activation analysis, which is especially useful for the detection of trace metals in the cell-free BAL fluid, showing high concentrations of tungsten (W), tantalum (Ta) and cobalt (Co) in hard metal lung disease [163].

The quantification of asbestos bodies is best done by filtration of 5–15 ml fresh BAL fluid, cells included, onto millipore filters, and counting the number of asbestos bodies [179]. Uncoated asbestos fibres can only be counted by electron microscopy [177], but this is, so far, without clinical value.

Asbestos body counts correlate with the type of asbestos related disorder being higher in those with benign pleural disease or malignant mesothelioma [179]. Asbestos body counts in BAL correlate closely with concentrations of asbestos bodies in lung tissue obtained by biopsy or at autopsy. A BAL count of more than one asbestos body per ml is highly indicative of a lung concentration exceeding 1,000 asbestos bodies per g dry tissue [180, 181]. Only seven percent of non-asbestos exposed white collar workers have asbestos bodies at concentrations $>1 \cdot ml^{-1}$ BAL fluid [179]. In general, demonstration of dust in the lungs is an indication of exposure but is no evidence of disease. On the other hand, a minority of patients with definite asbestos exposure and disease may have no detectable asbestos bodies in their BAL fluid [179]. Demonstration of dust in BAL is especially useful in patients with ILD or pleural disease who have previously unknown or uncertain exposure to asbestos or other dusts.

Value of BAL for clinical diagnosis and management

The demonstration of dust in BAL fluid or cells is indicative for exposure, but is no evidence of disease. There is currently no known BAL level of particles above which development of disease is inevitable. ILD has to be proven by routine clinical methods like chest radiography, computerized tomographic (CT) scanning and lung function test.

There is no clinical value of differential cell counts in ILD due to occupational dust exposure, except for chronic beryllium disease.

For the management of patients with known ILD due to dust exposure, BAL is currently of no proven value, except for chronic beryllium disease and for the recognition of the co-existence of another disorder of different cause, such as sarcoidosis, hypersensitivity pneumonitis, haemorrhage syndrome and others [182].

The clinical role of BAL in pulmonary histiocytosis X

C. Danel, D. Israel-Biet, U. Costabel, G.A. Rossi, B. Wallaert

Pulmonary histiocytosis X (PHX) is a rare chronic granulomatous disorder involving cells of the monophagocytic system. The diagnostic feature of this disease is the finding of Langerhans cells (LC) which react with the monoclonal antibody CD1 (OKT6) and which contain characteristic cytoplasmic organelles [183, 184]. After its introduction as a new means of studying peripheral lung and alveolar cell populations, BAL has rapidly proved useful in the diagnosis of PHX [185].

Diagnostic value of BAL in PHX

Several studies have shown the major value of BAL in the diagnosis of PHX [185, 186]. The total cell count is usually increased. HANCE *et al.* have reported that 90% of their PHX patients were smokers [186]. It is well known that the total cell recovery is usually higher in smokers than in nonsmokers. Besides, the nonsmoking patients with PHX have a normal alveolar cell count. The differential cell count shows a high percentage of alveolar macrophages (AM), a slight increase of neutrophils and eosinophils [185]. On electron microscopy, a significant percentage of Langerhans cells (LC) display highly specific pentalaminar structures of constant width, with a tennis racket shape at one end [183, 185]. As this ultrastructural analysis is time consuming, a more rapid and sensitive technique has been developed using monoclonal antibodies to LC (CD1 positive cells) [184]. For some other authors, the finding of PS 100 BAL positive cells could ensure the diagnosis of PHX. However, this antibody is far less specific of LC than CD1 and its use is therefore not recommended.

The actual value of BAL and in particular the presence of LC in the diagnosis of PHX is difficult to assess. Some authors have reported a mean of 5% CD1 positive cells in the BAL of patients with PHX, while in other interstitial lung diseases, less than 3% of the total cells were found to be CD1 positive [184].

In fact, recent studies have shown that LC are normally present in the lower respiratory tract and in lung parenchyma of normal subjects, particularly in smokers [186, 187]. Alteration of this epithelium seems to be an important stimulus in attracting LC to the lung [130], and cigarette smoking is known to produce such epithelial abnormalities in the lower respiratory tract. Besides, cigarette smoke actually increases the number of LC found in BAL fluid [186].

Furthermore, LC have been found in the lung of patients with diseases other than PHX, in fibrotic lung disorders, benign inflammatory conditions or bronchoalveolar carcinoma for instance [65, 167, 168]. Therefore, as the mere presence of LC in BAL is not pathognomonic of PHX, particularly in smoking patients, a percentage of at least 5% of CD1 labelled alveolar cells is required to confirm the diagnosis.

