infection each year while 2 million deaths are annually attributed to the disease.[1] Global rise in HIV infection has significantly boosted tuberculosis prevalence, with worse challenge of multi drug resistant mycobacteria. Unrecognized transition in diet, lifestyle, and stressors in sections of society, undermine immune status causing people groups more vulnerable to contracting tuberculosis.

1. The infective microorganism

M. tuberculosis, the causative organism measuring 0.5 μm in width and 3 μm in length are classified as acid fast bacilli by staining features. These possess unique cell wall structure with considerable fatty acid, mycolic acid in covalent bonding to underlying polysaccharide arabino-galactan. The structure creates extraordinary barrier that contributes to bacterial survival resisting host defense mechanisms and even chemotherapeutic agents. Cell wall constitution also determines growth rate and infectivity or virulence of the organism.[2] The outer cell membrane comprises lipo-arabino-mannan, the structural carbohydrate antigen. It is immunogenic and also helps the bacteria to survive inside macrophage cells of the host.[3] The understanding of genetic mechanisms of mycobacteria for synthesis of such cell wall is the major focus of research that intends to develop antimicrobial agents.

2. Commonest mode of infection

The person suffering pulmonary tuberculosis may be the source for spreading infection via small airborne droplet nuclei on coughing, sneezing and talking. Such droplets may remain floating in air for hours. The number of organisms in the droplet, virulence of the organism, extent of exposure of droplets to ultraviolet light, ventilation and occasions for

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aerolisation are important determinants in transmission of the infection through inhalation route.[4] Host lungs are primary site for infection that may spread to lymphatic tissue, pleura, bones, joints, meninges etc.

Majority of bacteria inhaled are trapped in outer airways due to mucus. The cilia on surface of airway remain in constant motion to propel mucus upwards for removal. Most of physical defense preventing nidation of infection is provided by ciliary mechanism.[5] Macrophages are abundant in alveolar spaces and constitute the next line of host defense by engulfing and destroying mycobacteria that bypass muco-ciliary clearance and reach alveoli.[6] Many macrophage receptors and mechanisms participate in capturing the bacteria. Key ligand for receptors on macrophages is the lipo-arabino-mannan of mycobacterial cell wall.[7] Phagocytosis of the microbes is facilitated also by complement system.[8] Thus, complement protein C-3 binds bacterial cell wall to mark them for recognition by macrophages (opsonisation), without need for past exposure to mycobacterium.[9] Phagocytosis may successfully check the infection or cascade of events in progression to primary tuberculosis disease, as per the balance of defense mechanisms against mycobacterial virulence.[10]

3. Host defense–mycobacterium interaction

Following ingestion by macrophages, the mycobacterium can continue to slowly multiply in 2–3 days intervals. The macrophages produce proteolytic enzymes and cytokines to destroy the bacteria. The cytokines recruit T lymphocytes invoking cell mediated immune response. The macrophages present antigen from degraded mycobacteria on their surface, for T cells to interact. These initial events continue over up to 12 weeks. The mycobacterium in macrophages may continue to multiply in quantity to generate magnitude of cell mediated response that can be detected by a skin test.[6]

Intact cell mediated immune function results in formation of defensive granuloma around the mycobacterial,[11] limiting replication and spread. Such environment destroys macrophages with necrosed centre in the lesion, while the bacilli are able to adapt and survive.[12] The adaptation includes change in expressed phenotype of the mycobacteria. By 2–3 weeks the necrotic soft debris appears cheese like and called caseation, in which the oxygen level, nutrients and pH are all very low. The mycobacteria in caseous environment therefore stop growing. When immune function is good, the caseous material undergoes fibrosis and calcification with embedded dormant mycobacteria in 'healed' lesions. No such eventuality in immune deficient state, allows primary progressive tuberculosis. In state of poor immunity, the caseous material becomes liquefied and may drain in to nearby bronchus or blood vessel, leaving behind an airfilled cavity. Mycobacteria carrying droplets may finally be coughed out from the bronchus route. From vascular route, infection is carried to extrapulmonary sites. Bacilli can also drain in to lymphatics and tracheo-bronchial lymphnodes in affected lungs, creating new caseous granulomas.

As per differences in immune states, different course of tuberculosis infection in people is understandable. The course manifests stages e.g. latent infection, primary progressive disease, extrapulmonary disease, each with different clinical manifestation.

4. Latent disease

Mycobacterium is difficult to completely eradicate but instead, can be enclosed, checking disease manifestation or infectivity. Such enclosed organisms remain viable within the caseous grave for years, and may reactivate disease under compromised states of immunity. People older above 65 years, uncontrolled diabetes, sepsis, renal failure, malnutrition, heavy smoking and prolonged corticosteroid medications are prominent grounds for reactivation of latent infection, in addition to cancer chemotherapy or HIV co-infection.[13]

5. Primary disease

Very often primary pulmonary tuberculosis is asymptomatic and revealed only through diagnostic tests. As bacilli in lungs spread through lymphatics, paratracheal lymphadenopathy is likely to result. Enlarging primary lesion in lung may cause pleural effusion as distinguishing finding. The effusion may resolve by itself or increase with inflammatory and mechanical symptoms. The affected lung tissue is defective for gas exchange and significant involvement results in dyspnoea.

6. Primary progressive disease

5 to 10 percent of people invaded by *M.tuberculosis* develop active disease. Early symptoms and signs of setting active disease remain non-specific. These include progressive fatigability, sense of malaise, weight loss and low grade fever with chills and night sweats. A classical feature of tuberculosis is wasting. This is consequent to the inflammatory and immune response that alters metabolism and decreases appetite. Both fat and lean tissue is lost and decreased muscle mass causes fatigability.[14] A late sign of poor oxygenation is finger clubbing, but does not precisely indicate extent of disease.[15]

Most patients eventually develop cough, which subsequently carries purulent sputum, and may contain blood. Damaged vessel in cavity is source for haemoptysis. Diffuse inflammation in pulmonary interstitium reduces gas exchange and causes pruritic pain. Dyspnoea and even orthopnoea would associate such state. Particularly after cough, rales may be heard aver afflicted lung area. Anaemia becomes major comorbidity. Infection also causes large leucocytosis.

7. Extrapulmonarry tuberculosis

Small contingent of immunocompetent people would suffer extrapulmonary disease but poor immunity increases the risk. Most serious is infection in central nervous system, where meningitis and tuberculomas may result. These carry high risk of mortality. Mycobacterial dissemination in blood may cause multiple organ involvement.[16] Military tuberculosis worsens rapidly with nonspecific features posing difficulty for clinical