CASE REPORT

Anti-synthetase Syndrome with Dermatomyositis Responding to Combination of Mycophenolate mofetil and Cyclosporin: A Case Report.

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Abstract

Anti-synthetase syndrome (ASS) is a rare inflammatory muscle disorder associated with dermatomyositis and polymyositis, characterized by autoantibodies targeting aminoacyl-tRNA synthetases. Clinical manifestations vary but typically include mechanic's hands, interstitial lung disease (ILD), and Raynaud's phenomenon. We report the case of a 42-year-old woman with a positive anti-Jo1 autoantibody, who initially presented with respiratory symptoms that progressed to myositis, along with severe, painful mechanic's hands and feet. Her condition improved with a combination of mycophenolate mofetil (MMF), corticosteroids, and cyclosporine.

Keywords: *Anti-synthetase syndrome, dermatomyositis, polymyositis, anti-aminoacyl-tRNA synthetase, anti-Jo1 antibody, mechanic's hands, interstitial lung disease, corticosteroid, mycophenolate mofetil, cyclosporin.*

Introduction

Anti-synthetase syndrome (ASS) is a rare autoimmune inflammatory myopathy classified under idiopathic inflammatory myopathies (IIM). The exact aetiology and pathogenesis remain unclear. ASS is defined by the presence of autoantibodies against aminoacyl-tRNA synthetases (anti-ARS), occurring in approximately 30% of patients with inflammatory myopathies [1]. Common clinical features include mechanic's hands, ILD, myositis, arthritis, and Raynaud's phenomenon [2].

Anti-Jo1 (histidyl-tRNA synthetase) is the most common anti-ARS antibody, though others, such as anti-PL-12, anti-PL-7, and anti-EJ, have also been reported [3]. ILD affects 70-90% of patients with anti-Jo1 [4, 5] and is more prevalent in ASS than in dermatomyositis and polymyositis [6].

Here, we report the case of a 42-year-old woman with severe mechanic's hands, ILD, arthritis, and myositis, positive for anti-Jo1 antibodies. Interestingly, ASS was not suspected during her initial presentation with respiratory symptoms. Despite severe ILD, her respiratory function was preserved, and she responded well to a combination of MMF, corticosteroids, and cyclosporine.

Case Report

A 42-year-old Indian woman, with no significant medical history, presented with progressive dyspnoea, chest pain, low-grade fever, and a productive cough with yellowish sputum. She was initially diagnosed with pneumonia based on chest radiographs showing bilateral mid-to-lower zone infiltrates. Blood investigations revealed an elevated erythrocyte sedimentation rate (ESR) of 64 mm/hour and C-reactive protein (CRP) of 33 mg/L. Additionally, creatinine kinase (CK) was mildly elevated at 420 U/L, with lactate dehydrogenase (LDH) at 484 U/L and aspartate transaminase (AST) at 92 U/L.

Despite completing antibiotic therapy, her symptoms persisted. A follow-up chest radiograph revealed persistent bilateral consolidations. Over time, she developed painful hyperkeratotic lesions with fissures on both hands and feet. Mild proximal muscle weakness and arthritis also emerged. However, Raynaud's phenomenon, oral ulcers, vasculitis, or lupus-related rashes were absent.

On examination, she exhibited severe mechanic's hands, characterized by dry, scaly, hyperkeratotic lesions on the fingers and toes (Figure 1). Additionally, symmetrical erythematous plaques covered the soles and palms, and stage 2 finger clubbing was noted. Mild proximal myopathy with quadriceps tenderness was present. There were no Gottron's papules, heliotrope rash, or telangiectasia. Fine and coarse crackles were audible in the lower lung fields, although her respiratory function remained stable.

Laboratory tests confirmed positive anti-nuclear antibody (ANA) at a titer of 1:320 (speckled pattern) and strongly positive anti-Jo1 and anti-Ro52 antibodies. High-resolution computed tomography (HRCT) of the thorax revealed bilateral patchy consolidations in the lower lobes (Figure 2A, 2B).

Based on her clinical and serological findings, she was diagnosed with ASS with myositis and ILD. Treatment was initiated with oral methylprednisolone (1 mg/kg/day), MMF (500 mg twice daily), and hydroxychloroquine (200 mg daily), along with topical treatments for her skin lesions.

After one month, her skin condition worsened, and her muscle weakness progressed. CK levels rose to 1437 U/L, CRP to 59 mg/L, LDH to 656 U/L, and AST to 52 U/L. Repeat HRCT revealed the resolution of consolidations but showed ground-glass opacities, subpleural fibrosis, and mild upper-lobe involvement (Figure 2C, 2D).

