ORIGINAL ARTICLES

Diagnoses and Diagnostic Procedures in 500 Consecutive Patients With Clinical Suspicion of Interstitial Lung Disease

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OBJECTIVE: To determine the diagnostic yield achieved with the application of current recommendations for evaluating patients with suspected interstitial lung disease (ILD) and the procedures that must be applied to reach a definitive diagnosis.

PATIENTS AND METHODS: Over a 10-year period, 500 consecutive patients attending an ILD outpatient clinic who showed features of diffuse lung involvement were assessed with a single diagnostic protocol. Results were introduced in a dedicated database and diagnoses for idiopathic interstitial pneumonia were established according to a recent consensus classification.

RESULTS: A definitive diagnosis was reached in 427 (85%) patients: in 125 without invasive procedures and in 302 with invasive procedures. In 73 (14.6%) cases a definitive diagnosis was not reached, and patients were placed in the group of unclassifiable interstitial pneumonia. Idiopathic interstitial pneumonia was the predominant group with 193 (39%) patients. The main specific entities included sarcoidosis with 93 (19%) patients, usual interstitial pneumonia with 84 (17%) patients, and hypersensitivity pneumonitis with 75 (15%) patients. Thirty (6%) patients were diagnosed with an illness other than ILD (false ILD). In 332 patients, we performed a total of 433 invasive procedures: transbronchial biopsy in 252 (direct diagnostic yield, 38%, or if used also to exclude other specific diagnosis, 50%), bronchoalveolar lavage in 260 (yield, 5%), and open lung biopsy in 141 (yield, 93%). Hence, following the current diagnostic approach, a definitive diagnosis was established for 85% of patients, for 25% solely on clinical grounds and imaging criteria and for 60% on the basis of invasive procedures. Diagnosis by open lung biopsy was still required for 141 (28%) patients.

CONCLUSIONS: The diagnostic yield was high when the recommended study protocol was followed. A quarter of the diagnoses were reached with clinical criteria alone, but another quarter could only be made after open lung biopsy.

Key words: *Interstitial lung diseases. Idiopathic interstitial pneumonias. Unclassified interstitial pneumonia. Nonspecific interstitial pneumonia. Sarcoidosis. Hypersensitivity pneumonitis. Diagnostic yield. Open lung biopsy. Bronchoalveolar lavage.*

Diagnósticos y procedimientos diagnósticos en 500 pacientes consecutivos con sospecha clínica de enfermedad pulmonar intersticial

OBJETIVO: Determinar las tasas de diagnósticos alcanzados con el seguimiento de las directrices actuales y los procedimientos que deben utilizarse para establecer el diagnóstico definitivo mediante la aplicación del nuevo protocolo en la evaluación de los pacientes con sospecha de enfermedad pulmonar intersticial (EPI).

PACIENTES Y MÉTODOS: Durante un período de 10 años se evaluó, mediante un único protocolo diagnóstico, a 500 pacientes consecutivos atendidos en una consulta ambulatoria de EPI que presentaban las características de esta enfermedad. Los resultados se introdujeron en una base de datos específica y los diagnósticos de neumonía intersticial idiopática (NII) se establecieron siguiendo los criterios del reciente Consenso.

RESULTADOS: Se estableció un diagnóstico definitivo en 427 pacientes (85%), en 125 de ellos sin procedimientos invasivos y en 302 con procedimientos invasivos. En 73 casos (14,6%) no se alcanzó un diagnóstico definitivo y en estos pacientes se estableció el diagnóstico de neumonía intersticial no clasificable. La NII constituyó el grupo predominante, con 193 casos (39%). Las entidades específicas principales fueron: sarcoidosis (n = 93; 19%), neumonía intersticial usual (n = 84; 17%) y neumonitis por hipersensibilidad (n = 75; 15%). En 30 pacientes (6%) se estableció el diagnóstico de una enfermedad distinta a la EPI (falsa neumonía inters-

