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Original Article

Interstitial Lung Disease Associated with Autoimmune Rheumatic Diseases: An Experience from Türkiye

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Abstract

Objective: Interstitial lung disease (ILD) is one of the most challenging involvement of autoimmune rheumatic diseases (ARDs) and could lead to significant morbidity and mortality. In this article, a collaborative work of tertiary rheumatology and pulmonology centers describing demographic, serological, and radiological findings of patients with ARD associated with ILD (ARD-ILD) is presented.

Methods: A descriptive, retrospective study, and data related to demographics, clinical, laboratory, radiologic, or histopathological findings of ILD were collected from the study participants' charts.

Results: Around 212 patients with ARD-ILD were evaluated. Of the patients, 172 (81.1%) were female and 40 (18.9%) were male. The distribution of the rheumatic diseases was as follows: systemic sclerosis in 114 (53.8%), rheumatoid arthritis in 47 (22.2%), Sjögren's syndrome in 14 (6.6%), inflammatory myopathy in 16 (7.5%) patients, interstitial pneumonia with autoimmune features (IPAF) in 9 (4%) patients, undifferentiated connective tissue disease in 8 (3.8%), and systemic lupus erythematosus in 4 (1.9%). According to the radiological patterns, 71.7% of the patients had nonspecific interstitial pneumonia (NSIP), 13.7% had definite usual interstitial pneumonia (UIP), 8.5% had probable UIP, 3.8% had lymphocytic interstitial pneumonia, 1.9% had organizing pneumonia, and 0.5% had an atypical pattern.

Conclusion: This study showed that the most common rheumatic disease causing ILD is still systemic sclerosis, and NSIP is more prominent as a radiological pattern. IPAF, a disease that has entered the literature in recent years, is also an important type of ILD. Given the multisystemic involvement of ARDs, collaboration among different disciplines is undoubtedly crucial in the diagnosis and management of these diseases.

Keywords: Autoimmune rheumatic disease, interstitial lung disease, interstitial pneumonia with autoimmune features, nonspecific interstitial pneumonia

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Introduction

Interstitial lung disease (ILD) is one of the most challenging involvement of autoimmune rheumatic diseases (ARDs) and could lead to significant morbidity and mortality. ARD associated with ILD (ARD-ILD) is defined in various ARDs, namely systemic sclerosis (SSc), rheumatoid arthritis (RA), idiopathic inflammatory myopathies (IIMs), Sjögren's syndrome (SjS), undifferentiated connective tissue disease (UCTD), and systemic lupus erythematosus (SLE), with different frequencies, severity, and distinctive types of involvement patterns.[1,2] Among the aforementioned ARDs, systemic sclerosis is the most common rheumatic disease leading to ILD and followed by IIM, UCTD, SjS, and RA.[3] Although RA does not lead to ILD as frequently as systemic sclerosis (SSc) or IIMs like anti-synthetase syndrome, its higher overall prevalence results in RA-ILD being the second most common cause of ARD-ILD.[2,3] Another recently defined entity is interstitial pneumonia with autoimmune features (IPAF), which includes a group of diseases that do not meet the criteria of a specific rheumatic disease but are considered to be of rheumatic origin with certain clinical, radiological, or serological features.[4]

Autoimmune rheumatic disease associated with interstitial lung disease is diagnosed by means of computer tomography (CT) and histopathologically, when necessary. The classification of ILD includes usual interstitial pneumonia (UIP) (definite or probable UIP), nonspecific interstitial pneumonia (NSIP), organizing pneumonia (OP), acute interstitial pneumonia, and lymphoid interstitial pneumonia (LIP).[5,6] The examples of NSIP and UIP patterns of the authors' own patients are presented in Figures 1 and 2.

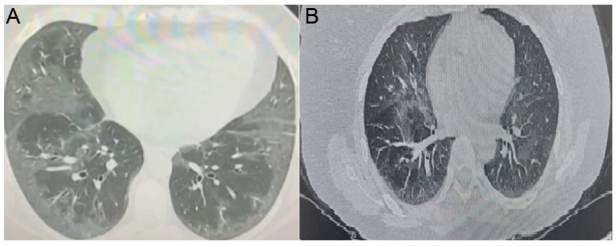

Figure 1. Nonspecific interstitial pneumonia pattern in a patient with systemic sclerosis (left), nonspecific interstitial pneumonia pattern in a patient with interstitial pneumonia with autoimmune features (right).