A skin biopsy demonstrated mild epidermal atrophy, focal hyperkeratosis, and pigment incontinence, along with lymphoplasmacytic infiltration surrounding hair follicles. Mucin accumulation was prominent in the dermis. No vasculitis was detected, and deeper dermis and appendages appeared normal. Immunofluorescence showed granular deposits of IgG and C3 at the dermo-epidermal junction and blood vessels, consistent with dermatomyositis (Figure 3).

Intravenous methylprednisolone (500 mg daily for three days) was administered, and the MMF dose was increased to 1 g twice daily. Cyclosporine (150 mg/day) was added to her regimen. After one month, her skin lesions and muscle strength improved, with CK levels reducing to 405 U/L and normalization of CRP and AST. She remained stable on tapering doses of methylprednisolone, MMF, hydroxychloroquine, cyclosporine, and topical treatments.

Discussion

ASS is a rare autoimmune disorder with diverse clinical manifestations, frequently involving ILD and inflammatory myopathy. This patient fulfilled the diagnostic criteria for ASS, presenting with anti-Jo1 antibodies, myositis, and ILD, as outlined by the Bohan and Peter criteria [6-8]. Anti-Jo1 antibodies are found in approximately 80% of ASS cases and serve as a key diagnostic marker [9].

ILD is a major concern in ASS and significantly influences prognosis. Around 70% of patients with ASS develop ILD, with anti-PL7 and anti-PL12 antibodies associated with more aggressive forms [10, 11]. HRCT findings often reveal patterns consistent with non-specific interstitial pneumonia (NSIP) [12].

In this patient, the presence of both anti-Jo1 and anti-Ro52 antibodies contributed to severe ILD. Anti-Ro52 has been linked to increased ILD severity and recurrence [13-15]. Treatment typically involves corticosteroids, with MMF, azathioprine, or calcineurin inhibitors recommended for ILD management [16].

This patient responded well to corticosteroids, MMF, and cyclosporine, achieving clinical stability despite severe ILD. MMF is known to improve pulmonary function in connective tissue disease-associated ILD, supporting its use in this case [17-19].

Conclusion

ASS is a rare autoimmune disease with significant heterogeneity in presentation, often involving ILD and myositis. Early diagnosis and appropriate treatment are essential to prevent irreversible damage. HRCT is crucial for differentiating ASS-ILD from other ILDs. This case emphasizes the importance of a multidisciplinary approach, involving rheumatologists, dermatologists, and pulmonologists, for optimal management. The patient showed significant improvement with corticosteroids, MMF, and cyclosporine, highlighting the efficacy of this combination.

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Informed Consent: Written informed consent was obtained from the patient for the publication of this report and the accompanying images.
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Authors contribution: WS: Case management, data collection, and manuscript writing; HFBB: case management and review of the manuscript; LBR: histopathology interpretation and review of manuscript.

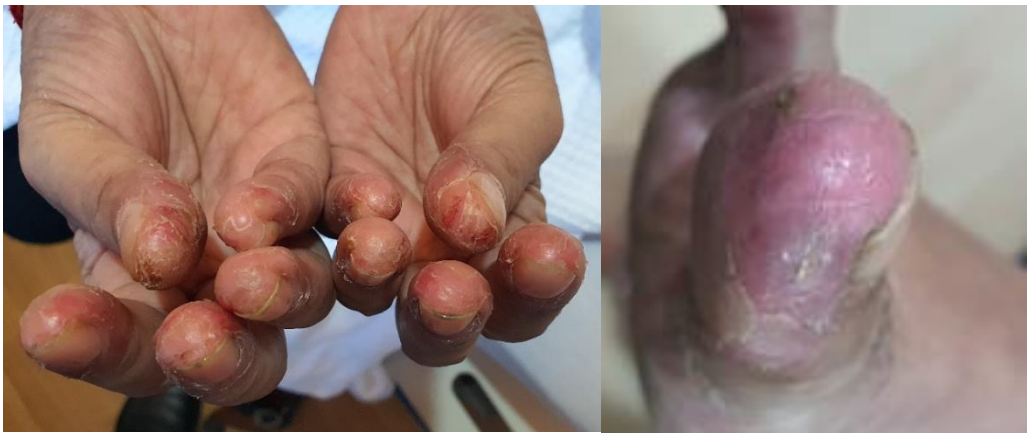

Figure 1. Mechanic's hands: Hyperkeratotic skin with fissures mainly at tips of the fingers and toes.

