Bronchoalveolar Lavage and Histopathologic Diagnosis Based on Biopsy


Yukihiko SUGIYAMA

Professor, Division of Pulmonary Medicine, Department of Medicine, Jichi Medical School

Abstract: The diagnostic significance of bronchoalveolar lavage (BAL) in idiopathic interstitial pneumonias (IIPs) is rather low, in that BAL merely enables exclusion of infections and such disorders as pulmonary alveolar proteinosis, which can be specifically diagnosed by this procedure, and suggests likelihood of eosinophilic pneumonia, BOOP or NSIP if assessments of cell fractions show an increase in eosinophils or lymphocytes alone. However, it is feasible to analyze disease states using components collected via BAL. In histopathologic diagnosis based on biopsy, it is impracticable to determine individual disease forms of IIPs by transbronchial lung biopsy (TBLB) because of the size of specimens obtainable, so surgical lung biopsy is required. Surgical lung biopsy procedures include open lung biopsy (OLB) and thoracoscopic lung biopsy. Lung biopsy with video-assisted thoracoscopy (VATS) is less invasive than OLB, and is performed in practically all applicable cases at present. For individual disease forms of IIPs, histopathologic diagnosis is currently carried out using this procedure at many medical institutions.

Key words: Bronchoalveolar lavage; TBLB; Surgical lung biopsy; Idiopathic interstitial pneumonia; Idiopathic pulmonary fibrosis

This article deals with “bronchoalveolar lavage and histopathologic diagnosis based on biopsy” as a current problem concerning interstitial pneumonia of unknown causes, i.e., idiopathic interstitial pneumonias (IIPs).

Bronchoalveolar Lavage

As for bronchoalveolar lavage (BAL) in IIPs (Fig. 1), to begin with, the BAL technique is an examination method initially devised in the 1970’s that can be said to be epochal, and has been progressing with the development of fiberoptic bronchoscopy. Bronchus of the relevant lung segment are irrigated in the case of a localized lesion, or the middle lobe of the right lung or the left lingular segments are lavated in patients with diffuse lung diseases. The procedure is
that the tip of a fiberbronchoscope is wedged into the target bronchus and a total volume of 100–200 mL of lukewarm physiological saline fluid is injected through that endoscope in aliquots of 20–50 mL, followed by collection of the lavage fluid. The first collection of fluid may not be used for examination because it eventually contains high concentrations of regional components of the airway.

The lavage fluid yield is usually about 60%. If the recovery rate is extremely low, it becomes difficult to evaluate BAL findings. Liquid components and cellular components in the collected BAL fluid specimen are examined and used for diagnosis and research. From the diagnostic viewpoint, the condition best indicated by BAL is pulmonary alveolar proteinosis, for which a whitish turbid liquid reminiscent of rice grain washings is obtained and is definitely diagnostic. The procedure is employed for specific diagnosis of alveolar hemorrhage, infections such as tuberculosis, mycosis, and Pneumocystis carinii pneumonia, asbestos pneumoconiosis verified by demonstrating asbestos bodies in the lavage fluid, pulmonary Langerhans’ cell histiocytosis (granulomatosis) diagnosed by noting increased CD1-positive cells, or malignant tumors.1)

Other conditions where BAL is relatively highly useful for diagnosis include chronic or acute eosinophilic pneumonia where a marked increase of eosinophils is observed in the lavage fluid, sarcoidosis in which there is a marked increase in lymphocytes with elevated CD4/8 ratio (when supported by other findings), and summer-type hypersensitivity pneumonitis simi-
larly with markedly increased lymphocytes yet with lowered CD4/8 ratio.

An important point in making evaluations of BAL findings is that the cellular pattern changes with cigarette smoking, and in interpreting BAL findings one needs to consider whether the subject under test is a smoker or a non-smoker. One should exercise caution in that an increased cell population collected in lavage fluid with an increase in percent macrophages, a decrease in percent lymphocytes and a decreased CD4/8 ratio are noted in healthy smokers, hence presenting a cellular pattern different from that seen in non-smokers.