Type of radiological or histopathological involvement is important in tailoring the treatment, together with the symptom severity and the functional capacity of the patient as well as monitoring the progression rate. The progression rate, irrespective of the underlying disease or serological positivity in cases such as IPAF, is routinely evaluated during follow-up visits by monitoring dynamic changes. This involves thoracic CT imaging as well as functional assessments, including the 6-minute walk test, functional vital capacity, lung diffusion capacity testing (DLCO), DLCO/VA ratio, and transthoracic echocardiography, particularly focusing on pulmonary artery pressure measurements.

The lack of robust data and scarcity of studies in this specific subgroup of patients poses a challange in treatment and follow-up. Therefore, cooperation between pulmonologists and rheumatologists is essential. In this article, the data of ARD-ILD patients who had been followed conjointly by rheumatologists and pulmonologists were presented.

Main Points

- Systemic sclerosis and rheumatoid arthritis are the most common autoimmune rheumatic diseases associated with interstitial lung disease in the Turkish cohort, with the majority being female patients.
- Nonspecific interstitial pneumonia is the predominant radiological pattern, especially in systemic sclerosis patients, while rheumatoid arthritis patients exhibit a more balanced distribution between nonspecific interstitial pneumonia and usual interstitial pneumonia.
- Mycophenolate mofetil and rituximab are the most frequently used immunosuppressive agents, particularly mycophenolate mofetil for nonspecific interstitial pneumonia patterns and rheumatoid arthritis–related interstitial lung disease cases.
- Effective management of autoimmune rheumatic disease associated with interstitial lung diseases requires close collaboration between the rheumatology and pulmonology disciplines, emphasizing the need for integrated care for optimal patient outcomes.
- Interstitial pneumonia with autoimmune features, though recently defined, shows promising responses to immunosuppressive therapy, necessitating increased clinical awareness for early diagnosis and management.

Material and Methods

Patients

A total of 212 patients who applied to the rheumatology outpatient clinic and/or chest diseases outpatient clinic between 2016 and 2023 were evaluated retrospectively. Patients with ARDs including SSc, RA, SjS, IIM, IPAF, UCTD, and SLE were included. Patients were evaluated by both a rheumatologist and a pulmonologist during the diagnostic work-up, with physical examination, laboratory tests, high-resolution computed tomography, and histopathology, if necessary.

The study was approved by the Başakşehir Çam ve Sakura Şehir Hastanesi Klinik Araştırmalar Etik Komitesi with the number 2024-17 on 17.01.2024. Throughout the study, the Declaration of Helsinki was adhered to. In this retrospective study, additional informed consent was not needed.

Data Collection

The data were obtained from patients' electronic medical records. Patients recruited in this cohort had all data from blood tests, all autoimmune series including disease-specific antibody series, and chest high resolution computed tomography scans. All patients' data were used anonymously.

Statistical Analysis

The normality of data was analyzed with the Kolmogorov–Smirnov distribution test. Data were presented as mean ± SD or median with range for continuous variables, according to distribution of data, and as percentages for qualitative variables. Considering the non-homogeneous distribution of continuous variables and heterogeneity among sample sizes of subgroups, a non-parametric test was used in assessment. The difference between 2 groups was analyzed by independent t-test or Mann–Whitney *U* test, and for multiple comparisons of independent samples, one-way ANOVA or Kruskal–Wallis test with Bonferroni's correction applied according to distribution. For the comparison of categorical variables between groups, the X^2 test was used. A *P* value of <.05 was considered significant. Statistical analyses were performed using SPSS Statistics for Windows, version 29.0 (IBM SPSS Corp.; Armonk, NY, USA).

Results

A total of 212 patients with ARD-ILD were evaluated. Of the patients, 172 (81.1%) were female and 40 (18.9%) were male. The mean age of the patients was 60.12 ± 12.5 years, and the median duration of follow-up was 28.0 (1-106) months (Table 1).

