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# Complementariness of the radiological finding and transbronchial lung biopsy for definitive diagnosis of diffuse interstitial lung diseases

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*In this study 52 patients admitted to hospital for transbronchial biopsy of the lungs (TBB) due to anamnestically, clinically and radiologically suspected diffuse interstitial lung disease (DILD) were examined. Using classical radiological symptomatology tele radiograms were recorded (F-F 180 cm) of the chest PA and profile, by high voltage technique (125 kV). The patients were selected with regard to contraindications for general anaesthesia, and TBB. TBB was carried out under general anaesthesia with combined use of a rigid and flexibile bronchoscope, without radiological control. The percentage of adequate biopsy findings was very satisfactory (94 %), as was also the case with regard to sufficient pathoanatomic (51 %) and radiological (42 %) findings, by which a definitive clinical diagnosis can be made without the need for other tests. In the same way the percentages of adequately sufficient pathoanatomic (16 %) and radiological (39 %) findings were very statisfactory, by which, combined with other tests, definitive clinical diagnosis can be concluded. In no single disease were both findings insufficient, which indicates their complementariness, and in this way they are sufficient judging by the clinical status, BAL and biochemical findings, with regard to the final clinical diagnosis.*

*Key words:* lung diseases, interstitial-pathology; biopsy; thoracic radiography

## Introduction

Interstitial lung diseases are a heterogeneous group of diseases characterized by damage to the supportive structure of the lung units for gas exchange, periaveolar and alveoral tissue. In the acute phase alveolitis occurs, accompanied by prolonged, unrestrained inflammation of neighbouring parts of the interstitium and blood-vessels, and after a long period the inflammatory changes and consequent interstitial lung fibrosis damage the lung parenchyma, leading to impairment of gas exchange and ventilation. This diverse group of approximately 125 diseases has many common characteristics, including similar clinical symptomatology, graded radiological findings, consistent alterations in lung functions and typical cytological and histological appearance.

Bronchoscopy demonstrated its great value by facilitating the use of biopsy forceps to take tissue samples for histological and cytological analysis. Probably no other diagnostic or therapeutic technique changed pulmological work so radically in such a short time.

Interstitial disease have recently become the subject of great interest for radiologists. On the chest X-rays and imaging techniques this special group of diseases is characterized by multiple diffusely

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distributed lesions. According to these radiological criteria, complex clinical symptomatology, consistent changes in lung function, bronchoalveolar lavage (BAL), approximate pathoanatomic diagnosis can be made. The interstitial sample is an antithesis for the consolidatory alveolar process. It is a disorder within the lung architecture caused by an abnormal accummulation of tissue in the parenchymal lung interstitium.

In this study we compared the findings of transbronchial lung biopsy (TBB), which is accepted as suitable in histopathological diagnosis of diffuse interstitial lung diseases (DILD), with the radiological finding. The aim of the study was to determine the specific diagnostic value of each method separately and the possible additional benefit when both methods are interpreted simultaneously.

## Patients and methods

In this investigation 52 hospitalized patients were examined (27 women and 25 men, range 16–76 years) in the Bronchoscopy unit at The Clinical Hospital for Lung Diseases – Jordanovac.

The patients were admitted for bronchological examination with transbronchial lung biopsy (TBB) because of anamnestically, clinically and radiologically suspected disease of the lung interstitium.

Teleradiograms (F-F 180 cm) of the chest PA and profile were recorded by high voltage technique (125 kV) on a Thoramat Siemens aparatus and, when necessary, tomography was performed. Such a radiological technique facilitated the taking of a biopsy sample in the area of the pathological process, with maximum accuracy, and without the use of a discope. As patients with DILD are regularly followed up long-term, it is essential to reduce the dose of exposure to ionizing radiation. Namely, during one minute of diascopy patients receive a dose which is equivalent to one hundred chest X-rays.

Although unrelated to ILO classification, the interstitial lesions were considered as patognomonic for certain diffuse interstitial lung disease.