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ticial). Se realizó un total de 433 procedimientos invasivos en 332 pacientes (66%): biopsia transbronquial en 252 (rendimiento diagnóstico directo: 38% y rendimiento diagnóstico cuando se utilizó para excluir otros diagnósticos específicos: 50%); lavado broncoalveolar en 260 (rendimiento diagnóstico: 5%), y biopsia pulmonar quirúrgica en 141 (rendimiento diagnóstico: 93%). Por lo tanto, siguiendo el protocolo diagnóstico actual, se estableció un diagnóstico definitivo en el 85% de los pacientes; de ellos, en el 25% el diagnóstico se estableció únicamente en función de los datos clínicos y de los criterios de imagen, mientras que en el 60% se realizó con procedimientos invasivos. En 141 pacientes (28%) fue necesaria la biopsia pulmonar quirúrgica para establecer el diagnóstico.

CONCLUSIONES: La tasa de diagnósticos es elevada cuando se utiliza el protocolo de estudio recomendado. La cuarta parte de los diagnósticos se efectúa mediante criterios clínicos como procedimiento único; sin embargo, otra cuarta parte de los diagnósticos requiere la realización de una biopsia pulmonar quirúrgica.

Palabras clave: *Neumonitis intersticial. Procedimientos diagnósticos. Rendimiento diagnóstico. Enfermedad pulmonar intersticial (EPI). Neumonías intersticiales idiopáticas. Neumonía intersticial usual. Neumonía intersticial no clasificable. Neumonía intersticial no específica. Biopsia pulmonar quirúrgica. Sarcoidosis. Neumonitis por hipersensibilidad. Lavado broncoalveolar.*

Introduction

The term interstitial lung disease (ILD) encompasses a heterogeneous group of more than 150 clinical entities with diffuse lung involvement.[1] There are few epidemiological studies on ILD and they differ both in the methods used to establish the diagnosis and in the frequencies of the various clinical entities studied.[2-8] The diagnostic guidelines on idiopathic pulmonary fibrosis (IPF) put forth by the American Thoracic Society (ATS)[9] and the European Respiratory Society (ERS)[10] recommend adherence to standardized diagnostic protocols and the use of more invasive diagnostic techniques, such as transbronchial biopsy (TBB) and open lung biopsy (OLB), when required. The fact that there may be no effective treatment for some conditions once the diagnostic study has been completed has meant that clinicians often fail to follow all the tests required to arrive at a precise diagnosis.[11] This attitude has made it hard to determine the real incidence, and prevalence, of the different entities comprising the group of ILDs and has led to a low percentage of proven diagnoses in clinical practice.[2-8]

Besides the 511 cases recorded in the Spanish Registry of ILD in 2000 and 2001,[8] only a single large series of 94 patients has been described in Spain.[12] That study, by our group, was published in 1982 and concerned the diagnostic yield of OLB. In the present investigation, carried out 25 years after that first study, we have adhered to the current diagnostic recommendations for ILD[13] and recent consensus classifications for idiopathic interstitial pneumonia[9,10] in order to determine the diagnostic rates achieved when adopting these recommendations and the procedures that must be applied to reach a definitive diagnosis. Some entities included in our study are not true interstitial diseases. However, patients who sometimes show a diffuse interstitial pattern on a chest x-ray or computed tomography (CT) scan are referred to the ILD outpatient clinic. Hence, in routine practice, these processes are included in the differential diagnosis of ILD.

Material and Methods

Patients

From January 1995 through March 2004 we studied 500 consecutive patients in our ILD outpatient clinic according to a specific, recommended diagnostic protocol.[13] Classification took into account the new consensus recommendations for IPF and idiopathic interstitial pneumonia published by the ATS and the ERS.[9,10] All patients who showed features of diffuse lung involvement on a chest x-ray or CT scan were included in the study.

Diagnostic Protocol, Criteria, and Classification

The following information was recorded in a database designed for this purpose: age, sex, medical history, prior medication, complete occupational history, prior contact with antigens or potentially noxious substances, and contact with animals, particularly birds and poultry. The signs and symptoms found in the initial physical examination were also included. The following analyses were requested for all patients: hemogram; total and differential leukocyte counts; levels of fibrinogen, angiotensin converting enzyme, antinuclear antibodies, calcium, and lactic dehydrogenase and its 5 isoenzymes in blood; and calcium levels in 24-hour urine samples.