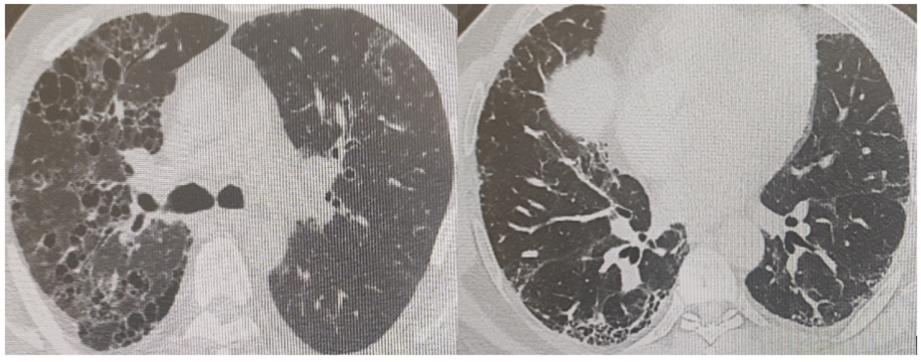

Figure 2. Usual interstitial pneumonia pattern in a patient with rheumatoid arthritis (left), usual interstitial pneumonia pattern in a patient with interstitial pneumonia with autoimmune features (right).

Table 1. Patient Charecteristics

Rheumatic diseases	RA	SSc	SjS	UCTD	IIM	SLE	IPAF	Total	*P*
n, %	47 (22.2)	114 (53.8)	14 (6.6)	8 (3.8)	16 (7.5)	4 (1.9)	9 (4.2)	212	
Female/Male (n)	32/15	100/14	13/1	6/2	10/6	4/0	7/2	172/40	.024
Female/Male (%)	68.1/31.9	87.7/12.3	92.9/7.1	75.0/25.0	62.5/37.5	100/0	77.8/22.2	81.1/18.9	.024
Age (mean ± SD)	67.0 ± 11.6	56.8 ± 12.0	63.3 ± 10.5	57.3 ± 14.5	56.8 ± 11.1	58.5 ± 11.1	70.6 ± 10.1	60.12 ± 12.5	.001
Follow-up duration, month (mean ± SD)	61.9 ± 24.0	33.9 ± 28.5	50.4 ± 41.9	12.8 ± 17.7	22.9 ± 20.2	60.3 ± 36.4	4.9 ± 3.3	38.8 ± 31.2	.001
Follow-up duration, month (med-range)	68 (2-96)	23 (1-106)	58 (4-106)	4 (3-50)	19 (3-86)	68.5 (10-94)	4 (1-10)	28.0 (1-106)	.001
CRP, mg/dL (med-range)	9.5 (1-675)	13.0 (1-283)	7.0 (2-55)	14.5 (1-96)	17.5 (2-62)	6.5 (3-36)	14.0 (3-58)	12.0 (1-675)	.969
Smoking									
Smoker	2 (5.4)	8 (7.5)	1 (8.3)	2 (25.0)	3 (20.0)	0	1 (12.5)	17 (9.0)	.087
Non-smoker	26 (70.3)	91 (85.8)	9 (75.0)	4 (50.0)	8 (53.3)	2 (66.7)	6 (75.0)	146 (77.2)	
Ex-smoker	9 (24.3)	7 (6.6)	2 (16.7)	2 (25.0)	4 (26.7)	1 (33.3)	1 (12.5)	26 (13.8)	
Radiologic pattern									.017
Definite UIP	15 (31.9)	11 (9.6)	2 (14.3)	0	1 (6.3)	0	0	29 (13.7)	
Probable UIP	6 (12.8)	10 (8.8)	0	0	0	1 (25.0)	1 (11.1)	18 (8.5)	
NSIP	23 (48.9)	88 (77.2)	12 (85.7)	7 (85.7)	12 (75.0)	2 (50.0)	8 (88.9)	152 (71.7)	
LIP	3 (6.4)	2 (1.8)	0	0	1 (6.3)	1 (25.0)	0	8 (3.8)	
OP	0	2 (1.8)	0	0	2 (12.5)	0	0	4 (1.9)	
Atypical	0	1 (0.9)	0	0	0	0	0	1 (0.5)	
ANA	14 (29.8%)	100 (87.7%)	7 (50.0%)	6 (75.0%)	9 (56.3%)	3 (75.0%)	6 (66.7%)	145 (68.4%)	.001
RF									
Negative (0-20)	7 (14.9%)	38 (33.3%)	5 (35.7%)	2 (25.0%)	4 (25.0%)	1 (25.0%)	2 (22.2%)	59 (27.8%)	.071
Mild positive (20-42)	5 (10.6%)	10 (8.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (25.0%)	2 (22.2%)	18 (8.5%)	
Strong positive (>42)	23 (48.9%)	30 (26.3%)	8 (57.1%)	6 (75.0%)	4 (25.0%)	0 (0.0%)	4 (44.4%)	75 (35.4%)	
CCP	22 (46.8%)	6 (5.3%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	29 (13.7%)	.001
Scl-70	6 (12.8%)	47 (41.2%)	3 (21.4%)	2 (25.0%)	4 (25.0%)	0 (0.0%)	0 (0.0%)	62 (29.2%)	.004
Ro	7 (14.9%)	14 (12.3%)	3 (21.4%)	4 (50.0%)	5 (31.3%)	2 (50.0%)	2 (22.2%)	37 (17.5%)	.080
La	2 (4.3%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (1.4%)	.629
P-ANCA	0 (0.0%)	2 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.9%)	.880
C-ANCA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	N/A
Ds-DNA	2 (4.3%)	1 (0.9%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	1 (25.0%)	0 (0.0%)	5 (2.4%)	.894
Sm	1 (2.1%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (11.1%)	3 (1.4%)	.388
RNP	0 (0.0%)	3 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (11.1%)	4 (1.9%)	.625
Jo	2 (4.3%)	0 (0.0%)	3 (21.4%)	1 (12.5%)	3 (18.8%)	0 (0.0%)	0 (0.0%)	9 (4.2%)	.412
Centromer	0 (0.0%)	7 (6.1%)	0 (0.0%)	1 (12.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	8 (3.8%)	.652
Pm-Scl	0 (0.0%)	2 (1.8%)	2 (14.3%)	0 (0.0%)	1 (6.3%)	0 (0.0%)	1 (11.1%)	6 (2.8%)	.098
SAE-1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (6.3%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	N/A
SRP	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (11.1%)	1 (0.5%)	N/A

