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Case Report

Pulmonary fibrosis in systemic sclerosis and granulomatosis with polyangiitis: a case report

Fibrose pulmonaire révélant l'association d'une sclérodémie systémique et d'une granulomatose avec polyangéite : à propos d'un cas

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KEYWORDS

Pulmonary Fibrosis;

Systemic Sclerosis;

Granulomatosis with Polyangiitis;

Overlap Syndrome;

Interstitial Lung Disease;

ANCA-Associated Vasculitis.

Abstract

Introduction : Pulmonary fibrosis is a major cause of morbidity and mortality in systemic autoimmune diseases. Systemic sclerosis (SSc) is frequently associated with interstitial lung disease, whereas granulomatosis with polyangiitis (GPA) rarely presents with fibrotic lung involvement. The coexistence of these two conditions constitutes an exceptional overlap syndrome and poses diagnostic and therapeutic challenges.

Methods : We report the case of a 64-year-old male presenting with progressive dyspnea and chronic cough evolving over three years, associated with nasal congestion, Raynaud's phenomenon, and skin thickening. High-resolution computed tomography (HRCT) revealed a non-specific interstitial pneumonia (NSIP) pattern. Immunological investigations showed positivity for anti-Scl-70 and anti-proteinase 3 (PR3) antibodies.

Results : A multidisciplinary assessment established the diagnosis of pulmonary fibrosis secondary to overlapping SSc and GPA. Treatment with mycophenolate mofetil resulted in partial clinical improvement and stabilization of respiratory symptoms.

Conclusion : This case highlights the importance of systematic autoimmune evaluation in interstitial lung disease and illustrates the role of individualized immunosuppressive therapy in rare overlap syndromes involving both fibrotic and vasculitic mechanisms.

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MOTS CLÉS

Fibrose pulmonaire;

Sclérodémie systémique;

Résumé

Introduction : La fibrose pulmonaire constitue une cause majeure de morbi-mortalité au cours des maladies auto-immunes systémiques. La sclérodémie systémique (ScS) est fréquemment associée aux pneumopathies interstitielles diffuses, tandis que la granulomatose avec polyangéite (GPA) s'exprime plus rarement par une atteinte fibrosante

Granulomatose avec
polyangéite,

Syndrome de
chevauchement ;

pneumopathie
interstitielle diffuse ;

Vascularite à ANCA

pulmonaire. Leur association définit un syndrome de chevauchement exceptionnel.

Méthodes : Nous rapportons le cas d'un patient de 64 ans présentant une dyspnée progressive et une toux chronique évoluant depuis trois ans, associées à une obstruction nasale, un phénomène de Raynaud et un épaissement cutané. La tomodensitométrie thoracique haute résolution a mis en évidence un aspect de pneumopathie interstitielle non spécifique (PINS). Le bilan immunologique retrouvait des anticorps anti-Scl-70 et anti-protéinase 3 (PR3).

Résultats : Une concertation multidisciplinaire a permis de retenir le diagnostic de fibrose pulmonaire secondaire à un syndrome de chevauchement ScS-GPA. Le traitement par mycophénolate mofétil a permis une amélioration clinique partielle.

Conclusion : Cette observation souligne l'intérêt d'un bilan immunologique exhaustif devant toute pneumopathie interstitielle diffuse et l'importance d'une prise en charge individualisée dans les syndromes de chevauchement auto-immuns.

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Introduction

Pulmonary fibrosis represents a heterogeneous group of chronic interstitial lung diseases characterized by progressive scarring of the lung parenchyma, resulting in irreversible architectural distortion, impaired gas exchange, and ultimately respiratory failure. It is the final common pathway of various injurious processes involving repetitive alveolar epithelial damage, abnormal wound-healing responses, fibroblast proliferation, and excessive extracellular matrix deposition [1,2]. These mechanisms are driven by complex interactions between epithelial cells, fibroblasts, immune cells, and profibrotic mediators such as transforming growth factor- β (TGF- β), platelet-derived growth factor, and connective tissue growth factor [3].

Among connective tissue diseases, systemic sclerosis (SSc) is the most frequently associated with interstitial lung disease (ILD), with a prevalence ranging from 40% to 70% depending on the diagnostic method used [4]. ILD is the leading cause of disease-related mortality in SSc, surpassing pulmonary arterial hypertension [5]. The most common radiological and histopathological pattern observed is non-specific interstitial pneumonia (NSIP), reflecting a predominantly immune-mediated and fibrotic process rather than irreversible honeycombing seen in usual interstitial pneumonia [6]. Risk factors for SSc-associated ILD include diffuse cutaneous involvement, male sex, African ancestry, and the presence of anti-topoisomerase I (anti-Scl-70) antibodies [7].

