ORIGINAL ARTICLES

Variability Among Pathologists in the Histological Diagnosis of Diffuse Interstitial Lung Diseases

J.M. Sánchez-Varilla,[a] S. Recio-Gallardo,[b] J.M. Benítez-Moya,[a] V. Almadana-Pacheco,[a] J. Peña de Bustillo,[a] and V. Martínez-Puentes[a]

[a]Servicio de Neumología, Hospital Universitario Virgen Macarena, Sevilla, Spain.
[b]Servicio de Radiología, Hospital Universitario Virgen Macarena, Sevilla, Spain.

OBJECTIVE: Diffuse interstitial lung diseases (DILD) form a group of diseases which affect the alveolar interstitial space and share very similar clinical, radiological, and functional features, making lung biopsy essential for establishing diagnosis, prognosis, and treatment in many cases. We aimed to see whether there was agreement in histopathological diagnosis among different groups of pathologists in their assessment of these diseases.

MATERIAL AND METHODS: Biopsies were studied from 33 patients suffering from noninfectious, nontumorous DILD. The biopsies had been assessed by 2 groups of pathologists: one specializing in this type of disease and another which was not a specialist group.

RESULTS: There was disagreement in the histology reports of 10 out of the 33 cases studied (30.3%): 9 cases in the group of 22 cases of idiopathic interstitial pneumonia (40.9%) and 1 in the group of 3 DILD with known or associated causes. No discrepancies were found, however, in the diagnosis of primary DILD or DILD associated with other, less well-defined processes.

CONCLUSIONS: We believe that idiopathic interstitial pneumonias are the DILD which pose most problems for pathologists. Therefore, the study of DILD requires specific dedication by pathologists and other professionals and specialists.

Key words: *Diffuse idiopathic interstitial pneumonia. Variability. Histology. Agreement.*

Variabilidad entre patólogos en el diagnóstico histológico de las enfermedades intersticiales difusas del pulmón

OBJETIVO: Las enfermedades pulmonares intersticiales difusas (EPID) son un conjunto de enfermedades que afecta al espacio alveolointersticial, con manifestaciones clínicas, radiológicas y funcionales muy similares, por lo que en muchos casos el estudio de la biopsia pulmonar será fundamental para el diagnóstico, pronóstico y tratamiento. Hemos querido ver si hay o no concordancia histopatológica diagnóstica, entre diferentes grupos de patólogos, en la valoración de estas enfermedades.

MATERIAL Y MÉTODOS: Se han estudiado las biopsias de 33 pacientes afectados de EPID no infecciosa ni tumoral, las cuales han sido valoradas por 2 grupos de patólogos: uno con especial interés por este tipo de enfermedades, y otro grupo no dedicado especialmente a esta enfermedad.

RESULTADOS: Al confrontar posteriormente los resultados, observamos en los informes histológicos una discordancia en el diagnóstico de 10 de los 33 casos estudiados (30,3%), 9 de ellos en el grupo de las 22 neumonías intersticiales idiopáticas (40,9%) y un caso en el grupo de las 3 EPID de causas conocidas o asociadas. Sin embargo, no encontramos ninguna discrepancia en el grupo de EPID primarias o asociadas a otros procesos no bien conocidos.

CONCLUSIONES: Creemos que las neumonías intersticiales idiopáticas son el grupo de EPID que más problemas de diagnóstico histológico pueden plantear al patólogo. Por tanto, es fundamental una especial dedicación por parte de estos profesionales y de los distintos especialistas que están relacionados con el estudio de las EPID.