Next I would like to discuss the usefulness of BAL from the angle of diagnosis of IIPs. Firstly, the usefulness of BAL consists in that the above-mentioned specific diseases can be excluded by analysis of BAL fluid from among a variety of diseases that present diffuse opacities in the lungs. It is infeasible, nevertheless, to make a diagnosis of IIPs on the grounds of BAL findings, nor is it possible to diagnose various disease forms of IIPs. The usefulness of BAL as a research tool is unquestioned, but the value of BAL from the viewpoint of diagnosis is limited.

In idiopathic pulmonary fibrosis (IPF), the central clinical entity among IIPs, it is generally recognized that the BAL cellular pattern is macrophage-predominant and close to a normal pattern. Furthermore, an increase in neutrophils by ≥5% is observed in 70–90% of patients with this disorder, and an increase in eosinophils by ≥5% is noted in 40–60% of patients. Besides these changes, an increase in lymphocytes is demonstrable in only 10–20% of patients, and an increase in lymphocytes alone is noted in less than 10%.1)

If there is only an increase in lymphocytes, therefore, it may be said that other disorders than IPF should rather be suspected, such as sarcoidosis, hypersensitivity pneumonitis, bronchiolitis obliterans with organizing pneumonia (BOOP), nonspecific interstitial pneumonia (NSIP), or lymphoid interstitial pneumonia (LIP). In cases, especially where the increased lymphocytes mostly comprise CD8-positive cells with a CD4/8 ratio of ≤1, BOOP or NSIP would be more likely than other IIPs and further differentiation between them according to lung imaging pattern may be possible.

The next problem to be discussed is whether BAL can be utilized for prognostic estimation. This, too, has limitations as regards IPF. Some reports suggest that the prognosis is unfavorable in patients showing increased percentages of neutrophils and/or eosinophils, but these reports are not authoritatively supported. Increased lymphocytes are observed in less than 20% of cases of IPF as mentioned above, and it is generally recognized that the increase in lymphocytes on BAL correlates with cellular infiltration type in biopsied specimens, responses to corticosteroids can be anticipated, and honeycomb lung is rare. BAL is not so invasive as an examination but there have been a report that acute exacerbation occurred due to BAL;2) it is not a frequently repeatable procedure. Therefore, the cellular pattern on BAL performed as part of initial diagnostic evaluation may possibly be useful for prognostic estimation, but will require technical skill at the institution and scrupulous care in the interpretation of results.

Thus, BAL is used solely for the limited purpose of excluding other disorders in the diagnosis of IIPs. However, studies on the disease state of various diffuse lung diseases have been making rapid progress thanks to gene analysis using cells collected by means of BAL and analysis of components in the BAL fluid. The role of BAL in pathophysiologic studies of IIPs may be said to be extremely prominent.

Transbronchial Lung Biopsy

This section deals with transbronchial lung biopsy (TBLB) (Table 1). Specimens obtained by TBLB are quite small, measuring up to 5mm in diameter. It is difficult consequently to accurately determine the extent of fibrosis or
inflammation and its pattern, and it is impossible to pathologically differentiate disease forms of IIPs from such TBLB specimens. With the specimens obtained by TBLB, however, it is feasible to definitely rule out in the first place such granulomatous lung diseases as sarcoidosis, hypersensitivity pneumonitis and pulmonary Langerhans cell histiocytosis, infections by tubercle bacilli or mycotic agents, various malignant tumors or malignant lymphomas, eosinophilic pneumonia, and pulmonary alveolar proteinosis.

There is also the possibility that BOOP, among other IIPs, may be diagnosed to some extent by TBLB because of its characteristic pathologic features. Tissues at the peripheral alveolar level immediately subjacent to the pleura are sampled under fiberbronchoscopy. More concretely, the biopsy forceps are advanced to immediately subjacent to the pleura under fluoroscopic control with the patient holding his/her breath once, then the forceps are pulled back a little and opened, and the tissue is sampled in harmony with patient’s breathing motion. It is a common practice to biopsy the site possibly best reflecting the disease on imaging in diffuse lung diseases as well, with S3a and S8a usually being chosen for the biopsy.

TBLB also is not so invasive as an examination but is impracticable in a patient unable to hold his/her breath for a short time due to coughing or hypoxemia. There have been cases in which acute exacerbation of IPF followed TBLB-associated pneumothorax; here too, needless to say, caution must be observed.