Prior to bronchoscopy the following tests were carried out: gas analysis of arterial blood, coagulogram, haemogram, electrolytes, urea, creatinine clearence and an ECG.

The patients were selected with regard to contraindications for this examination (pulmonary hypertension, hemorrhagic diathesis, asthma, hypoxia where pO2 is less than 8,7 kPA inspite of oxygen administration, acute hypercapnia where pCO2 is more than 6 kPA, severe arhithmias, status within 3 months after the myocardial infarction, bad general condition, haemogram, electrolytes, local finding of the bronchial mucosa).

Following premedication with 0.8–1 mg Atropin, the anesthesized (narcotic, hypnotic and depolarizing muscle relaxants) patient was intubated with a rigid bronchoscope ("Wolf"). During the bronchoscopy the patient was ventilated according to Venturi's method, and a fiberbronchoscope (Olympus BS 10") was then introduced by which 2–3 biopsy samples were taken (by a standard technique) of TBB from the pathologically changed lung parenchyma, without using radiological control. The biopsy sample was placed in 10 % formalin and sent to the Institute for Pathology, Clinical Hospital Centre Rebro for pathoanatomical analysis. After the procedure the patient rested for 25 hours, with an obligatory control X-ray within 8 hours of the procedure.

**Table 1.** Dependence of succesful TBB on examination techniques. Comparison of the results of this study with the results of other authors.

| Authors | Attempted biops. N | Adequate biops. N | % | Examination techniqe |
|---|---|---|---|---|
| Anderson i Fontana | 450 | 378 | 84 | Fiberbronchoscopy + dia. + local anaesthesia |
| R. Petit | 66 | 47 | 71 | Fiberbronchoscopy + dia. + local anaesthesia |
| J. Malenić | 66 | 59 | 89 | Combined + dia. + general anaesthesia |
| Wal | 53 | 50 | 94 | Fiberbronchoscopy + dia. + local anaesthesia |
| Own results | 52 | 49 | 94 | Combined without dia. + general anaesthesia |
| Levin | 22 | 21 | 95 | Fiberbronchoscopy + dia. + local anaesthesia |

Mean (apart from own results)

**Table 2.** Complimentariness of radiological and pathoanatomic findings in the diagnostics of DILD.

| | Pathoanatomic finding | | Radiological finding | |
|---|---|---|---|---|
| | N | % | N | % |
| Sufficient | 25 | 51 | 21 | 43 |
| Adequately sufficient | 8 | 16 | 19 | 39 |
| Insufficient | 16 | 33 | 9 | 18 |
| Total | 49 | 100 | 49 | 100 |

**Table 3.** Complimentariness of radiological and pathoanatomic findings in the final diagnosis of DILD.

| Final dg. DILD | N | Sufficient PA | Sufficient RTG | Adequately sufficient PA | Adequately sufficient RTG | Insufficient PA | Insufficient RTG |
|---|---|---|---|---|---|---|---|
| Fibrosis | 20 | 16 | 5 | 2 | 9 | 2 | 6 |
| Sarcoidosis | 16 | 5 | 11 | 2 | 4 | 9 | 1 |
| Pneumonia interstitial | 2 | 2 | | | 2 | | |
| Vasculitis necrotisans | 2 | 1 | | 1 | | 1 | 1 |
| Hypersensitive pneumonitis | 2 | | | | 1 | 2 | 1 |
| Microlithiasis | 1 | 1 | 1 | | | | |
| Granulomatosis Wegener | 1 | | 1 | 1 | | | |
| Granulomatosis Lymphomatoides | 1 | | 1 | | 1 | | |
| TBC milliaris | 1 | | | | 1 | | |
| TBC + sarcoidosis | 1 | 1 | | | 1 | | |
| Silicosis | 1 | | 1 | 1 | | | |
| Asbestosis | 1 | | | 1 | 1 | | |
| Total | 49 | 25 | 21 | 8 | 18 | 17 | 9 |

## Results

By simultaneous use of priliminary radiological diagnostic treatment and combined TBB technique, the number of satisfactory samples was very high, up to 94 %. This result is comparable with the percentages of other techniques (bronchofiberscopy with radiological control, combined techniques with radiological control) in approximately the same number of cases (Table 1).