ANA, anti-nuclear antibody; ANCA, anti-neutrophil cytoplasmic antibody; CCP, cyclic citrullinated peptide; CRP, C-reactive protein; IIM, idiopathic inflammatory myositis; IPAF, interstitial pneumonia with autoimmune features; LIP, lenfositic interstitial pneumonia; NSIP, non spesific interstitial pneumonia; OP, organizing pneumonia; RA, rheumatoid arthritis; RF, rheumatoid factor; RNP, ribonucleoprotein; SAE, small ubiquitin-like modifier activating enzyme; SjS, sjögren syndrome; SLE, systemic lupus erythematosus; SRP, signal recognition particle; SSc, systemic sclerosis; UCTD, undifferantiated connective tissuse disease; UIP, usual interstitial pneumonia.

*Patients with anti-CCP positivity classified under SSc exhibited typical skin manifestations without inflammatory arthritis, whereas those with Scl-70 positivity in the RA group fulfilled the clinical criteria for RA with inflammatory polyarthritis but did not meet the diagnostic criteria for SSc.

The distribution of the rheumatic diseases was as follows: SSc in 114 (53.8%), RA in 47 (22.2%), SjS in 14 (6.6%), IIM in 16 (7.5%), IPAF in 9 (4%), UCTD in 8 (3.8%), and SLE in 4 (1.9%) patients (Figure 3). According to the ILD classification, 71.7% of the patients had NSIP, 13.7% definite UIP, 8.5% probable UIP, 3.8% LIP, 1.9% OP, and 0.5% atypical pattern. The most common ILD pattern in SSc patients was NSIP (77.2%). In RA