### Surgical Lung Biopsy

The following surgical lung biopsy procedures are to be undertaken in further focusing the diagnosis after disorders specifically diagnosable by BAL and/or TBLB have been excluded. Surgical lung biopsy procedures include open lung biopsy (OLB) and thorascopic lung biopsy, including lung biopsy with video-assisted thoracoscopy (VATS). Both procedures are performed under general anesthesia, and lung biopsy is carried out using VATS in practically all cases currently because it is less invasive and requires shorter durations of drainage and hospital stay. A marked advance made in recent years has been that, with the development of VATS, surgical lung biopsy can now be performed far more easily.

The purpose for which surgical lung biopsy is carried out is to attain an ultimate histopathologic diagnosis in a patient whose diffuse
lung disease has not been diagnostically ascertained by BAL and/or TBLB. As disease forms of IIPs cannot be diagnosed by BAL and/or TBLB, surgical lung biopsy is aimed at determination of the disease form. The primary objective is thus to differentiate between IPF generally unresponsive to steroid therapy (histologically, usual interstitial pneumonia: UIP) and NSIP, desquamative interstitial pneumonia (DIP) or BOOP/COP (cryptogenic organizing pneumonia) which are usually responsive to steroid therapy. However, there is a high degree of possibility of IPF/UIP in chronic cases where IIPs are suspected with typical image findings and obvious honeycomb lung features on high-resolution CT (HRCT) scan. The diagnostic strategy usually does not proceed up to VATS in such cases. In IIPs, VATS may be said to be an examination performed to obtain histopathologic evidence to ascertain indication for steroid therapy in patients in whom IPF/UIP has been ruled out.

IPF is precisely defined as a disease presenting histopathologic features of UIP. Pathologically, the disease is generally recognized to be characterized by diverse phases of changes with a patchy, especially subpleural, distribution of lesions with the presence of honeycomb lung and fibroblastic foci. In NSIP reported by Katzenstein et al. in 1994, in contrast, lesions are diffuse and temporally homogeneous with characteristically concordant phases and respond well to steroid therapy, thus differing in these respects from IPF.

As regards the group III (fibrotic type) of NSIP, problems have often arisen for histopathologic features in the differential diagnosis from UIP, and opinions vary even among pathologists. The issues are still to be clarified.

It is generally thought that the points described below should be taken into account in order to improve the certainty of pathologic diagnosis in undertaking VATS.

As for the problem of tissue sampling sites, it has been suggested that it is most desirable to take samples from three different sites, i.e., the area of the most pronounced lesion, the area where the most incipient change is likely to be present, and an area of intermediate change.

It is generally thought advisable that apical regions of the middle and lower lobes, where nonspecific subpleural collapse often occurs, are to be avoided. Specimens obtained by VATS are a few cm in size, hence more than 10 times as large as those sampled by TBLB, and therefore can provide information that enables determination of the distribution of lesions (patchy or diffuse), their relation to the airway, and the destruction/modification pattern of alveolar structures. Only with this approach, it is possible to differentiate histologic patterns among such entities included in IIPs as UIP, NSIP, DIP, acute interstitial pneumonia (AIP), BOOP/COP and respiratory bronchiolitis-interstitial lung diseases (RB-ILD), and thus to permit an ultimate diagnosis. However, there are still conditions which cannot be placed under any of the above-mentioned histologic patterns, even by the surgical biopsy VATS. Such conditions have to be taken as unclassifiable. One should note that VATS is not an omnipotent examination.

As is the case with BAL or TBLB, there have been clinical cases of IIP in which acute exacerbation occurred due to surgical lung biopsy including VATS, thus one must stress the need for careful consideration in applying this technique. Risk factors involved in surgical lung biopsy have been described as excluding patients over 70 years of age, and patients with intercurrent cardiac disorders, markedly depressed pulmonary function, and severe obesity.

We have reviewed above the roles of bronchoalveolar lavage, transbronchial lung biopsy, and surgical lung biopsy especially as means of diagnostic approach in cases of idiopathic interstitial pneumonias.

REFERENCES


