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ANTI-PL-7 ANTISYNTHETASE SYNDROME WITH ONSET OF DIFFUSE INTERSTITIAL LUNG DISEASE AND MYOPATHY: A CASE REPORT

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ABSTRACT – ***Introduction:*** Antisynthetase syndrome (ASyS) is a rare autoimmune disorder belonging to the spectrum of idiopathic inflammatory myopathies, with an estimated incidence of 0.56 cases per 100,000 person-years and a prevalence of 9.21 per 100,000 inhabitants. It is characterized by the presence of autoantibodies directed against aminoacyl-tRNA synthetases. Among them, the anti-PL-7 antibody is uncommon and is associated with a high frequency of severe interstitial lung disease (ILD) and an unfavorable prognosis.

Case Presentation: We report the case of a 41-year-old man with no significant past medical history who presented with proximal muscle weakness and elevated muscle enzymes, findings consistent with inflammatory myopathy. He was initially treated with corticosteroids and cyclophosphamide, followed by maintenance therapy with azathioprine. Several months later, during a subsequent hospitalization, he developed progressive dyspnea and was diagnosed with antisynthetase syndrome (ASyS) with anti-PL-7 positivity, confirmed through an extended myopathy antibody panel, associated with interstitial lung disease (ILD), pulmonary hypertension, and signs of myopathy. Immunosuppressive therapy was adjusted, but with poor clinical response, leading to progression of ILD and worsening pulmonary hypertension. A new therapeutic adjustment with cyclophosphamide was initiated, achieving clinical stability and hospital discharge.

Conclusions: This case highlights the importance of early clinical suspicion and an aggressive therapeutic approach in antisynthetase syndrome (ASyS), particularly in the presence of the anti-PL-7 antibody, a marker of poor prognosis and strong association with interstitial lung disease (ILD). Timely identification of this variant allows for individualized immunosuppressive management and may improve patients' clinical outcomes. This report underscores the need to include anti-PL-7 serology in the evaluation of patients with ILD of undetermined cause.

KEYWORDS: Anti-PL-7 antibody, Antisynthetase syndrome, Case report, Inflammatory myopathies, Interstitial lung disease, Pulmonary hypertension.

INTRODUCTION

Antisynthetase syndrome (ASyS) is a systemic autoimmune disease included within the group of idiopathic inflammatory myopathies (IIM), characterized by the presence of autoantibodies directed against aminoacyl-tRNA synthetase enzymes, which catalyze the binding of amino acids to their corresponding transfer ribonucleic acid (tRNA) during the aminoacylation process. In 2011, Solomon et al. proposed diagnostic criteria that integrate the positivity for an antisynthetase autoantibody with specific clinical manifestations, thereby establishing a standardized framework for the diagnosis of the syndrome. These criteria are currently the most widely used and recognized in clinical practice for identifying ASyS[1].

The estimated incidence of ASyS is 0.56 cases per 100,000 person-years, with a peak onset between 50 and 59 years of age. Its prevalence is 9.21 cases per 100,000 inhabitants[2], classifying it as a rare disease. The distribution of autoantibodies in ASyS shows predominance of anti-Jo-1 in 46% of cases, followed by anti-PL-12 (32%), anti-PL-7 (16%), anti-OJ (12%), and anti-EJ (6%), with anti-PL-7 antibodies being particularly uncommon within the syndrome spectrum[3]. In South America, data remains limited. In Latin America, and specifically in Colombia, the information is scarce; however, a prevalence of 5.8% among IIMs has been reported, with a marked association between anti-PL-7 positivity and pulmonary involvement[4].

Clinically, the syndrome is characterized by a variable combination of non-erosive arthritis, myositis, Raynaud's phenomenon, unexplained fever, interstitial lung disease (ILD), and mechanic's hands[5]. Certain clinical phenotypes are associated with specific autoantibodies; in particular, anti-PL-7 has been linked to more severe pulmonary involvement with rapid interstitial progression[6].

