EDITORIAL

BRONCHOALVEOLAR LAVAGE STUDIES IN PULMONARY TUBERCULOSIS

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Bronchoalveolar lavage (BAL) studies are useful to assess the lower respiratory tract inflammation and to study the pathogenesis of various lung diseases (1). Even though potent chemotherapeutic regimens are available currently to treat patients with pulmonary tuberculosis, radiographic and pulmonary function abnormalities persist in a proportion of tuberculosis patients despite treatment (2). Evaluation of lung immune process in pulmonary tuberculosis using BAL may aid in understanding the mechanism of lung injury and fibrosis which, in turn, may help to formulate modalities of treatment that prevent fibrosis. In addition, since BAL samples the epithelial lining fluid of the alveoli, it is possible that it may aid in early diagnosis of sputum smear negative pulmonary tuberculosis.

Studies on pathogenesis

BAL studies in 27 sputum smear negative but radiographic probable pulmonary tuberculosis patients, confirmed as active pulmonary tuberculosis by isolation of *Mycobacterium tuberculosis* in culture from sputum and/or lavage specimens, had shown that two distinct cell profiles could be identified in smear negative pulmonary tuberculosis patients (3). One group (macrophage predominant) had significantly elevated total cells and alveolar macrophages in both radiologically normal and abnormal lobes. The other group (lymphocyte predominant) had expanded numbers of total cells, lymphocytes and granulocytes in radiologically abnormal lobe only. Sputum smear positive pulmonary tuberculosis patients had been shown to have lymphocytosis in BAL fluid (4-7). In addition, eosinophilic pneumonia was also demonstrated in three bacteriologically confirmed pulmonary tuberculosis (8). In two patients, pulmonary eosinophilia was present only at the site of lesion and the third had eosinophilia in both peripheral blood and lung. There was complete elimination of eosinophilic inflammatory process in two patients who had successfully completed antituberculosis treatment (8). BAL studies in miliary tuberculosis show lymphocytic alveolitis (9,10). Elevated levels of immunoglobulins (IgG, IgA, IgM) and fibronectin were demonstrated in BAL fluid from patients with miliary tuberculosis (10). Lymphocytic alveolitis (9,10,) and raised immunoglobulins (IgG and IgA) persisted in BAL fluid despite treatment (10).

Alveolar macrophages from patients with active pulmonary tuberculosis produced significantly higher hydrogen peroxide (11). Alveolar macrophages that were resistant to OK la (anti-DR monoclonal antibody and complement treated) in fact produced increased levels of hydrogen peroxide (12). Alveolar lining material of patients with active pulmonary tuberculosis has less bactericidal activity against bacterial infections such as *Staphyococcus aureus* (13). It had also been demonstrated that there was increased production of procoagulant activity by alveolar macrophages, in collaboration with lymphocytes and other cells at the site of tuberculosis lesions and this may lead to fibrin formation (14). It had been reported that a decreased CD4/CD8 ratio with an increase in CD8 cells in the alveolar space was associated with slow disease regression in patients with active pulmonary tuberculosis suggesting that the balance of T lymphocyte subsets may play a central role in the modulation of host defence against mycobacterial infection (15). Further studies utilizing BAL in patients with pulmonary tuberculosis with or without HIV infection are required to understand the local immune mechanisms which may aid in formulating treatment modalities especially for prevention of lung fibrosis.

Studies on diagnostic utility

Patients with positive tuberculin skin tests and abnormal chest radiographs compatible with tuberculosis pose diagnostic problems and therapeutic dilemma (to treat or not to treat for tuberculosis) to chest Physicians. Fibreoptic bronchoscopic studies provide various types of specimens (aspirates, brushes, lavage fluids and biopsies) for early diagnosis of sputum smear negative pulmonary tuberculosis (16-22).

In a retrospective review of patients over a six-year period, Baughman et al (23) observed that bronchoscopy with BAL was useful in the diagnosis of pulmonary tuberculosis. In their study there were 30 patients whose pre-bronchoscopy expectorated sputum smaples were negative for acid fast bacilli (AFB). Of these

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30, bronchoscopy specimens were smear positive in 26 (87%). Only nine (30%) had sputum culture positivity. In another study (24), out of a total of 71 suspected patients, sputum culture was positive in 33 (46.5%) while BAL culture was positive only in 24 (34%) patients and in whom sputum cultures were also positive. In none of the patients, tuberculosis was diagnosed by BAL culture alone, despite BAL specimens were cultured in several different media. Lavage smear positivity enabling a rapid diagnosis was possible in three (9%) of 33 patients proved to be tuberculosis by culture examination (24). Thus, a single bronchoscopic procedure such as BAL fluid obtained by instillation of normal saline and cultured for *M. tuberculosis* is not, therefore, superior to sputum culture examination for the diagnosis of sputum smear negative, X-ray positive pulmonary tuberculosis. Kennedy et al had reported in a retrospective analysis of 112 patients that 91% of prebronchoscopy sputum samples (all smear negative) had positive culture results, but only 63% of BAL specimens were positive for *M. tuberculosis* (25). Sputum smear negative pulmonary tuberculosis is a paucibacillary condition and the dilution of epithelial lining fluid by the instilled saline might be responsible for the low yield from BAL specimens. In addition, the local anesthetic used for bronchoscopy might have also suppressed the growth of *M. tuberculosis* (26). In childhood pulmonary tuberculosis, Somu et al found that gastric lavage was superior to BAL fluid for isolation of *M. tuberculosis* in culture (27).

Kennedy et al (25) had further observed that early diagnosis of sputum smear negative pulmonary tuberculosis was possible in 38% of patients if different bronchoscopic procedures such as transbronchial biopsy (TBB) and post-bronchoscopy sputum in addition to BAL were studied. Panda et al reported that immediate diagnosis was possible in 35% of patients using TBB and bronchoscopy lavage (28). Chasroenratankul et al also found that the diagnostic yield of overall bronchoscopic procedures (BAL smear and culture and TBB) was 32.5% in patients with suspected smear negative pulmonary tuberculosis (29). Thus an early diagnosis of tuberculosis is possible if different bronchoscopic procedures are employed instead of a single procedure alone during bronchoscopy. In a decision analysis model to assess the overall utility of BAL in clinically suspected sputum smear negative pulmonary tuberculosis, it has been suggested, in a region of high tuberculosis prevalence, empirical treatment is the best course of action. BAL in such circumstance can be reserved for further investigation of Patients not responding to empirical antituberculosis treatments (30).

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