The percentages of sufficient interpretations of pathoanatomic (51 %) and radiological findings (43 %) were very satisfactory and would enable a definitive diagnosis, without other clinical data, and also adequately sufficient pathoanatomic (16 %) and radiological findings (39 %) with which, together with clinical data, the final diagnosis could be made. The percentage of insufficient pathoanatomic findings was higher (33 %) than radiological findings (18 %) (Table 2).

As to the pathoanatomic criteria, the initial diffuse interstitial fibrosis is a dominant finding. Pulmonary fibrosis, which is in fact compatible with the definitive stage of other interstitial diffuse lung diseases, was found in 18 patients, while radiological findings of sarcoidosis was found in 15 patients.

In interstitial pneumonia the radiological finding was sufficient while the pathoanatomical finding was not. Both the pathoanatomic and radiologic findings were sufficiently adequate in pulmonary alveolar microlithiasis, as well as sufficient in asbestosis. In hypersensitive pneumonitis only the radiological finding was sufficient. In other diagnoses both pathoanatomic and radiological findings were adequately sufficient and therefore in no disease were they both insufficient, which indicates their complementariness (Table 3).

## Discussion

Interstitial lung diseases are currently the object of lively interest because of their great frequency, both due to air pollution and other harmful effects in the environment and because of the increasing number of circulating harmful agents. They have become a great health problem because of their acute stadium, different dynamism and response to therapy and finally their chronic forms, with regard to invalidity, i.e. remaining work ability.[1-3]

The protective reaction of the lungs which can include all types of immunological responses, can occasionally lead to one of many diffuse diseases of the lung interstitium.[4–5] Diffuse diseases of the lung interstitium are more frequent in their final stadium of pulmonary fibrosis with lung function impairment of prognosis. They are extremely difficult to classify as there are approximately 125 different diseases, the features of which are often common.

Diseases can be classified into known and unknown etiology. Of the diseases of known etiology the largest group comprises occupational diseases due to exposure to atmospheric pollutants. In the case of diseases of unknown etiology the largest group includes idiopathic lung fibrosis, collagen-vascular diseases (CVD), and granulomatous sarcoidosis. In many diffuse diseases of the lung interstitium similar conditions are present during their immunopathological course. They are judged by the clinical status, characteristic radiological finding, histological samples, bronchoalveolar lavage, scintigraphy with Ga-67 and biochemical findings.[6–12]

By using bronchoscopy it is possible, by a special technique, to obtain a sample of the lung parenchyma, avoiding open-lung biopsy.[13] Transbronchial lung biopsy was first carried out by Andersen[14] in 1965 an later in 1975. It was improved by Zavala and became the most modern technique in the diagnostics of DILD.[15] Current research in this field has shown that the piece of tissue obtained by TBB is usually small, and there is a possibility that widespread changes are not always gripped by the biopsy forceps. Consequently the biopsy sample is frequently taken 3 to 6 times, compared to only 2 to 3 times in our patients. The greater the number of pieces of tissue taken increases the chance of a sucessful diagnosis.[16–17]

Pneumothorax is the most frequent complication of the lung biopsy, (1–5 %, Herf, Zavala).[18, 19] In our series. there were two cases of pneumothorax (3,8 %), which required a conservative treatment. Significant hemorrhage (more than 50 ml of blood) is the second most frequent complication (1.3 % Herf, 5–9 % Zavala).[18, 19] We had a moderate hemorrhage, which ended spontaneously, in two patients.