A battery of delayed cutaneous hypersensitivity tests was performed.[14] When hypersensitivity pneumonitis was suspected, specific immunoglobulin G determinations (precipitation techniques or enzyme-linked immunoassay) were requested, as well as specific skin testing and bronchial challenge testing with the suspected antigen.[15] Lung function tests were evaluated using the Mediterranean population reference values of Roca et al.[16] All patients underwent chest x-ray and chest high-resolution CT scanning. When indicated, fiberoptic bronchoscopy with bronchoalveolar lavage (BAL) was performed for cytology to determine T- and B-lymphocyte percentages and T-lymphocyte subpopulations, and, in cases of suspected Langerhans cell histiocytosis, specific CD1 receptors were also quantified. Culture for common microorganisms and *Mycobacterium tuberculosis* bacilli was performed in all cases. When indicated, 4 TBBs were routinely carried out. In certain patients, extrapulmonary biopsy was performed to investigate involvement of organs other than the lungs. If a definite diagnosis had not been established after these tests and the patient was younger than 75 years old, OLB was undertaken if there were no contraindications and the patient accepted the procedure after being informed of its benefits and risks.

Statistical Analysis

Information on demographic variables, sex and age, and diagnostic tests collected for study. The distribution of patients by type of ILD and the distribution of ILD types by sex were determined and expressed as numbers and percentages. The

Fisher exact test and the *t* test were used to compare categorical and continuous variables, respectively. Significance was established at a 2-sided *P* value of .05 and the statistical analysis was performed with SAS software, version 8.2 (SAS Institute, Cary, North Carolina, USA). Data were expressed as mean (SD).

Results

Diagnosis, Age, and Sex

From January 1995 through March 2004 we studied 500 consecutive patients, 276 (55%) women and 224 (45%) men, with a mean age of 56.2 (16.3) years (range, 12-91 years). Table 1 shows that idiopathic interstitial pneumonia was the largest diagnostic group. Sarcoidosis was the most frequently diagnosed entity, followed by usual interstitial pneumonia (UIP)/IPF, and hypersensitivity pneumonitis. The mean age was lower in the patients with lymphangioleiomyomatosis, Langerhans cell histiocytosis, and sarcoidosis. In contrast, the mean age was higher in the groups of patients with unclassifiable interstitial pneumonia and UIP/IPF. More men than women were diagnosed with UIP/IPF, nonspecific interstitial pneumonia, respiratory bronchiolitis/desquamative interstitial pneumonia ILD (RB/DIP-ILD), and Langerhans cell histiocytosis. Conversely, women predominated in the sarcoidosis and hypersensitivity pneumonitis groups.

The prevalences of diagnoses are compared to those reported in other published series in Table 2.

Procedures and Diagnostic Yield

In total, 433 invasive procedures (BAL, TBB, OLB, and extrapulmonary biopsies) were performed in 332 (66%) of the 500 patients, and in 168 (34%) patients these procedures were not performed. TBB was undertaken in 252 (50%) and BAL in 260 (52%). OLB was performed in 141 (28%). Extrapulmonary biopsies were taken in 33 (7%) patients, 30 of them from the sarcoidosis group. More than a single invasive procedure was required in 142 (28%) patients. The highest diagnostic yield was obtained with OLB, with a definite diagnosis achieved in 131 out of 141 cases (93%). The next highest yield was obtained with specific bronchial challenge testing, which led to 30 diagnoses (for 60% of the 50 patients in whom it was performed). TBB provided direct diagnostic findings in 95 (38%) of the 252 procedures performed; additionally, after including 32 (6% of the 500) other patients with clinical and radiologic findings of IPF in which TBB served diagnosis by ruling out granulomas and other characteristic lesions, the total diagnostic yield of TBB was 50%. BAL had the lowest diagnostic yield, with definite diagnoses in only 12 (5%) out of 260 patients.