Palabras clave: *Neumonía intersticial difusa idiopática. Variabilidad. Histología. Discordancia.*

Introduction

Diffuse interstitial lung diseases (DILD) form a group of entities with similar clinical, radiological, and functional features and with histological abnormalities that affect the alveoli and interstitial spaces of the lung.[1] Because of the similarity of these features, histology will, in many cases, be essential for diagnosis and thus prognosis and treatment of these diseases. Studies of observational variations among pathologists working with lung diseases refer to neoplastic diseases and few studies have been performed on the reproducibility of histological classifications in other contexts.[2]

We wanted to verify the accuracy of the histological studies in our center when biopsy samples from patients

Correspondence: Dr. J.M. Sánchez-Varilla.
Alejandro Collantes 26, P 2, 2.º B. 41005 Sevilla. España.
E-mail: sanchezva@terra.es

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with DILD are examined by different groups of pathologists. We used the currently accepted DILD classifications, ie, the consensus classification of the American Thoracic Society (ATS) and the European Respiratory Society (ERS).[3]

Material and Methods

We reviewed the records of patients diagnosed with noninfectious, nontumorous DILD who were admitted between 1997 and 2002 to the Hospital Universitario Virgen Macarena in Seville and who had undergone biopsy procedures by means of videoassisted thoracoscopy. The cases of 33 patients were studied (19 men and 14 women) between 29 and 75 years of age, with a mean age of 55.8 years. The biopsies taken from these patients (3 samples of more than 1 lobe) were studied retrospectively by 2 groups of pathologists who, from the clinical data, knew only that a noninfectious, nontumorous interstitial lung disease was present. One group consisted of pathologists who had trained with a special interest in interstitial diseases ("specialist pathologists") and the other group consisted of pathologists with no special training in this type of disease ("general pathologists"). The findings of both groups were compared.

In order to compare the histological results of the biopsies, we grouped the DILD, using the histology reports of the "specialist pathologists," into *a)* idiopathic interstitial pneumonia (IIP); *b)* primary DILD or DILD associated with other less well defined processes; and *c)* DILD with known or associated causes. Diagnoses were established collectively by majority and all members of the group studied each sample.

Results

The first DILD group (IIP) contained 22 patients, the second group (primary DILD or DILD associated with other less well defined processes) contained 8 patients and the third group (DILD with known or associated causes) contained 3 patients. In the first group, we found 11 cases of usual interstitial pneumonia (UIP), 1 case of desquamative interstitial pneumonia, 5 cases of cryptogenic organizing pneumonia, 2 cases of respiratory bronchiolitis with diffuse lung disease, 2 cases of nonspecific interstitial pneumonia, and 1 case of lymphoid pneumonia (Table 1). Of the 8 patients in the second group (primary DILD or DILD associated with other less well defined processes), there was 1 case of eosinophilic pneumonia, 3 cases of sarcoidosis, and 1 case each of pulmonary hemosiderosis, histiocytosis X, alveolar proteinosis, and lymphangioleiomyomatosis (Table 2). The third group comprised 3 cases of hypersensitivity pneumonia (Table 3). Comparison of the histology reports on the biopsies studied by the 2 groups of pathologists showed disagreement in 10 of the 33 cases (30.3%), 9 of which were in the group of the 22 IIP cases (40.9%). In 5 cases (22.8%) for which there was disagreement, the diagnosis was non-specific. In the statistical analysis of this group, agreement was 62% (95% confidence interval, 0.42-0.82). In the second group (primary DILD or DILD associated with other less well defined processes), the histology reports of both groups of pathologists coincided in 100% of cases, and in the third group (DILD with known or associated causes), there was one case for which there was considerable disagreement.

TABLE 1
Idiopathic Interstitial Pneumonia: Histological Diagnoses*

General Pathologists	Specialist Pathologists
PF	UIP
UIP	DIP
UIP	COP
IP	RB
UIP	UIP
UIP	RB
IP	NSIP
UIP	UIP
UIP	COP
PF	NSIP
UIP	UIP
UIP	UIP
UIP	UIP
UIP	UIP
UIP	UIP
UIP	UIP
PF	UIP
COP	COP
LP	LP
UIP	UIP
COP	COP
COP	COP

*PF indicates pulmonary fibrosis; UIP, usual interstitial pneumonia; DIP, desquamative interstitial pneumonia; RB, respiratory bronchiolitis with diffuse lung disease; IP, interstitial pneumonia; NSIP, nonspecific interstitial pneumonia; COP, cryptogenic organizing pneumonia; LP, lymphoid pneumonia.

