Chapter

Introductory Chapter: Diagnosis of Interstitial Lung Disease

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1. Introduction

Interstitial lung diseases are rare diffuse lung disease characterized by a specific clinical picture and radiological (imaging) and pathohistological findings. It is considered that these diseases represent about 15% of all respiratory diseases [1].

Diffuse changes of the lung parenchyma in each type of these diseases are characterized by various morphological patterns which are reflected by a different imaging finding and a specific clinical picture [2–4]. The clinical picture at an early stage of the disease is not specific, and it is hard to suspect interstitial lung disease. Symptoms of interstitial lung disease are dry cough, short breath, fever, and fatigue. A specific high resolution - computed tomographyn (HR-CT) finding indicates an interstitial lung disease which is proven by biopsy. Transbronchial biopsy primarily excludes specific granulomatous lung diseases, primary malignancy and metastatic as well as eosinophilic pneumonia, alveolar proteinosis, and pulmonary histiocytosis. If a bioptized lung sample has nonspecific morphological pattern, it is necessary to perform an open lung biopsy or video-assisted thoracoscopic surgery (VATS). Open lung biopsy procedure requires a multidisciplinary approach that includes a chest surgeon. An agreement on taking large number of lung tissue samples characterized by change evolution increases the efficiency and accuracy of the diagnosis [5].

Integrated clinical and radiological data help the pathologist to establish an accurate diagnosis of the type of interstitial lung disease. Besides pulmonologist, radiologist, and pathologist, microbiologist and immunologist also participate in diagnostic procedure [2–4].

2. Pathohistological diagnosis of interstitial lung disease in open lung biopsy

It is necessary to take the entire surgical material for processing and microscopic analysis. Before all, it is necessary to completely instill 10% buffered formalin into the lung parenchyma with a needle for injection but in a moderate amount, in order to not provoke artifacts in the lung parenchyma. In such a manner, alveolar spaces are as if they were in the air-inspiration phase, and also damages on the lung parenchyma caused by a forceps during biopsy performed by a surgeon are avoided. After fixation that lasts 24 h, the entire material is sampled into thin sections which are fixed in the buffered formalin, alcohol, and xylol. After that, they are embedded into paraffin and then cut and stained with a classical hematoxylin-eosin staining.

The pathologist at first performs microscopic examination on a low-powered-field microscope in order to see the distribution of changes, that is, whether they are confluent or not. Then he observes localization of changes and their peribronchial or

perivascular presence or connective subpleural, interlobular, or interalveolar septa. On highermicrosopic microscopic field enlargements, the cellularity of changes is noted, as well as the type of cells that contain changes and then the presence and degree of fibrosis. By connective tissue staining, it is desirable to confirm the degree of fibrosis and with other methods to determine type of cells and presence of microorganisms. Immunohistochemical technique can detect the type of cells in the analyzed changes [5].

On the basis of the overall finding, descriptive diagnosis that correlates with the disease entity is made. Diagnosis must correlate with the clinical and imaging picture by the type of change. For this purpose, current classification of interstitial lung diseases is used [5].

The first used classification of interstitial diseases in different subtypes is according to Liebow and Carrington [6]. By consensus of the American Thoracic Society and European Respiratory Society (ATS/ERS), current classification of interstitial lung diseases is determined. This classification defines different clinical-pathological entities according to clinical, radiological, and histological criteria. By using this classification, it is possible to predict the course of the disease, treatment, and outcome. Therapy and monitoring of the disease course require consultative decisions. The medical advisory board consists of experienced pulmonologists, radiologists, and pulmonary pathologists. If the course of the disease is not satisfactory even with applied therapy, treatment may be evaluated, and in exceptional circumstances, archived tissue samples can be reexamined and diagnosis can be changed [1]. In addition to the therapy, in order to improve lung function which is tested by various functional tests, physical therapy is also desirable.

The ATS/ERS classification of these diffuse lung diseases divides them into those of known and those of unknown etiologies [1]. According to ATS/ERS classification, morphological image in the lung parenchyma should correspond to clinical-pathological diagnosis (in this part of the text, insert **Table 1** from the bottom of the text).

Diffuse diseases of known etiology, such as connective tissue diseases or diseases caused by taking some drugs, are less common. Allergic alveolitis or hypersensitivity pneumonitis is a specific entity of generally known etiology. Diseases of unknown etiology, that is, idiopathic diseases such as idiopathic lung disease, nonspecific interstitial lung disease, desquamative interstitial pneumonia, respiratory bronchiolitis, organized pneumonia, acute interstitial pneumonia, and lymphoid interstitial pneumonia, are more frequent. This group of diseases includes granulomatosis of which the most common is sarcoidosis characterized by the presence of epithelial, non-necrotizing granulomas [1].

Histological pattern	Clinicopathological diagnosis
Usual interstitial pneumonia (UIP)	Idiopathic pulmonary fibrosis (IPF)/cryptogenic fibrosing alveolitis (CFA)
Nonspecific interstitial pneumonia (NSIP)	Nonspecific pneumonia
Organizing pneumonia	Cryptogenic organizing pneumonia
Diffuse alveolar damage (DAD)	Acute interstitial pneumonia
Desquamative interstitial pneumonia (DIP)	Desquamative interstitial pneumonia
Respiratory bronchiolitis	Respiratory bronchiolitis-interstitial lung disease (RB-ILD)
Lymphocytic interstitial pneumonia (LIP)	Lymphocytic interstitial pneumonia

Table 1.
Morphological image which corresponds to a certain clinical-pathological diagnosis according to the ATS/ERS classification [1].

By using the said formulations, uniformity of the findings is achieved and therapy is specified. If good treatment results fail, it comes to a stage known as "end-stage lung disease." In such a case, lung transplantation is proposed which lately requires a special chapter in each textbook about these diseases. Selection of the transplantation type (single, bilateral, or heart-lungs) depends on the type of interstitial lung disease and other factors. The success of transplantation depends on the type of organism reaction on the presence of the transplanted lung or the type of rejection which can be subacute, acute, and chronic. Changes in rejection reactions are localized around the blood vessels of the lungs or bronchi. The intensity of rejection reaction depends on the extent of the changes spreading in the pulmonary interstitium and the type of inflammatory infiltrate. Prevention and treatment of rejection are regulated by immunosuppressive drugs. Therefore, it is necessary to control the presence of microorganisms in the transplanted lung by microbiological tests and transbronchial biopsy [7–9].

However, the future of the treatment of interstitial lung diseases depends on the molecular changes in the cells found in the lesions. miRNAs profiling in lung tissue in various interstitial lung diseases in a variety of cells that contain lung lesions: endothelium, alveolar epithelium, inflammatory cells, fibroblast and myofibroblast. This profiling can determine the type of therapy and their outcome or success.

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