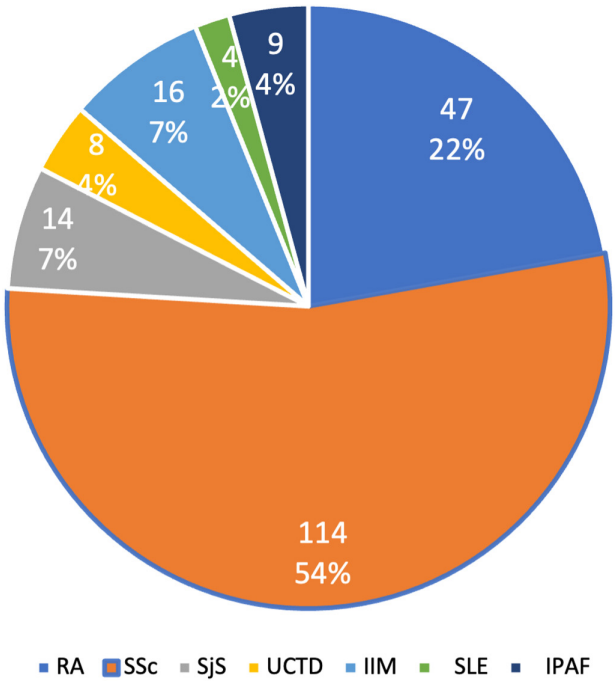

Figure 3. The distribution of patients according to disease subgroups (IIM, idiopathic inflammatory myositis; IPAF, interstitial pneumonia with autoimmune features; RA, rheumatoid arthritis; SjS, Sjögren syndrome; SLE, systemic lupus erythematosus; SSc, systemic sclerosis; UCTD, undifferantiated connective tissuse disease).

patients, the frequency of NSIP was 48.9% and UIP was 44.5%. Eight of 9 patients with IPAF had the NSIP pattern (88.9%) (Table 1). Rituximab (RTX) (29%) was the most commonly used drug in patients with RA-related interstitial lung disease (RA-ILD), while the use of mycophenolate mofetil (MMF) (50%) was more prominent in other ARDs, namely SSc-related interstitial lung disease (SSc-ILD).

Thirty-four percent of patients with RA did not require specific treatment for ILD and remained stable in terms of clinical, radiological, and functional lung capacity during their follow-up, while this rate was 8% in patients with SSc. Considering the treatments used according to the radiological pattern, MMF (58%) was most frequently used in patients with NSIP, while azathioprine (AZA) was used at a rate of 37% in patients with UIP (both UIP and probable UIP). It was observed that the pulmonary findings of 3 patients with OP regressed with the steroid treatment and did not require an extra specific agent for OP. The treatment regimens received by the patients according to the diseases and radiological patterns are shown in Tables 2 and 3, respectively. The agents given in the tables were options used to target both the inflammatory condition and lung involvement. Specific drugs targeting only inflammatory disease, like non-steroid anti-inflammatory drugs and intra-articular treatments, etc., were not included.

Table 2. The Distribution of Treatment Agents According to Diseases

Drug/Disease, n/N (%)	AZA	CYC	MMF	RTX	TOF	PIRF	NINT	No specific drug	Total (N)
RA	4 (11)	3 (9)	3 (9)	10 (29)		1 (2)		12 (34)	35
SSc	16 (16)	20 (20)	50 (50)	12 (12)	1 (1)		1 (1)	8 (8)	100
SjS		2 (20)	7 (70)	3 (30)				1 (10)	10
UCTD			6 (85)	2 (28)				1 (14)	7
IIM	2 (13)			2 (13)	10 (67)			1 (7)	15
SLE	3 (75)		1 (25)						4
IPAF			6 (66)					3 (34)	9

AZA, azathioprine; CYC, cyclophosphamide; IIM, idiopathic inflammatory myositis; IPAF, interstitial pneumonia with autoimmune features; MMF, mycophenolate mophetil; NINT, nintedanib; PIRF, pirfenidone; RA, rheumatoid arthritis; RTX, rituximab; SjS, sjögren syndrome; SLE, systemic lupus erythematosus; SSc, systemic sclerosis; TOF, tofacitinib; UCTD, undifferantiated connective tissuse disease.

Patients followed with the diagnosis of IPAF in the cohort had the most common radiological pattern of NSIP (88.9%), and the most common autoantibody detected in this patient group was anti-nuclear antibody (66.6%). It was noteworthy that the mean age of the patients with IPAF was 70.6 ± 10.1. The clinical and radiological features of patients with IPAF are shown in Table 4.

Discussion

In this article, the data of ARD-ILD patients who had been followed conjointly by rheumatologists and pulmonologists were presented. Systemic sclerosis (53.8%) and RA (22.2%) patients constituted the vast majority of the ARD-ILD patients. In SSc patients, the most common ILD pattern was NSIP (77%), with a significant proportion of anti-Scl-70 positivity (44.8%). Mycophenolate mofetil (50%) and cyclophosphamide (CYC) (20%) were the most commonly used agents in SSc-ILD. Similarly to SSc, the NSIP pattern (48%) was the most common ILD type in RA, which is followed by the UIP pattern (44%), with an rheumatoid factor (RF) positivity of 65% and anti-CCP positivity of 59% in the whole RA cohort. Thirty-four percent of patients with RA-ILD did not require additional treatment for pulmonary involvement and continued their follow-up without any lung-directed therapy. RTX (29%) and AZA (11%) were the most commonly used drugs in patients with RA-ILD in this cohort. Current clinical practice and guidelines also prioritize MMF for patients with RA and pulmonary involvement. However, a significant proportion of the cohort consists of patients who were previously initiated on AZA, which accounts for their notable representation in the study. Although current clinical practice and guidelines also prioritize MMF for patients with RA and pulmonary involvement, a significant proportion of the cohort consists of patients who were previously initiated on AZA, which accounts for their notable representation in this study.