Interstitial diseases are also currently the object of lively interest of radiologists. According to radiological criteria this particular group of diseases differs with regard to the multiple diffusely disseminated lesions on the chest X-rays and imaging techniques, and within the complex of clinical symptomatology, consistent changes in lung function, bronchoalveolar lavage and cell study approximates pathoanatomic diagnosis. These diseases may, primarily, be lung diseases or they may be a "reflection" of systemic diseases. They were initially described as milliary diseases, because the lesions were the size of a grain of millet,[20, 21] later as "diffuse disseminated",[21] or "nodular and reticular".[22] They are currently known as interstitial diseases. However, as these diseases encompass occasionally histologically determined both the interstitium and alveolar area some authors consider that "chronic diffuse infiltrative disease" is more appropriate. Radiological criteria for these anatomic locations was developed by Felson and later Fraser and Pare as alveolar or acinous lesions, and interstitial lesions.[23–25] The finest interstitial pattern is "ground-glass", consisting of discretely swollen connective structure and inflammatory infiltration without bronchiectasis, not covering the outline of the blood vessels. Nodular opacities are interstitial, 1–2 mm in size, which cover the outline of the blood vessels (apart from the interstitium they can also be in the alveolars and bronchioles). The reticular pattern relates to swollen interlobular septa with exudation – early stage of fibrosis – chronic stage. The linear pattern – honey combing – typical areas 5–10 mm in diameter. The reticulonodular pattern corresponds to the size of the nodular opacities and is characteristic for granulomatosis.[24] Theve have been many classifications, particularly for sarcoidosis, since 1940, King.[26] Wurn, Reindell and Heimeyer, classified sarcoidosis in three radiological stadia, taking into account the course and prognosis of disease, which was the case in our patients.[27]

As there is in fact no correlation between different parameters with regard to disease activity (lung function tests, BAL, ACE, scintigraphy with Ga-67) the radiological stage remains the most sensitive in the prognostics of these diseases.[27]

Because of the need to systematically evaluate radiological changes caused by inhalation of silicia dusts in various parts of the world the first International Classification for Pneumoconiosis was produced in 1930 by the International Bureau for Work in Geneva and reviewed in 1955, 1958, 1968, 1971 and 1980.[28] The ILO classification with standard proposals is clearly written and does not adopt pathoanatomic hypotheses. It only describes the round and irregular opacities according to size and profusion and does not go into the morphology of lesions which can be misleading.[29, 30] McLoud et al. were the first to apply the modified ILO classification to

other diffuse diseases of the lung interstitian, added as a description of reticulonodular pattern, characteristic for granulomatosis.[31] In our patients reticular and reticulonodular patterns were dominant in the radiograms, although without ILO classification of lesion.

In our investigation the percentage of satisfactory biopsies during which an adequate sample was obtained, was very high (94 %). As such biopsy material contains at least one piece of tissue with diffuse pathological changes of the lung, this sample was considered representative. This percentage agrees with the tests performed by the techniques of other authors[14, 32–35] with approximately the same number of patients with an average (apart from individual results) of 85 % (Table 1).

The same percentage of reliable pathoanatomic (51 %) and radiological (43 %) findings (39 %) compared to adequately sufficient pathoanatomic findings (16 %) and greater percentage of insufficient pathoanatomical findings (33 %) compared to insufficient radiological findings (18 %) (Table 2).

The most frequent were definitive clinical diagnoses of interstitial lung fibroses and sarcoidosis. Both pathoanatomically and radiologically reliable findings were of the same etiology. Pathoanatomically reliable findings were most frequent in interstitial lung fibroses (18 patients) and radiologically reliable findings in sarcoidosis (15 patients) (Table 3). In no single disease were they both insufficient, which indicates their complementariness, and they are therefore sufficient judging by the clinical status, BAL, and biochemical finding, with regard to the final clinical diagnosis. With respect to immunopathogenesis, in many diffuse diseases of the lung interstitium similar conditions are combined in their immunopathological course, which is another complicating factor in their differentiation. Definitive evaluation of the evolutiveness of DILD is facilitated by bronchoalveolar lavage (BAL) and cell analysis, and in the complex of clinical symptomatology and consistent changes of lung functional findings it is possible to make an approximate pathoanatomic diagnosis, and thus TBB, in this case, is an inferior test.

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