Granulomatosis with polyangiitis (GPA) is a necrotizing small-vessel vasculitis belonging to the spectrum of ANCA-associated vasculitides. It classically involves the upper and lower respiratory tracts and kidneys, with pulmonary manifestations occurring in up to 85% of patients during the disease course [8]. Typical radiological findings include pulmonary nodules, cavitory lesions, alveolar infiltrates, and diffuse alveolar hemorrhage. However, interstitial lung disease and pulmonary fibrosis have increasingly been reported, particularly in patients with PR3-ANCA positivity, suggesting that chronic inflammation and repeated vascular injury may promote fibrotic remodeling of the lung parenchyma [9,10].

The coexistence of systemic sclerosis and granulomatosis with polyangiitis represents a rare autoimmune overlap syndrome, with only isolated cases reported in the literature. This association raises important diagnostic and therapeutic challenges, as it reflects the convergence of distinct but potentially overlapping immunopathogenic mechanisms, combining fibrotic pathways characteristic of SSc with vasculitic and neutrophil-mediated injury typical of GPA [11]. We report a case of pulmonary fibrosis revealing this exceptional overlap, highlighting the importance of comprehensive autoimmune evaluation and multidisciplinary management.

Case presentation

A 64-year-old male, former smoker (20 pack-years), with no significant occupational exposures, presented with a complaint of progressive dyspnea (mMRC class

II) and a chronic, non-productive cough evolving over three years. He reported concomitant symptoms of persistent nasal congestion. A review of extra-respiratory systems was positive for Raynaud's phenomenon (Figure 01) and tightening of the skin on his hands.

On physical examination, vital signs were normal. Dermatological examination confirmed sclerodactyly. Cardiopulmonary auscultation revealed fine, bilateral end-inspiratory "Velcro" crackles predominating in the lower lung zones. The initial diagnostic workup was systematically pursued:

- **Imaging:** A chest X-ray showed subtle bilateral interstitial opacities in the lung bases (Figure 02). High-resolution computed tomography (HRCT) of the chest confirmed the presence of bilateral, peripheral predominant ground-glass opacities with fine reticulation and traction bronchiectasis, consistent with a radiological pattern of non-specific interstitial pneumonia (NSIP) (Figure 03)

- **Laboratory Investigations:** Routine hematology and biochemistry were within normal limits. Autoimmune serology revealed a positive antinuclear antibody (ANA) with a speckled pattern. Specific antibody testing was strongly positive for anti-Scl-70 (anti-topoisomerase I). Concurrently, cytoplasmic-ANCA (c-ANCA) was detected and confirmed to be directed against proteinase 3 (PR3). Inflammatory markers as C-reactive protein were mildly elevated.

- **Bronchoscopic Evaluation:** To exclude infectious etiologies and further characterize the interstitial process, a flexible bronchoscopy was performed. Direct examination revealed a normal-appearing bronchial mucosa with all segmental orifices patent and catheterizable. All carinal spurs were noted to be sharp, with the exception of the left upper lobe bronchus spur which appeared widened. Bronchoalveolar lavage (BAL) fluid analysis revealed an inflammatory cytology with a differential count of 86% macrophages, 10% lymphocytes, and 4% polymorphonuclear neutrophils (PNNs). Biopsies of the bronchial mucosa showed only mild, non-specific inflammatory changes.

- **Pulmonary Function Tests:** Spirometry showed a conserved forced vital capacity (FVC). However, the diffusion capacity for carbon monoxide (DLCO) was severely impaired at 46% of the predicted value, indicating a significant gas exchange abnormality.



Figure 01



Figure 02

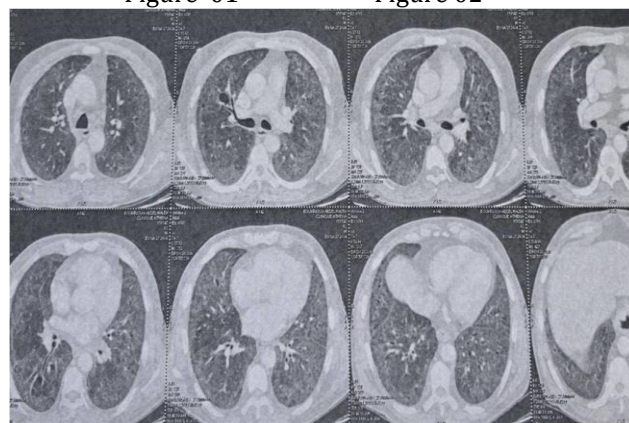


Figure 03

Figure 01: Raynaud's syndrome interesting the anular and little fingers

Figure 02: Anteroposterior Chest X-ray. Subtle bilateral interstitial opacities in the lung bases.