The present case is noteworthy for its representative clinical course of ASyS with anti-PL-7 positivity, the development of ILD, and secondary pulmonary hypertension. Although pulmonary involvement is common in ASyS, the coexistence of anti-PL-7 antibodies and pulmonary hypertension is infrequently reported and carries a guarded prognosis. Therefore, this case provides an opportunity to illustrate the clinical behavior and therapeutic approach of this uncommon phenotype.

CASE PRESENTATION

We present the case of a 41-year-old Caucasian male from the city of Pasto, Colombia, a cabinetmaker by occupation, with no significant past medical history, who reported a six-year history of progressive proximal muscle weakness and dyspnea on exertion. He was initially hospitalized at a tertiary care center, where markedly elevated creatine phosphokinase (CPK) levels (19,000 U/L) were detected. He received initial treatment with corticosteroids, followed by six monthly cycles of cyclophosphamide, and later transitioned to oral azathioprine for maintenance therapy.

In January 2025, he required rehospitalization due to lower-limb edema, dyspnea on minimal exertion, and persistent proximal muscle weakness. On physical examination, muscle strength was 4/5 on the Daniels scale. During this admission, Raynaud's phenomenon was documented, along with ulcerative, desquamative, and hyperkeratotic lesions on the fingers and toes (Figure 1). Immunoserological testing revealed positive ANA titers (1:160 IU/mL) with speckled and ribosomal patterns, normal total CPK levels, and a negative remaining profile (Table 1). High-resolution computed tomography (HRCT) of the chest demonstrated interstitial involvement (Table 2, Figure 2). Due to suspected myopathic compromise, electromyography and an extended myopathy antibody panel were requested for outpatient evaluation. Right heart catheterization (Table 2) revealed pre-capillary pulmonary hypertension. Pulmonology recommended home oxygen therapy *via* nasal cannula at 2 L/min, along with vasodilator and antifibrotic therapy for outpatient management.

In June, during a rheumatology follow-up visit, the patient presented results from the extended myopathy antibody panel by immunoblot, showing positivity for anti-PL-7, and an electromyography consistent with muscle fiber disease (Table 2), confirming the diagnosis of antisynthetase syndrome (ASyS). During follow-up, the patient reported increasing oxygen requirements, and on physical examination, lower-limb edema was observed, prompting referral to the emergency department.

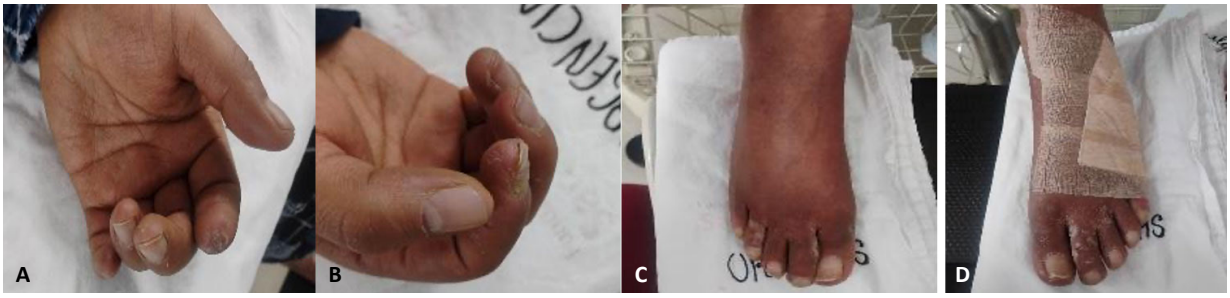

Figure 1. Mechanic's hands with hyperkeratotic lesions on the fingers and toes (June 2025). *A-B*, Figures A and B show "mechanic's hands." *C-D*, Figures C and D display hyperkeratotic and crusted lesions on the feet.

Table 1. Laboratory test results.