Regarding the given serological findings and diagnosis, there are issues to highlight. Firstly, there was no access to U1RNP antibody testing, which would have been necessary to diagnose mixed connective tissue disorders. While some patients exhibited overlapping serological findings, they either lacked clinical manifestations consistent with their expected disease phenotype or presented

Table 3. The Distribution of Treatment Agents According to Radiologic Pattern

Drug/Patern, n/N (%)	AZA	CYC	MMF	RTX	TOF	PIRF	NINT	No Specific Drug	Total (N)
UIP	10(43)	6(23)		1(4)		1(4)		4(17)	23
PUIP	4(26)	5(33)		3(20)			1(7)	3(20)	15
NSIP	12(9)	13(10)	77(58)	20(15)	1(0,7)			18(14)	132
LIP			4(66)	1(16)				2(33)	6
OP								3(100)	3

AZA, azathioprine; CYC, cyclophosphamide; LIP, lenfositic interstitial pneumonia; MMF, mycophenolate mophetil; NINT, nintedanib; NSIP, non-spesific interstitial pneumonia; OP, organizing pneumonia; PIRF, pirfenidone; PUIP, probable usual interstitial pneumonia; RTX, rituximab; TOF, tofacitinib; UIP, usual interstitial pneumonia.

with low-titer antibodies that were not diagnostically significant.

None of the p-ANCA positive patients were solely positive for p-ANCA; all had at least 1 additional serological marker that contributed to their final diagnosis. The clinical diagnoses based on the EULAR/ACR classification criteria for each disease entity were established, ensuring a standardized approach to diagnosis.

Table 4. The Characteristics of the Patients with IPAF

Radiologic pattern, n, n/N (%)	
Probable UIP	1 (11.1)
NSIP	8 (88.9)
Gender	
Female/Male	7 (77.8) / 2(22.2)
Age (mean ± SD)	70.6 ± 10.1
Symptom duration, month (mean ± SD)	4.9 ± 3.3
Smoking, n, n/N (%)	
Smoker	1 (12.5)
Non-smoker	6 (75.0)
Ex-smoker	1 (12.5)
RF, n, n/N (%)	
Negative (0-20)	2 (25.0)
Mild positive (20-42)	2 (25.0)
Strong positive (>42)	4 (50.0)
Anti-CCP, n, n/N (%)	
Negative	9 (100)
Positive	0
ANA positivity, n, n/N (%)	
Negative	3 (33.3)
Positive	6 (66.6)
ANA titer, n, n/N (%)	
Unknown	1 (11.1)
Negative	3 (33.3)
1/320	1 (11.1)
1/1000	3 (33.3)
1/3200	1 (11.1)

ANA, anti-nuclear antibody;cCCP, cyclic citrullinated peptide; IPAF, interstitial pneumonia with autoimmune features; NSIP, non-spesific interstitial pneumonia; RF, rheumatoid factor; UIP, usual interstitial pneumonia.

One notable issue raised was the absence of overlap syndromes in the diagnostic groups. While the potential risk of underdiagnosing overlap syndromes was acknowledged, classifying any patients as having an overlap syndrome to maintain diagnostic clarity and avoid ambiguity was intentionally refrained from doing so.

Finally, although specific autoantibodies such as anti-CCP and Scl-70 are highly suggestive of RA and SSc, respectively, their presence alone does not establish a definitive diagnosis. Clinical features remain the cornerstone of disease classification. In this cohort, patients with anti-CCP positivity classified under SSc exhibited typical skin manifestations without inflammatory arthritis, whereas those with Scl-70 positivity in the RA group fulfilled the clinical criteria for RA with inflammatory polyarthritis but did not meet the diagnostic criteria for SSc.