Figure 03: High-Resolution Computed Tomography (HRCT) of the chest at the level of the lung bases. Axial image demonstrates bilateral, peripheral predominant ground-glass opacities with associated fine reticulation and mild traction bronchiectasis (arrows), consistent with a non-specific interstitial pneumonia (NSIP) pattern.

Management and outcome

Following a multidisciplinary discussion involving pulmonology and internal medicine, a definitive diagnosis of pulmonary fibrosis secondary to overlapping Systemic Sclerosis and GPA was established. Given the predominance of the fibrotic NSIP pattern associated with SSc and the patient's serology, the treatment strategy was tailored to concurrently address both the fibrotic and vasculitic components. The patient was initiated on Mycophenolate Mofetil (MMF) monotherapy at a target dose of 1500 mg twice daily. This agent was selected for its dual capacity to modulate the immune pathways driving both systemic sclerosis-associated interstitial lung disease and granulomatosis with polyangiitis.

After two months of therapy with MMF monotherapy, the patient reported subjective improvement in dyspnea and cough. A follow-up clinical assessment showed stabilization of respiratory symptoms with no new clinical signs of active vasculitis. A repeat pulmonary function test and clinical evaluation are

planned at three months to objectively assess the therapeutic response. The patient continues under close multidisciplinary surveillance for monitoring of disease activity and medication tolerance.

Discussion

This case illustrates a rare autoimmune overlap between systemic sclerosis and granulomatosis with polyangiitis, revealed by progressive pulmonary fibrosis. While interstitial lung disease is a classical and well-recognized manifestation of SSc, fibrotic lung involvement in GPA remains uncommon and is often underdiagnosed, particularly when it precedes or masks typical vasculitic manifestations [9,12].

In systemic sclerosis, pulmonary fibrosis results from immune-mediated endothelial and epithelial injury, leading to persistent activation of fibroblasts and myofibroblasts, excessive collagen deposition, and progressive destruction of alveolar architecture [3,13]. The presence of anti-Scl-70 antibodies, as observed in our patient, is strongly associated with diffuse cutaneous disease and an increased risk of severe ILD and rapid functional decline [7,14].

In contrast, lung involvement in GPA is primarily driven by ANCA-mediated neutrophil activation and small-vessel vasculitis, resulting in necrotizing inflammation of the pulmonary capillaries and arterioles [15]. Although pulmonary fibrosis is not considered a hallmark of GPA, several studies have reported its occurrence, particularly in patients with chronic disease or persistent PR3-ANCA positivity. Recurrent inflammatory injury, microvascular ischemia, and aberrant repair processes may contribute to fibrotic remodeling in these patients [10,16].

Pathophysiological overlap hypothesis

The coexistence of SSc and GPA in the same patient suggests shared or convergent pathogenic mechanisms characterized by endothelial dysfunction, immune dysregulation, and aberrant repair responses. Endothelial injury represents a central event in SSc, leading to vascular rarefaction and tissue hypoxia, while in GPA, ANCA-mediated neutrophil activation induces direct endothelial damage through the release of reactive oxygen species and proteolytic enzymes [8,15]. These convergent vascular insults may promote chronic ischemia and trigger profibrotic signaling pathways.

Furthermore, innate and adaptive immune responses overlap in both conditions, with activation of Th17 cells, macrophages, and B lymphocytes contributing to sustained inflammation. Profibrotic cytokines such as TGF- β and IL-6, implicated in SSc-related fibrosis, may also be upregulated following repeated vasculitic injury

in GPA, favoring fibroblast activation and extracellular matrix deposition. This immuno-fibrotic continuum may explain the development of NSIP-pattern fibrosis in overlap cases and supports the rationale for immunomodulatory therapies targeting both inflammatory and fibrotic pathways.

Radiologically, the NSIP pattern identified on high-resolution computed tomography strongly supports SSc-associated ILD, as this pattern is rarely predominant in isolated GPA, where nodular or hemorrhagic lesions are more typical [6,12].

