20 Post-primary Pulmonary Tuberculosis

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Post-primary pulmonary tuberculosis is a chronic disease commonly caused by either endogenous reactivation of a latent infection or exogenous re-infection by Mycobacterium tuberculosis. It has other synonyms derived mostly from the route of transmission of the infection or from the age of the patient at the onset of the disease, including endogenous reactivation primary tuberculosis, exogenous re-infection pulmonary tuberculosis, or adult-onset pulmonary tuberculosis. The term being used here is 'post-primary pulmonary tuberculosis' to include both re-infection and reactivation forms. The clinical features of the disease are not specific, and the imaging features are suggestive but can simulate other diseases. The definitive diagnosis depends on the identification of M. tuberculosis bacilli, using conventional microbiological methods of sputum smear and culture or radiometric culture methods such as BACTEC or DNA probe PCR-based assays which can identify drug-resistant strains as well. Sputum smear and culture remain the most important investigative methods. Smear-negative sputum may delay the diagnosis for 4–8 weeks or longer if the culture is also negative. A presumptive diagnosis based on the clinical and radiographic features should be made with initiation of treatment after the exclusion of other possible causes of the radiographic findings.

Infection with HIV is a great risk for the development of either endogenous reactivation or exogenous re-infection pulmonary disease (Millar and Horne 1979; Barnes et al. 1991; Heyderman et al. 1998). The development of drug-resistant pulmonary tuberculosis is a real global concern that indicates a failure of the tuberculosis control program. The current treatment is both toxic and expensive, and new drug development is sparse at present.

20.1 Pathogenesis and Pathology

The development of post-primary pulmonary tuberculosis as a result of endogenous reactivation or exog-
enous re-infection in low-risk and high-risk areas has been debated for many years among authors (Glynn et al. 2001). Balasubramanian and colleagues reviewed the world literature on these issues and added their own views (Balasubramanian et al. 1994). Schools of thought adopted by those researchers based on microbiological studies of tissue specimens from the lung and lymph nodes of the primary complex. Some authors quoted by reviewers suggested that the primary complex is sterile within 5 years, while other authors suggest that virulent bacilli lie dormant in a metastatic site seeded hematogenously within the vulnerable region. Cultures of apical lung lesions yielded viable bacilli in 25%–76% as reported by some of the quoted authors, and transmission via the bloodstream was suggested.

Other researchers examined the sputum and urine cultures in patients living in Bangalore, India, and compared the bacilli virulence, INH sensitivity, and phage typing of the isolates and drew conclusions about the biological evidence of exogenous re-infection in that study. Epidemiologists have noted that high- or low-risk incidence rates of infection in different areas of the world played an important role (in exogenous re-infection or endogenous reactivation). In areas with a risk greater than 1% of developing countries, with the likelihood of repeated episodes of droplet infection via the airway, the disease is more likely to be due to exogenous re-infection. In areas of low-risk (less than 0.05%), as in developed countries, endogenous reactivation is more likely to be the cause of the disease. Some other authors gave evidence of the contributions of both exogenous re-infection as well as endogenous reactivation. Balasubramanian et al. hypothesized that the implantation of the vulnerable region is directly transmitted via the airway (exogenous re-infection). They also concluded that more studies using genetic fingerprinting of \textit{Mycobacterium} bacilli isolates would help in the future in disease control in endemic areas and in the development of new vaccines. Immune suppression resulting from HIV infection leads to higher rates of co-infection with tuberculosis.

Recent molecular epidemiological studies have indicated that up to 40% of newly diagnosed tuberculous patients and over 70% of recurrences may be due to exogenous re-infection (Stead and Bates 2000; Bates et al. 2001). Among the immunosuppressed patients due to HIV, exogenous re-infection was the leading mechanism. Endogenous reactivation contributed to only 16% of patients in a low-risk area in developed countries and more than 70% in a high-risk area in developing countries (Alland et al. 1994; Brande et al. 1998; Small et al. 1994; van Rie et al. 1999; McDonough et al. 2000; Rook and Zumla 2001; Caminero et al. 2001; Banadera et al. 2001; Wallis and Johnson 2001).

Caminero and colleagues (2001) reported 912 patients with culture-proved pulmonary tuberculosis between 1991 and 1996 on a Spanish island with a moderate risk rate of incidence. They were treated and followed up for at least 12 months after completing chemotherapy and were culture-negative. Twenty-three patients (2.5%) became culture positive again. DNA fingerprinting results were available from 18 patients with recurrence of the disease. DNA fingerprinting was available of pretreatment and recurrent isolates and was reviewed. In 8 patients (44%), the genotype of the recurrent isolate showed a different pattern to the pretreatment isolate. These authors concluded that in 8 patients, 2 of them HIV-positive, exogenous re-infection was the cause of the recurrent pulmonary tuberculosis. Immune suppression or reduction of immune responses may also occur in certain diseases such as silicosis, diabetes mellitus, or with corticosteroid and other immunosuppressive drugs used for malignancies or connective tissue diseases.

Regardless of the mode of infection (exogenous or endogenous), the apex of the lung (apical-posterior segments) is the most common site of post-primary pulmonary tuberculosis. Specific factors permitting the progression of tuberculosis in most cases are not yet known (Wallis and Johnson 2001).

The host immune response and the role of the cell-mediated immunity of activated macrophages and T-cells and the expression of cytokines (Garcia et al. 2002) in response to \textit{M. tuberculosis} glycolipids and lipoproteins have been discussed in the pathogenesis of primary pulmonary tuberculosis in Chap. 17. Post-primary pulmonary tuberculosis commonly affects the apical and posterior segments of the upper lobe or the superior segment of a lower lobe. After its localization, inflammatory granulomatous nodular formations with cellular infiltrates, fibrosis, central necrosis, and caseation may take place. Hilar and parastracheal lymphadenitis (Woodring 1986) in post-primary tuberculosis is a rare occurrence and reported in approximately 5% of patients (see Figs. 23.18, 23.20, 23.21, 23.22, 23.39, 23.40b). Healing with fibrosis and calcification (Fig. z.25) of lung parenchymal lesion may occur, leading to traction of the trachea (Fig.23.21, 23.22, 23.23), and in late advanced stages when the lung is destroyed and replaced by extensive fibrosis, displacement of the mediastinum may occur (Fig. 23.24).

The initial upper lobe infiltration may form a pneumatic consolidation, and cavitation often