Regarding IPAF, it was observed that the mean age was significantly higher, unlike other rheumatological disease subgroups ($P < .001$). The NSIP pattern was dominant in radiologic assessment, and MMF was most frequently used treatment. In this study, the most common primary connective tissue disease of patients with ILD was SSc.

In the retrospective cohort study published by Chan et al[7] in 2019, 359 patients with ILD-ARD were evaluated, and the most common diseases in this cohort were SSc (57%) and RA (14%). Patients with SSc and RA in the cohort showed similar characteristics to these cohorts in terms of age, gender, and radiological pattern distribution.

While lung parenchymal pathologies in SSc are detected in 80%-90% of HRCT (high resolution computed tomography) scan screenings, only 40% of patients develop clinically significant and symptomatic lung disease. Nevertheless, the presence of ILD in SSc patients remains the main cause of mortality.[8,9] It is known from previous studies that the NSIP pattern is the most frequently seen pattern in HRCT of SSc-ILD and that anti-Scl-70 antibody positivity is associated with poor prognosis.[10,11] The efficacy of these 2 drugs in patients with SSc-ILD has been demonstrated in previous studies.[12] Again, consistent with the data, the most commonly used treatments in patients with SSc-ILD were CYC (35.1%) and MMF (25%) in an American cohort of 77 patients.[13]

The prevalence of ILD in patients with RA is highly variable in the literature, ranging from 7.7% to 67%.[14] This may be due to the frequently milder progress of pulmonary involvement in RA and its lesser effect on mortality compared to SSc. Overall, both might lead to the absence of standard lung screening approaches that have developed over time in SSc but not yet been fully established in RA. Also, among all rheumatic disease-associated ILDs of this cohort, the group in which the UIP pattern was most common was RA. This distribution was consistent with previous literature data.[15-17] Matson et al[17] evaluated 212 patients with RA-ILD and found that 43.4% of the patients were treated with AZA, 36.3% with MMF, and 20.3% with RTX. Again, in a multicenter study published by Kelly et al[18] in 2021, the most commonly used drugs were presented as AZA (22%), MMF (17%), and RTX (15%) in 290 patients with RA-ILD. Another important issue regarding RA-ILD is that not every patient may require treatment. As emphasized in previous studies, in the case of partial parenchymal involvement that does not affect the functional capacity of the patient or in patients with involvement patterns of fibrosis such as fibrotic NSIP or UIP patterns, patients can be followed without immunosuppressive therapy for the lung.[19] In this regard, another remarkable data in this cohort was that while the group of patients with IPAF in this cohort showed similar characteristics to the previous

studies investigating IPAF in terms of radiological pattern and drugs used, the mean age was higher than the other cohorts.[20-22]

Our study highlights the role of antibody profiles in ARD-ILD, as these markers provide insight into disease mechanisms and clinical outcomes. For instance, anti-Jo-1 antibodies, which are frequently associated with IIM, are linked to severe ILD patterns and carry prognostic significance. Similarly, the presence of Scl-70 antibodies in SSc-ILD suggests a higher likelihood of rapid disease progression and more extensive pulmonary fibrosis. These profiles not only guide diagnosis but also inform treatment strategies, as certain antibodies correlate with therapeutic response or the need for more aggressive management. Understanding these relationships is critical for tailoring individualized treatment plans and improving long-term outcomes in ARD-ILD.

Among ARD, the most common cause of ILD is SSc, and the most common radiological pattern is NSIP. Interstitial pneumonia with autoimmune features is a relatively newly defined entity and constitutes an important disease group that needs increased awareness considering its good response to immunosuppressive therapy. Patients might first present to chest diseases clinics with respiratory symptoms even before being diagnosed with any rheumatic diseases. The awareness and experience of the clinicians dealing with this patient group are important for early diagnosis and improvement of treatment approaches. While not every patient with a rheumatological disease and ILD findings requires treatment with immunosuppressives, lung findings may progress rapidly and be fatal in some disease subgroups. Therefore, patients should be followed by a team consisting of rheumatology, chest diseases, and radiology.

Data Availability Statement: The data that support the findings of this study are available upon request from the corresponding author.

Ethics Committee Approval: This study was approved by the Ethics Committee of University of Health Sciences Başakşehir Çam and Sakura City Hospital Ethical Committee (Approval no.: 17; Date: 17.01.2024).

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