Diagnoses Based on Clinical Criteria With the Addition of Various Diagnostic Tests

Table 3 shows the numbers of patients for whom a definitive diagnosis was established with noninvasive or invasive diagnostic procedures. The 73 patients (15%) for

TABLE 1
Diagnostic Classifications of 500 Patients With Suspected Interstitial Lung Diseases[a]

Interstitial Lung Diseases	Patients	Females	Males	P, Sex[b]	Mean (SD), Age	*P*, Age[c]
Idiopathic interstitial pneumonias, total	193 (38.6%)	88 (45.6%)	105 (54.4%)	.0001	63.4 (12.6)	.0001
UIP/IPF	84 (16.8%)	34 (40%)	50 (60%)	.003	62.8 (11.2)	.0001
Nonspecific interstitial pneumonia	19 (3.8%)	6 (32%)	13 (68%)	.05	59.4 (11.6)	.3
Cryptogenic organizing pneumonia	9 (1.8%)	7 (78%)	2 (22%)	.1	53.6 (13.6)	.6
RB/DIP ILD	7 (1.4%)	2 (29%)	5 (71%)	.2	59.1 (12.8)	.6
Lymphocytic interstitial pneumonia	1 (0.2%)	0	1 (100%)	.4		
Unclassifiable interstitial pneumonia	73 (14.6%)	39 (53%)	34 (46%)	.8	66.7 (13.6)	.0001
Sarcoidosis	93 (18.6%)	64 (69%)	29 (31%)	.003	47.6 (15.5)	.0001
Hypersensitivity pneumonitis	75 (15%)	47 (63%)	28 (37%)	.1	48.2 (14.6)	.0001
Miscellaneous ILD	54 (10.8%)	29 (54.7%)	25 (45.3%)	.5	64.0 (15.4)	.0009
Collagen vascular disease associated-ILD	17 (3.4%)	12 (71%)	5 (29%)	.2	60.5 (14.5)	.2
Chronic eosinophilic pneumonia	13 (2.6%)	10 (77%)	3 (23%)	.1	48.9 (20.8)	.1
Langerhans cell histiocytosis	13 (2.6%)	3 (23%)	10 (77%)	.02	36.5 (11.6)	.0001
Bronchiolitis, different types	7 (1.4%)	3 (43%)	4 (57%)	.7	49.6 (14.1)	.2
Lymphangioleiomyomatosis	5 (1.0%)	5 (100%)	0	.06	34.4 (8.0)	.002
False ILD	30 (6%)	15 (50%)	15 (50%)	.5	63.8 (12.5)	.03
Total	500 (100%)	276 (55.2%)	224 (44.8%)		56.2 (16.3)	

Abbreviations: ILD, interstitial lung disease; RB/DIP, respiratory bronchiolitis/desquamative interstitial pneumonia; UIP/IPF, usual interstitial pneumonia/idiopathic pulmonary fibrosis.
[a]Data are expressed as number of patients (%) or mean (SD).
[b]Fisher exact test.
[c]Student *t* test.

TABLE 2
ILD Diagnoses in Published Case Series[a]