TABLE 2
Primary Diffuse Interstitial Lung Disease or Diffuse Interstitial Lung Disease Associated With Other Less Well Known Processes: Histological Diagnoses

General Pathologists	Specialist Pathologists
Eosinophilic pneumonia	Eosinophilic pneumonia
Sarcoidosis	Sarcoidosis
Sarcoidosis	Sarcoidosis
Sarcoidosis	Sarcoidosis
Pulmonary hemosiderosis	Pulmonary hemosiderosis
Histiocytosis X	Histiocytosis X
Alveolar proteinosis	Alveolar proteinosis
Lymphangioleiomyomatosis	Lymphangioleiomyomatosis

TABLE 3
Diffuse Interstitial Lung Disease With Known or Associated Causes: Histological Diagnoses*

General Pathologists	Specialist Pathologists
COP	HP
HP	HP
HP	HP

*COP indicates cryptogenic organizing pneumonia; HP, hypersensitivity pneumonia.

Discussion

In 1969, Liebow and Carrington[4] proposed the histological classification of IIP diseases (usual interstitial pneumonia, desquamative interstitial pneumonia,

lymphoid pneumonia, obliterative bronchiolitis with interstitial pneumonia and diffuse alveolar damage, and giant-cell interstitial pneumonia). This classification was subsequently modified by other authors such as Katzenstein[5] and Müller and Colby.[6] Clinicians in the United States of America talked about idiopathic pulmonary fibrosis whereas in Europe they used the term cryptogenic fibrosing alveolitis, and in Japan, they referred to IIP. Later, due to the severe outcome of a subgroup of IIP, it was decided to remove this subgroup from the IIP group of diseases and give it the name of idiopathic pulmonary fibrosis.[7-9]

In our study of the 3 groups into which DILD are now classified, no problems with the histological diagnoses were observed in the second group (primary DILD or DILD associated with other less well defined processes). In the IIP group, however, we found disagreement in the diagnosis of 40.9% of cases—the group of "general pathologists" diagnosed as usual interstitial pneumonia cases for which the group of "specialist pathologists" had established a diagnosis of desquamative interstitial pneumonia, cryptogenic organizing pneumonia, or respiratory bronchiolitis with diffuse lung disease. Furthermore, the "general pathologists" diagnosed 3 cases as pulmonary fibrosis of which the "specialist pathologists" deemed 2 cases to be usual interstitial pneumonia and 1 case to be nonspecific interstitial pneumonia. The "general pathologists" also diagnosed 2 cases of interstitial pneumonia, which the "specialist pathologists" considered to be nonspecific interstitial pneumonia in one case and respiratory bronchiolitis with diffuse lung disease in the other. There was only one case of serious disagreement in the group of DILD with known or associated causes: a single biopsy sample was diagnosed as cryptogenic organizing pneumonia by the "general pathologists" and as hypersensitivity pneumonia by the "specialist pathologists." There were, however, only 3 cases in this group of DILD.

We believe that the discrepancy in the results for the IIP group is primarily due to the complexity of the nomenclature, changes to the classifications and to the diagnosis of these diseases. We also believe that the discrepancy is due to the fact that the pathologists who study the biopsies of these patients do not specialize in this type of illness. Changes to the classifications, new advances and the low incidence of these diseases (175 per 100 000 in people over 75 years of age in the cases of idiopathic pulmonary fibrosis) mean that they should be studied by specialists in this group of diseases as the lack of specialization leads to varying and inaccurate diagnoses.[10] In the literature, we also found variations in the histology reports of DILD biopsies studied by different pathologists, such as in the study by Nicholson et al,[11] where variations were found in more than 18% of histology reports, even though the pathologists had been instructed to report specific histological diagnoses and all of them had a special interest in DILD. Other studies also refer to disagreement between the histology reports on different samples of biopsies taken from patients suffering from DILD, even when they are taken from a single lobe.[12-15]

In conclusion, within DILD, the IIP group is the one that poses most problems in the histological diagnosis of lung biopsies. As with other infrequent diseases, it is essential that hospitals where DILD patients' biopsies are studied have specialists in this type of disease. Perhaps specialization in DILD together with the ATS/ERS consensus classification will help make disagreement in histology reports for these diseases a rare occurrence.

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