Test	Reference value	Result
ANAs: Antinuclear antibodies	Less or equal to 1/40-1/80	1/160 patrón moteado, patrón ribosomal 1/160
Anti-Ro antibody	Less than 20 RU/ml	5.07 RU/ml
Rheumatoid factor	Less than 9 RU/ml	8.6 RU/ml
Anti-Jo-1 antibody	Less than 20 RU/ml	13.2 RU/ml
Anti-RNP antibody	Less than 20 RU/ml	3.04 RU/ml
Anti-MPO antibody	Less than 20 RU/ml	2.6 RU/ml
Anti-PR3 antibody	Less than 20 RU/ml	2.7 RU/ml
Blood urea nitrogen (BUN)	6 a 20 mg/dL	32 mg/dl
C3: Complement component 3	88-165 mg/dl	87 mg/dl
C4: Complement component 4	14-44 mg/dl	12.7 mg/dl
Total CPK: Total creatine phosphokinase	55-170 U/L	45 U/L
Myopathy panel by immunoblot	N/A	Positive Anti PL-7
NT-proBNP: N-terminal pro–B-type natriuretic peptide	0-250 pg/ml	4840 pg/ml
Erythrocyte sedimentation rate (ESR)	Less than 20 mm/h	2 mm/h
C-reactive protein (CRP)	Less than 5 mg/dl	74.7 mg/dl
Creatinine	0.7 - 1.3 mg/dL	1.0 mg/dl

MPO: myeloperoxidase; **PR3:** proteinase 3; **RNP:** ribonucleoprotein.

Table 2. Extension studies.

Electromyography	Abnormal study showing electrophysiological evidence consistent with intrinsic muscle fiber injury, suggestive of myopathy.
Transthoracic echocardiogram	LVEF: 79%. Severe dilation of the right ventricle with severe systolic dysfunction. Marked biatrial enlargement. Moderate-to-severe tricuspid regurgitation with a high probability of pulmonary hypertension. Interventricular septum showing paradoxical motion and leftward displacement during diastole. Moderate homogeneous pericardial effusion encircling the anterior (18 mm) and posterior (12 mm) regions. Grade I diastolic dysfunction, consistent with impaired relaxation pattern
Right heart catheterization	Right atrial pressure: 18 mmHg, V wave 24 mmHg, SaO_2: 66%. Pulmonary artery pressure: 105/53/70 mmHg, SaO_2: 68%. Pulmonary capillary wedge pressure (PCWP): 2 mmHg. Right ventricular pressure: 101/18 mmHg. Mixed venous O_2 saturation: 68%. Cardiac output: 5.1 L/min. Pulmonary vascular resistance (PVR): 13 Wood units. Systemic vascular resistance (SVR): 21 Wood units.
High-resolution chest CT (June)	Usual interstitial pneumonia (UIP) pattern. Global cardiomegaly. Imaging findings consistent with pulmonary hypertension. Right pleural effusion. Passive basal atelectasis in the right lung. Degenerative bone changes.