On the other hand, with PHX having a patchy distribution, a localized BAL can miss the diagnosis, as well as a transbronchial biopsy. Confirmation by an open lung biopsy is therefore advisable.

Conclusions

There are strong arguments to support the usefulness of lavage cell analysis in the diagnosis of pulmonary histiocytosis X. However, false negative results can be related to the patchy distribution or to the stage of the disease. False positive results havealso been reported in heavy smokers or in bronchoalveolar carcinomas, for instance. This highlights the fact that BAL data should be interpreted carefully in the context of clinical and radiological data. One requires at least 5% of LC in BAL to confirm the diagnosis. This either gives sufficient diagnostic clues or else points to the necessity of an open lung biopsy.

The clinical role of BAL in eosinophilic lung diseases

C. Danel, D. Israel-Biet, U. Costabel, G.A. Rossi, B. Wallaert

Eosinophilic infiltrates in the lung can be encountered in a great variety of disorders such as asthma, eosinophilic pneumonia, allergic bronchopulmonary aspergillosis or Churg and Strauss vasculitis. In this chapter we will concentrate on eosinophilic pneumonia ranging from the acute but mild and remitting Loeffler's syndrome to the severe chronic eosinophilic pneumonia. As these diseases can be life-threatening but remarkably reversible under corticosteroid therapy, a rapid diagnosis is of major importance. Since no alveolar eosinophilia is ever observed in normal controls, any increase in the percentage of eosinophils in BAL argues for a pathological process. In any type of eosinophilic lung (EL), acute or chronic, BAL always displays a high alveolar eosinophilia, whether or not associated with a blood eosinophilia [190–193].

Besides its diagnostic value, BAL has also given clues to the pathogenesis of eosinophilic lung injury. Indeed, eosinophils secrete not only neutral proteases and oxygen radicals but also a major basic protein (MBP) and a cationic protein (ECP) known to be able to induce acute lung damage and pulmonary fibrosis [194]. Finally, BAL is also valuable in EL for the clinical follow-up of patients under treatment [195].

Diagnostic value of BAL in eosinophilic lung

As, in these disorders, eosinophils are largely located in air spaces, the diagnostic yield of BAL is very high, usually making more invasive techniques (open lung biopsy or transbronchial biopsy) unnecessary. The analysis of BAL and blood should be performed in parallel. The diagnostic value of a high alveolar eosinophilia is all the greater if the level of the blood eosinophilia is normal.

It is usually in eosinophilic pneumonia (EP) that the highest eosinophilic count is observed [190–193]. If the increase of total recovered cells is not always significant, the percentage of eosinophils is markedly abnormal, sometimes increased up to 90% of total cells, associated or not to a few mast cells, and always higher than the neutrophil count. A proportion of these eosinophils can undergo necrosis, and fine eosinophilic granules can be observed in alveolar macrophages. Nevertheless, such a high alveolar eosinophilia can also be observed in some parasitic disorders or in the Churg-Strauss syndrome [192]. Less pronounced eosinophil increases (5–10%) can be found in sarcoidosis, histiocytosis X, drug induced pneumonia, collagen vascular disease, asthma and idiopathic pulmonary fibrosis [190–192].

Conclusions

In eosinophilic lung diseases (EL), BAL is of great value not only for the diagnosis and the follow-up of patients treated, but also for the study of their pathogenesis. EL is one of the diseases in which BAL can give enough clues to the diagnosis to avoid, in many cases, an open lung biopsy. The highest eosinophil counts ever seen in BAL fluid are observed here, ranging from 20–90% of the cells. These results are most useful when the X-ray findings are atypical and peripheral eosinophilia absent.

The clinical role of BAL in alveolar proteinosis

C. Danel, D. Israel-Biet, U. Costabel, G.A. Rossi, B. Wallaert

Pulmonary alveolar proteinosis (PAP) is a rare disorder characterized by accumulation of periodic-acid-Schiff (PAS)-positive phospholipidic material in the alveolar spaces [196]. PAP can be idiopathic or secondary to various conditions, such as immunosuppression, malignant haematological disorders, silicosis or, more rarely, diffuse interstitial lung diseases [53, 196, 197].

As the clinical and radiological presentations are not specific, PAP can remain misdiagnosed. Segmental BAL appears to be essential in management of this disease for diagnosis, follow-up, and therapeutic purposes [197].