To better contextualize this observation, previously reported cases of overlap between systemic sclerosis and granulomatosis with polyangiitis with pulmonary involvement are summarized in Table 1, highlighting the heterogeneity of clinical presentation, radiological patterns, therapeutic strategies, and outcomes. The absence of alveolar hemorrhage, renal involvement, or other life-threatening vasculitic manifestations in our patient justified a less aggressive therapeutic approach. Mycophenolate mofetil (MMF) was selected as first-line therapy due to its established efficacy in stabilizing lung function in SSc-associated ILD, as demonstrated in the Scleroderma Lung Study II [17]. MMF inhibits lymphocyte proliferation and reduces fibroblast activation, thereby targeting both inflammatory and fibrotic pathways. In addition, MMF has been shown to be effective as a steroid-sparing agent for remission maintenance in ANCA-associated vasculitis, with a favorable safety profile compared to azathioprine or cyclophosphamide [18,19]. In the absence of organ- or life-threatening vasculitis, MMF monotherapy represented a rational and balanced therapeutic strategy.

This observation emphasizes the importance of multidisciplinary discussion and systematic immunological screening in patients presenting with interstitial lung disease of unclear etiology. Early recognition of autoimmune overlap syndromes allows tailored immunosuppressive therapy and may help prevent irreversible lung damage and disease progression [20].

Conclusion

Pulmonary fibrosis may reveal rare autoimmune overlap syndromes such as the association between systemic sclerosis and granulomatosis with polyangiitis. Early recognition through comprehensive clinical and immunological assessment allows individualized therapeutic strategies targeting both fibrotic and vasculitic components, with the potential to improve outcomes.

Conflicts of interest:

We declare no conflicts of interest

References :

1. Selman M, Pardo A. The epithelial-fibroblast axis in pulmonary fibrosis. *Eur Respir J*. 2014;44:157–168.
2. King TE Jr, Pardo A, Selman M. Idiopathic pulmonary fibrosis. *Lancet*. 2011;378:1949–1961.
3. Wynn TA. Cellular and molecular mechanisms of fibrosis. *J Pathol*. 2008;214:199–210.
4. Solomon JJ, Olson AL, Fischer A, et al. Scleroderma lung disease. *Eur Respir Rev*. 2013;22:6–19.
5. Tyndall AJ, Bannert B, Vonk M, et al. Causes and risk factors for death in systemic sclerosis. *Ann Rheum Dis*. 2010;69:1809–1815.
6. Lynch DA, Sverzellati N, Travis WD, et al. Diagnostic criteria for idiopathic interstitial pneumonias. *Radiology*. 2018;288:909–931.
7. Steen VD, Medsger TA Jr. Severe organ involvement in systemic sclerosis with anti-topoisomerase I antibodies. *Arthritis Rheum*. 2000;43:2437–2444.
8. Kallenberg CGM. Pathogenesis of ANCA-associated vasculitis. *Nat Rev Rheumatol*. 2014;10:484–493.
9. Comarmond C, Crestani B, Tazi A, et al. Pulmonary fibrosis in antineutrophil cytoplasmic antibody-associated vasculitides. *Autoimmun Rev*. 2014;13:1004–1010.
10. Hervier B, Pagnoux C, Agard C, et al. Pulmonary fibrosis associated with ANCA-associated vasculitis. *Respir Med*. 2009;103:194–201.
11. Guillevin L, et al. Overlap syndromes in systemic autoimmune diseases. *Autoimmun Rev*. 2012;11:727–735.
12. Ando M, Miyazaki E, Kurashima K, et al. Incidence of interstitial lung disease in granulomatosis with polyangiitis. *Clin Rheumatol*. 2013;32:169–174.
13. Varga J, Abraham D. Systemic sclerosis: a prototypic fibrotic disease. *J Clin Invest*. 2007;117:557–567.
14. Nihtyanova SI, Denton CP. Pathogenesis of systemic sclerosis-associated interstitial lung disease. *J Scleroderma Relat Disord*. 2020;5:3–16.
15. Falk RJ, Jennette JC. ANCA disease: where is this field heading? *J Am Soc Nephrol*. 2010;21:745–752.
16. Arulkumaran N, Periselneris N, Gaskin G, et al. Interstitial lung disease in ANCA-associated vasculitis. *Clin Exp Rheumatol*. 2014;32:S82–S89.
17. Tashkin DP, Roth MD, Clements PJ, et al. Mycophenolate mofetil versus oral cyclophosphamide in scleroderma-related interstitial lung disease (SLS II). *N Engl J Med*. 2016;374:255–265.
18. Hiemstra TF, Walsh M, Mahr A, et al. Mycophenolate mofetil vs azathioprine for remission maintenance in ANCA-associated vasculitis. *JAMA*. 2010;304:2381–2388.
19. Specks U, Merkel PA, Seo P, et al. Efficacy of remission-induction regimens for ANCA-associated vasculitis. *N Engl J Med*. 2013;369:417–427.
20. Wijsenbeek M, Cottin V. Spectrum of fibrotic lung diseases. *N Engl J Med*. 2020;383:958–968.