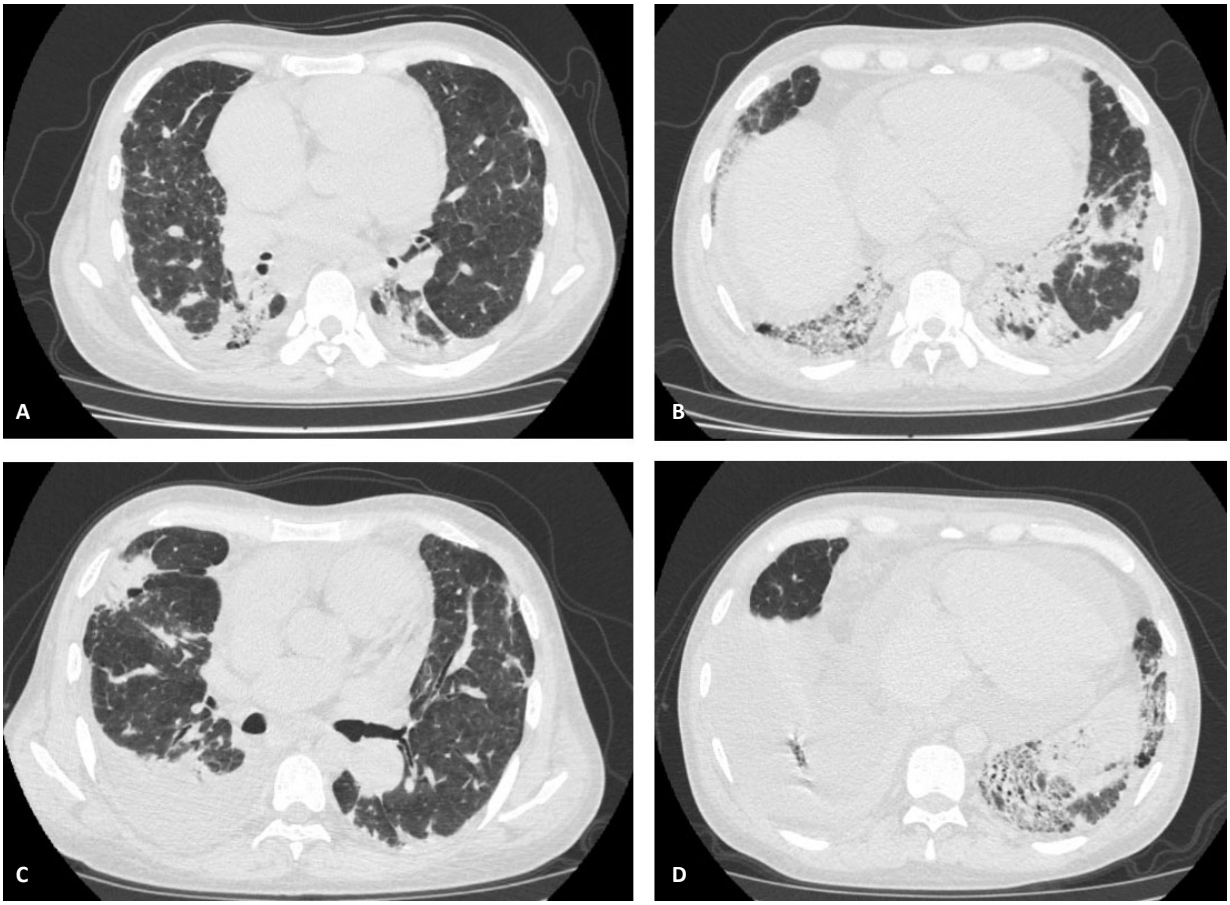

Figure 2. High-resolution chest CT (HRCT). *A-B*, January 2025 showing interstitial lung disease (ILD). *C-D*, June 2025 demonstrating interstitial progression and signs of pulmonary hypertension.

During this hospitalization, a repeat HRCT scan of the chest revealed pulmonary congestion and progression of interstitial disease (Figure 2). Physical examination showed 4/5 proximal muscle strength in the upper limbs (Daniels scale) and bibasilar crackles on pulmonary auscultation. The patient received depletive therapy with loop diuretics and, due to pulmonary involvement, was treated with three days of methylprednisolone pulses followed by monthly 1,000 mg cyclophosphamide infusions. A muscle biopsy was not performed given the confirmatory clinical and serological findings. The patient was discharged in stable clinical condition on oral corticosteroid maintenance therapy, home oxygen *via* nasal cannula at 2 L/min, without edema, and with minimal residual proximal muscle weakness in the upper limbs.

DISCUSSION

The present case represents a classic phenotype of antisynthetase syndrome (ASyS) associated with anti-PL-7 antibodies, characterized by interstitial lung disease (ILD), cutaneous-muscular manifestations without arthritis, and the development of pulmonary hypertension (PH). These findings are consistent with those described in the literature and highlight the progression of ILD despite appropriate immunosuppressive therapy.

In international series, the anti-PL-7 subtype has been consistently associated with greater pulmonary involvement and poorer clinical outcomes. In a Chinese cohort, rapidly progressive ILD had an overall prevalence of 8.9%, but this figure rose to 19.4% among patients with anti-PL-7 antibodies, who also showed a trend toward lower survival rates[6]. Similarly, precapillary pulmonary hypertension, though uncommon (7.9%), occurs more frequently in patients positive for anti-PL-7 or anti-PL-12, characterized by mean pulmonary arterial pressures exceeding 35 mmHg, coexistence with severe ILD, and an overall worse clinical prognosis[7].