	Hospital Vall d'Hebron Barcelona, Spain		Spain[8]		Italy[7]		Flandes, Belgium[5]		Germany[6]		United States[2]		Hospital Vall d'Hebron Barcelona, Spain[b,12]	
Years included	1995-2004		2000-2001		1998-1999		1992-1996		1995		1988-1990		1973-1979	
Year of publication	2008		2004		2001		2001		1996		1994		1982	
Patients, total	500		511		1382		362		234		257		94	
	No.	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**
Idiopathic interstitial pneumonias, total	193	38.6	285	55.8	589	42.6	105	29	104	44	141	54.9	35	37.2
UIP/idiopathic pulmonary fibrosis	84	16.8	197	38.6	520	37.6	72	19.8	76	32.4	58	23	31	32.9
Nonspecific interstitial pneumonia	19	3.8	9	1.7	0		0		0		0		0	
Cryptogenic organizing pneumonia	9	1.8	53	10.4	69	5.0	0		16	6.8	0		0	
RB/DIP ILD	7	1.4	0		0		0		0		0		2	
Lymphocytic interstitial pneumonia	1	0.2	0		0		0		0		0		1	
Unclassifiable interstitial pneumonia	73	14.6	26	5.1	0		33	9.1	12	5.1	83	32	1	1.1
Sarcoidosis	93	18.6	76	14.9	403	29.2	112	30.9	83	35.4	30	12	5	5.3
Hypersensitivity pneumonitis	75	15.0	34	6.6	51	3.7	47	12.9	31	13.2	0	1	1.1	
Miscellaneous ILD	54	10.8	17	3.3	23	1.7	31	8.6	6	2.5	38	14.8	8	8.5
Collagen vascular disease-associated ILD	17	3.4	51	9.9	18	1.3	27	7.4	5	2.1	33	134		
Langerhans cells histiocytosis	13	2.6	15	2.9	91	6.6	13	3.5	0	2	0.8	5	5.3	
Chronic eosinophilic pneumonia	13	2.6	9	1.7	26	1.9	0		0		3	1.2	0	
Bronchiolitis, different types	7	1.4	0		11	0.8	0				0		1	1.1
Lymphangioleiomyomatosis	5	1.0	0		35	2.5	0		0		0			
False ILD	30	6	0		0		0		0		0		17	18

Abbreviations: ILD, interstitial lung disease; RB/DIP ILD, respiratory bronchiolitis/desquamative interstitial pneumonia; UIP, usual interstitial pneumonia.
[a]Note that some entities were not known at the time of publication of other series (nonspecific interstitial pneumonia), and other entities were not included in those series since they are not properly ILD (bronchiolitis, false ILD).
[b]Open Lung Biopsy Series.

TABLE 3
Diagnoses and Diagnostic Procedures in 500 Patients With Suspected ILD[a]

Clinical diagnosis without invasive procedures	
Clinical findings + x-ray images + analyses + lung function tests	95 (19.0%)
Clinical features + x-ray images + RFT + SBCT (+)	30 (6.0%)
Total diagnoses	125 (25.0%)
Diagnosis by invasive procedures	
Clinical features + x-ray images + lung function tests + OLB (+)	131 (26.2%)
Clinical features + x-ray images + lung function tests + TBB (+)	127 (18.8%)[b]
Clinical features + x-ray images + lung function tests + extra-pulmonary biopsy (+)	33 (6.6%)
Clinical features + x-ray images + lung function tests + BAL (+)	12 (2.4%)
Total diagnoses	302 (60.4%)
Total definitive diagnoses (invasive + noninvasive procedures)	427 (85.4%)
No diagnosis reached	73 (14.6%)

Abbreviations: BAL, bronchoalveolar lavage; OLB, open lung biopsy; RFT, functional respiratory tests; SBCT, specific bronchial challenge tests; TBB, transbronchial biopsy.
[a]Data are number of patients and percentage of the series.
[b]Thirty-two patients were diagnosed with UIP/IPF by characteristic clinical and radiologic manifestations plus TBB to rule out malignant and granulomatous diseases.

whom a definitive diagnosis (with or without histology) could not be reached were ultimately included in the unclassifiable interstitial pneumonia group. In 119 (24%) patients more than 1 invasive procedure was needed. In the 125 patients (25%) who were diagnosed without the use of BAL, TBB, extrapulmonary biopsies, or OLB, the diagnoses were hypersensitivity pneumonitis in 45 patients (60% of the patients with this diagnosis); chronic eosinophilic pneumonia in 10 (77% of the 13 patients with this diagnosis); and false ILD in 30 (all of the patients with this diagnosis).

Other Diagnostic Entities

Thirty-five of the 73 (15%) patients who did not have a definitive diagnosis and were placed in the group with unclassifiable interstitial pneumonia had probable IPF-like clinical and radiologic characteristics, but invasive procedures could not be performed, or, when an invasive procedure was carried out, tissue samples were not diagnostic. Another group of 30 with nonspecific radiologic characteristics of fibrosis could not be diagnosed precisely despite analysis of lung tissue obtained by 6 OLB and 19 TBB, and 24 BAL procedures. Lastly, 8 patients had radiologic features of nonspecific fibrosis and did not undergo any invasive techniques because of advanced age or refusal to provide consent.

