

# PLEUROPARENCHYMAL FIBROELASTOSIS IN SYSTEMIC AUTOIMMUNE RHEUMATIC DISEASES: A CASE SERIES AND SYSTEMATIC REVIEW OF THE LITERATURE

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## BACKGROUND

Pleuroparenchymal fibroelastosis (PPFE) is a rare form of interstitial pneumonia characterised by fibrosis of the visceral pleura and subpleural pulmonary parenchyma, predominantly in the upper lobes. It can be idiopathic or secondary to multiple processes, including Systemic Autoimmune Rheumatic Diseases (SARDs). PPFE presents with a highly variable prognosis, sometimes evolving into an extremely severe condition. To date, no specific treatment has been established for this entity.

## OBJECTIVES

To investigate the association of PPFE with SARDs and to assess the clinical characteristics and prognosis in these cases.

## METHODS

We retrospectively reviewed all patients diagnosed with PPFE associated with SARDs at a Pulmonary Interstitial Functional Unit from 2013 (when this entity was included in the ATS/ERS classification of idiopathic interstitial pneumonias) to 2023. A systematic review of the literature (PubMed from inception to 31 December 2023) was also conducted to determine the relevance, prognosis, and the most appropriate treatment strategy for this complication.

## RESULTS

We identified 5 cases of PPFE-SARDs. Their main characteristics are summarised in *Table 1*.

The literature review revealed an additional 235 cases, totalling **240 patients** for the present analysis. The most common PPFE-associated disease (*Table 2*) was **Systemic Sclerosis** (54.5%; being most frequent in diffuse cutaneous forms), followed by Rheumatoid Arthritis (18.3%). Approximately 10% of published cases had autoimmune features potentially stemming from an underlying systemic autoimmune condition, but did not meet current rheumatological criteria for a defined connective tissue disease.

A majority of the patients (71.9%) were women, with an average age of 60.6±8.5 years. In most cases, the PPFE diagnosis was made simultaneously or after the SARDs diagnosis.

Diagnosis was based on findings in High-Resolution Computed Tomography (HRCT); histopathological confirmation was obtained in 49 cases through biopsy or autopsy.

**Table 2:** Frequency of Systemic Autoimmune Rheumatic Diseases associated PPFE.

Rheumatic diagnosis	N= 240
Systemic sclerosis	131 (54.5%)
Rheumatoid arthritis	44 (18.3%)
Primary Sjögren's Syndrome	13 (5.4%)
ANCA associated vasculitis	11 (4.6%)
Systemic lupus erythematosus	2 (0.8%)
Giant cell arteritis	2 (0.8%)
Inflammatory idiopathic myopathies	8 (3.3%)
Overlap syndrome	5 (2%)
IgG4 related disease	1 (0.4%)
Undifferentiated connective tissue disease	24 (10%)

Dyspnoea was the most frequently reported symptom (in over three quarters of cases), followed by cough and respiratory failure. All cases exhibited pulmonary functional involvement characterised by a restrictive pattern with a decline in %pDLCO. During follow-up, 40.6% of patients (72/177) worsened, with a mortality rate of 34.9% (59/169). Complications recorded included pneumothorax/pneumomediastinum in 13 and pulmonary arterial hypertension in 2. Use of antifibrotic therapy was documented in only 5 cases, including 3 of ours, with promising results. In our 3 patients, this treatment achieved functional stabilisation in all cases (Slope pre-antifibrotic: -4.7% / Slope post-antifibrotic: +6.6%; p=0.279).

**Table 1:** Main characteristics of the SARD-PPFE cases identified in our centre.

	Case 1	Case 2	Case 3	Case 4	Case 5
Age, years	45	43	67	66	55
Sex	Female	Female	Male	Male	Female
Smoking history	No	No	Yes	Yes	No
BMI, kg/m2	16	24	22	24	22
SARD	SLE	SS	ASS	AAV	SSc
Year of diagnosis, SARD	2017	2022	2022	2022	2000
PPFE	2017	2016	2022	2018	2021
PPFE diagnosis					
HRCT	Yes	Yes	Yes	Yes	Yes
Pulmonary biopsy	Yes	No	Yes	Yes	No
Immunology					
RF	Negative	Negative	Negative	Negative	NA
ACPA	Negative	Negative	Negative	Negative	NA
ANA	1/160	Negative	Negative	Negative	NA
Specific antibodies	Anti-dsDNA	Ro52	PL7	ANCA MPO	NA
PFT, first/last					
pFVC, %	58/64	111/130	65/62	91/82	113/116
pDLCO, %	63/65	83/73	73/42	66/46	61/64
PFT response	Stable	Stable	Worsening	Worsening	Stable
6MWT, first/last					
Distance, metres	480/583	NA/536	368/363	465/516	532/437
Treatment					
Immunosuppressive	No	No	MPA + RTX	MPA + RTX	RTX
Antifibrotic	Nintedanib	No	Nintedanib, Pirfenidone	Nintedanib	No
Oxygen therapy	No	No	No	No	No
Lung trasplant	No	No	Waitlist	Rejected	No
Exitus	No	No	No	No	No
Total follow-up, years	6,3	1.75	1,25	7,6	6,6

## CONCLUSIONS

PPFE may be present in rheumatic autoimmune diseases, especially systemic sclerosis. Rheumatologists should be aware of this new radiological pattern that implies a poor prognosis (mortality 34.9%). Based on the limited experience available, antifibrotic therapy could be a therapeutic option.