In the European series, most cases of precapillary pulmonary hypertension (PH) were associated with interstitial lung disease (ILD); however, disproportionately elevated pulmonary arterial pressures were documented relative to the degree of interstitial involvement—a phenomenon also observed in our patient. This pattern suggests primary pulmonary vascular involvement beyond parenchymal damage, possibly linked to endothelial dysfunction and immune-vascular mechanisms specific to ASyS. This finding is further supported by the coexistence of Raynaud's phenomenon and capillaroscopic abnormalities, features that indicate an intrinsic vasculopathic component[7]. Taken together, the findings in our case reflect an anti-PL-7 phenotype with ILD and PH of poor prognosis, underscoring the value of anti-PL-7 as a serological marker of unfavorable disease progression.

Regarding extrapulmonary manifestations, inflammatory myopathy represents the second most frequent feature in anti-PL-7–positive patients, as reported in a European cohort[3]. In this patient, the initial presentation with acute-onset proximal muscle weakness and a CPK elevation greater than ten times the upper normal limit was consistent with active inflammatory myopathy[8]. Electromyography helped exclude other neuromuscular causes, in line with descriptions of inflammatory myopathies[8], confirming the presence of intrinsic muscle fiber involvement.

With respect to cutaneous manifestations, "mechanic's hands" have been described in approximately 46.2% to 55% of cases, whereas Raynaud's phenomenon associated with ILD occurs in about 36.9%[9]. These clinical findings, present in this patient, further support the diagnosis within the spectrum of antisynthetase syndrome (ASyS).

The treatment of ASyS with severe pulmonary involvement is based on a stepwise approach, beginning with an induction phase using corticosteroids and cyclophosphamide, followed by maintenance therapy with azathioprine or mycophenolate mofetil. In this case, the patient initially received azathioprine with a favorable response and good tolerance; however, subsequent progression of ILD required the introduction of cyclophosphamide, consistent with current recommendations that reserve this agent for severe or refractory forms[10]. Although the literature has documented favorable responses to rituximab or tacrolimus[11], their use was not feasible due to local availability constraints. Despite therapeutic intensification, the persistence of pulmonary disease progression and the development of pulmonary hypertension illustrate the refractory course characteristic of the anti-PL-7 phenotype.

CONCLUSIONS

This case illustrates the clinical behavior of a rare antisynthetase syndrome (ASyS) phenotype characterized by anti-PL-7 positivity, presenting with interstitial lung disease (ILD) and pulmonary hypertension, both of which represent markers of poor prognosis and require early diagnosis and aggressive immunosuppressive management. This report emphasizes the importance of a multidisciplinary approach and close follow-up in anti-PL-7 ASyS, as well as the need for multicenter studies to further define optimal therapeutic strategies and prognostic factors for this subtype of inflammatory myopathy.

Conflict of Interest:
The authors declare that they have no conflicts of interest to disclose.

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Authors' Contributions:
Dr. Kevin Burbano (ORCID: 0000-0003-4450-8423), Dr. Mario Benavides (ORCID: 0000-0001-6208-2759), and Dr. José Zambrano (ORCID: 0000-0002-4959-9136) participated equally in the preparation of this manuscript. All authors contributed to the writing of the abstract, introduction, case presentation, discussion, and conclusions, as well as to the design and review of the tables and figures. All authors approve the final version of the manuscript and take full responsibility for its content.

Ethical Statement:
This case report was conducted in accordance with the ethical standards outlined in the Declaration of Helsinki, the principles recommended by the Committee on Publication Ethics (COPE), and the applicable national regulations (Resolution 8430 of 1993 and Law 1581 of 2012). The case was reviewed and approved by the Ethics Committee of Fundación Hospital San Pedro and was classified as a no-risk study.

Informed Consent:

Written informed consent was obtained from the patient for the publication of their clinical data and images. Confidentiality and anonymity were strictly maintained, and no identifiable information is presented.

Data Availability:

Clinical and complementary data used in the preparation of this report are available from the corresponding author upon reasonable request.

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