Seventeen patients were placed in the collagen-ILD group, including 10 with ILD and rheumatoid arthritis, 2 with ILD and ankylosing spondylitis, 2 with ILD and

dermatomyositis, 2 with ILD and lupus, and 1 with ILD and CREST syndrome (calcinosis, Raynaud phenomenon, esophageal dysfunction, sclerodactyly, and telangiectasia).

Fifty-four patients were included in the miscellaneous ILD group: 8 drug-related (6 amiodarone, 1 methotrexate, and 1 interferon-α), 8 silicosis, 7 diffuse fibrotic process and emphysema, 5 after acute respiratory distress syndrome, 4 post-radiotherapy, 3 asbestosis, 2 neuroendocrine cell hyperplasia, 2 carcinomatous lymphangitis, 2 pulmonary hemosiderosis, 2 alveolar proteinosis, 2 diffuse lymphoma of the lung, 1 pulmonary capillary hemangiomatosis, 1 alveolar microlithiasis, 1 diffuse pulmonary lymphangiomatosis, 1 metastasizing pulmonary leiomyomatosis, and 1 vasculitis (polyarteritis nodosa).

Lastly, the false-ILD group included 13 patients with bronchiectasis (1 bronchopulmonary aspergillosis), 9 patients with bilateral post-tuberculosis fibrosis, 4 patients in whom interstitial infiltrate disappeared during the early follow-up, and 4 with chronic obstructive pulmonary disease (emphysema plus suspicious interstitial x-ray image).

Discussion

Recommendations for the diagnosis and treatment of ILD,[13] specifically for idiopathic interstitial pneumonia and pulmonary fibrosis[9,10] have led to the standardization of diagnostic criteria and nomenclature used for the clinical entities that comprise this group of diseases. With time, this rigorous policy will allow more reliable comparison of the incidence and prevalence of these diseases between reported patient series and will facilitate further analyses to determine the yields of available diagnostic techniques.

The criteria for diagnosis in the present study first followed those of King, Cherniack, and Schwarz[13] and, in recent years, took into account the ATS/ERS consensus guidelines.[9,10] On this basis, 433 invasive procedures (BAL, TBB, OLB and extrapulmonary biopsies) were performed in 332 (66%) patients. The technique with the highest diagnostic yield was OLB (93%) and the one with the lowest was BAL (5%). The direct diagnostic yield of TBB was nearly 38%, a percentage that is influenced by the biopsies performed in patients with idiopathic interstitial pneumonia, in whom TBB is not considered sufficient to establish a diagnosis. However, if we include the 32 patients diagnosed with UIP in whom TBB ruled out the presence of other pulmonary processes such as malignant disease and granulomatosis, the yield of this procedure was 50%. Furthermore, the diagnostic yield of TBB was higher in specific entities, such as sarcoidosis, in which 70% of the procedures performed gave a positive result.

OLB was used in 141 (28%) patients, a percentage very similar to that reported in the series of Carrington and Gaensler[17] 25 years ago. The continued need for this technique may be explained by the fact that there are still no specific markers for differentiating pulmonary fibrotic diseases in TBB or BAL specimens; hence a precise diagnosis must be obtained by OLB. Also, the increased life expectancy in the general population and the new, promising protocols utilizing antifibrotic agents have encouraged the use of OLB in older patients (up to 75 years old in our hospital). In fact, although high-resolution CT findings can be highly indicative of UIP/IPF, the specificity and diagnostic accuracy of this technique continues to be around 80%.[18,19] Thus, in our opinion, until the specificity of diagnostic imaging increases or new specific markers are developed, diagnosis should be made through invasive methods when idiopathic interstitial pneumonia is suspected in research contexts.