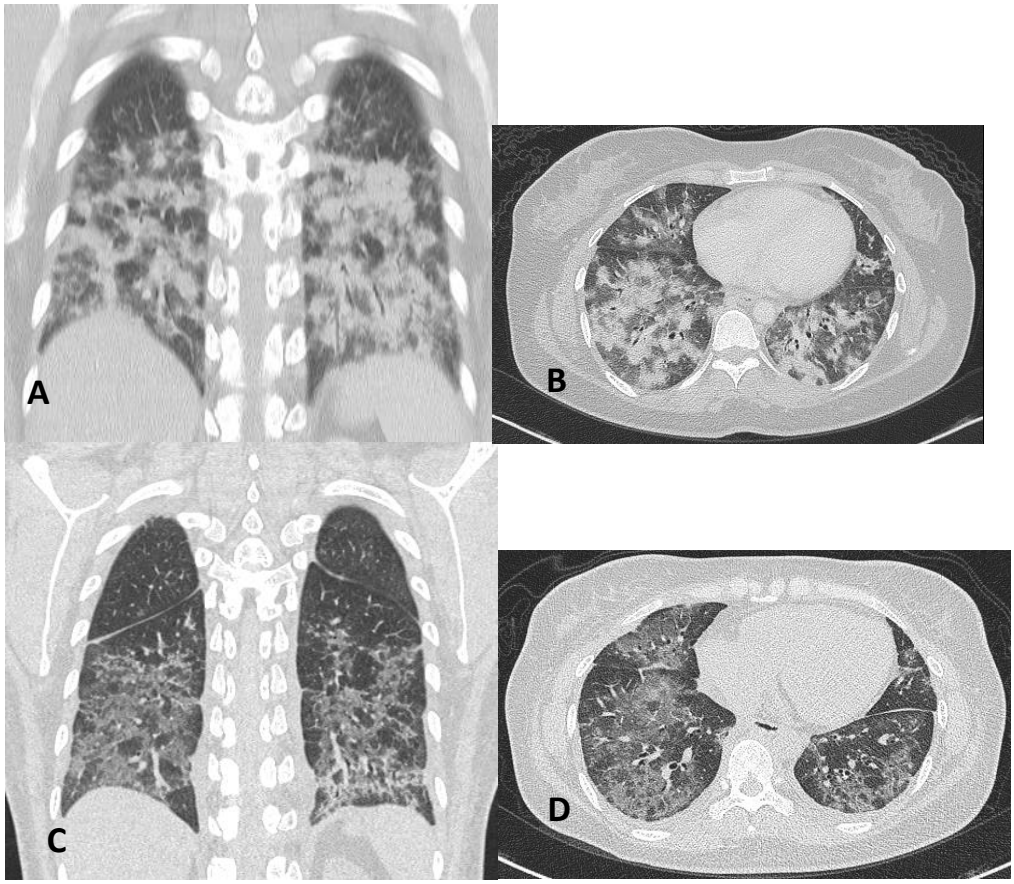

Figure 2. Coronal and transverse section HRCT thorax: A, B: Scattered patches of consolidations in the lower lobes bilaterally. C, D: after 5 months: HRCT thorax showing ground-glass opacities in both lungs are predominantly in both lower lobes with subpleural basal fibrosis.

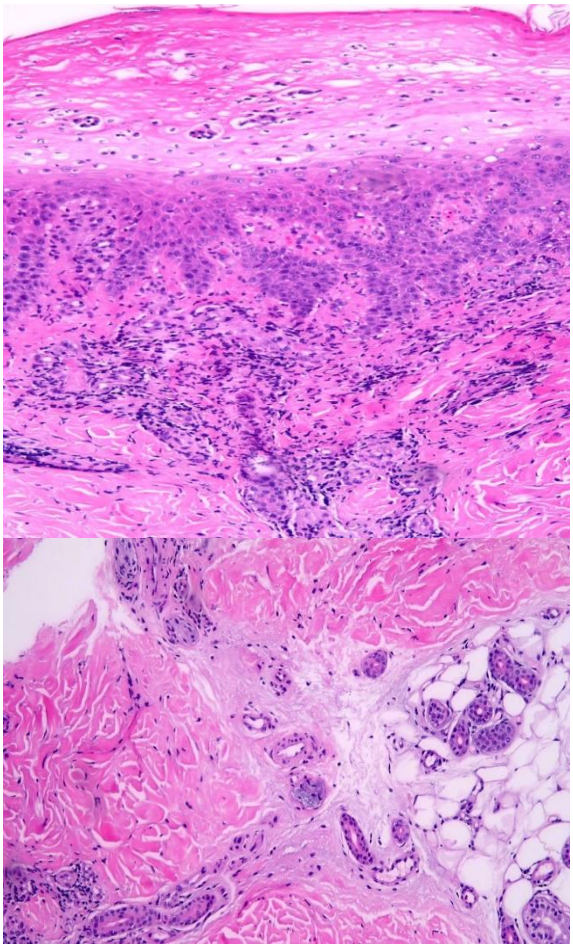

Figure 3. Histopathologic examination from skin biopsy showed lichenoid dermatitis with dermal mucin deposit and immunofluorescence (IF) consistent with dermatomyositis.

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