The OLB technique used in our center consists of a minithoracotomy directed toward the middle lobe (right lung) or lingula (left lung), depending on findings by high-resolution CT. We use this method instead of thoracoscopy because the morbidity and mortality rates associated with OLB in our hospital have been very low for several years.[12] The operation lasts less than 20 minutes, selective intubation to collapse the lung before biopsy is not usually required, and high levels of oxygenation are therefore maintained during the entire procedure. These are decisive factors, particularly in patients who are highly compromised physiologically. Moreover, the mean size of the lung tissue obtained is approximately $3 \times 3 \times 1$ cm, an amount of tissue that allowed a precise diagnosis to be reached in 93% of the biopsies performed. In fact, some biopsies showed areas of both UIP and NSIP involvement (4 patients), as has already been reported in relation to bilobar video-assisted thoracoscopy lung biopsies[20] and in explanted lungs.[21] Hence, the structural changes that might be seen in 2 different lobes can also be found in a single sample of lung when the size of the biopsy is large enough to allow in-depth study of these possible alterations.[22,23] In fact, no differences regarding diagnostic yield have been found between OLB and video-assisted thoracoscopic procedures in the only randomized controlled trial published.[22]

In the comparison of the results from our series of patients with those from previously published reports (Table 2), we should mention that this study and the findings from a Spanish registry published recently by Xaubet and colleagues[8] are the first to use the latest idiopathic interstitial pneumonia classification,[9] in which nonspecific interstitial pneumonia and other entities, such as unclassifiable interstitial pneumonia have been incorporated. In the present study, we found that the most common type of ILD in Catalonia, Spain, is idiopathic interstitial pneumonia, in keeping with the majority of published series. Among the specific diseases, sarcoidosis, UIP/IPF and hypersensitivity pneumonitis were the most common. There were fewer cases of sarcoidosis than in the rest of Europe, a finding also reported in the aforementioned Spanish study.[8] This might indicate that there is a higher index of suspicion for sarcoidosis in other countries, or that there is a lower incidence of the disease in Catalonia, as was suggested some years ago.[12,24]

The main difference between the present series and others that did not take the consensus guidelines into consideration is the high number of patients—73 (15%)

in the group of unclassifiable interstitial pneumonia—a discrepancy that underscores the reality of strict application of the diagnostic criteria to reach a definitive diagnosis. In fact, the unclassifiable group was mainly comprised of patients clinically considered to have UIP, but finally classified as probable UIP/UIP-like disease since they did not undergo invasive tests, usually because of advanced age. We believe that until the publication of the consensus,[9] other authors probably included these patients in the UIP group as the CT scan images were characteristic of that entity. In the unclassifiable group are also included those patients with nonspecific radiologic characteristics of fibrosis who underwent biopsy procedures (6 OLB, 19 TBB), but had lung tissue features characteristic of various processes, or nonspecific findings. Despite individual case assessment by clinicians, radiologists and pathologists, a definitive diagnosis could not be strictly established in these cases; hence, we preferred to treat them as doubtful, that is, unclassified.

Our series included patients with what we have termed false ILD. These patients were correctly referred to our specialized unit because diffuse interstitial infiltrates were observed in imaging studies; however, true interstitial disease was ruled out after applying the diagnostic protocol. The group was mainly comprised of patients with radiologic features of lines and dots who were ultimately found to have bronchiectasis or long-standing pneumonic infiltrates that in some cases disappeared; all of these entities are included in the real-life differential diagnosis of an interstitial radiologic pattern.

In summary, this study describes our experience with the use of current consensus guidelines[9,10,13] applied in routine practice in a hospital unit for diffuse lung disease. It demonstrates the advantages of following a diagnostic protocol, which achieved reliable classification of 85% of the patients, and illustrates the difficulties encountered, for many reasons, in trying to reach a precise diagnosis in the remaining 15%. This study establishes the spectrum and prevalence of clinical entities comprising the group of diffuse ILD in Spain, and it analyzes the procedures needed to reach these diagnoses and the diagnostic yield of each. Diagnosis was reached on clinical grounds alone in 25% of the patients but the persistent need to perform OLB in 28% of the patients studied is underscored.

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