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CASE REPORT

Anti-MDA5 Positive Dermatomyositis Overlapping with Rheumatoid Arthritis: A Case Report

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Abstract: We report a rare case of overlap syndrome between anti-MDA5-positive dermatomyositis (DM) and rheumatoid arthritis (RA) in a 65-year-old woman. Initially diagnosed with RA, the patient later developed characteristic DM manifestations including characteristic DM rash, generalized weakness, poor appetite, and unintentional weight loss. Laboratory findings revealed elevated muscle enzymes, positive anti-melanoma differentiation-associated gene 5 (MDA5) antibody and anti-Ro52 antibodies, and increased anti-citrullinated protein antibodies. The patient showed significant improvement following combination therapy with prednisone and mycophenolate mofetil, highlighting the importance of early recognition and appropriate management of this rare overlap syndrome.

Keywords: anti-MDA5 antibodies, dermatomyositis, interstitial lung disease, rheumatoid arthritis, overlap syndrome

Introduction

Idiopathic inflammatory myopathies (IIM) are a heterogeneous group of autoimmune disorders characterized by skeletal muscle weakness, inflammation, and distinctive cutaneous manifestations.[1] Dermatomyositis (DM), a major subtype of IIM, typically presents with symmetrical proximal muscle weakness and characteristic skin lesions.[2] The discovery of myositis-specific antibodies (MSAs) has significantly advanced our understanding of DM. Among these autoantibodies, the anti-melanoma differentiation-associated gene 5 (anti-MDA5) antibody has emerged as a crucial biomarker associated with a definite subset of dermatomyositis patients.[3] Anti-MDA5 antibody positivity is strongly associated with clinically amyopathic dermatomyositis (CADM) and rapidly progressive interstitial lung disease (RP-ILD), which carries a substantially poor prognosis, with mortality rates ranging from 33% to 66% within the first six months of diagnosis,[4,5] and overall mortality rates reaching 25.4% in anti-MDA5-positive dermatomyositis patients with RP-ILD.[4]

The literature documents various cases of overlap syndromes between DM and other autoimmune diseases.[6,7] However, the co-occurrence of anti-MDA5 antibody-associated CADM with rheumatoid arthritis (RA) has been documented in limited case reports. This overlap syndrome presents specific diagnostic and therapeutic challenges due to the complex interplay of autoimmune mechanisms and the clinical course of RP-ILD.

Here, we report a case of anti-MDA5 antibody-positive CADM overlapping with RA, highlighting its clinical features, diagnostic approach, and therapeutic considerations. This case contributes to the growing body of knowledge regarding anti-MDA5-associated diseases and provides valuable insights for the management of similar cases in clinical practice.

Case Presentation

A 65-year-old woman presented to the emergency department with a one-day history of fever. She reported a 10-month history of weight loss, poor appetite, fatigue, generalized weakness, alopecia, and rash. She had a one-year history of rheumatoid arthritis, for which she received irregular treatment and discontinued medication six months prior.

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On physical examination, she appeared fatigued. Her temperature was 37.6°C, pulse 106 beats per minute, respiratory rate 20 breaths per minute, and oxygen saturation 96% on room air. Examination of the skin revealed mild cyanosis of the lips, oral ulceration, hyperpigmentation, violaceous heliotrope rash with periorbital edema (Figure 1A), V-neck sign (Figure 1B), shawl sign (Figure 1C), Gottron's papules and joint deformities (Figure 1D), skin ulcers (Figure 1E), and psoriasiform changes and crusted lesions on the extensor surfaces (Figure 1F). The chest was symmetric without deformities, and lung expansion was bilaterally equal. Breath sounds were coarse bilaterally, but no crackles or wheezes were auscultated. The abdomen was soft, without tenderness or rebound tenderness. She had no palpable hepatosplenomegaly or lymphadenopathy, and no deficits were found on neurologic examination. There was no edema in the lower extremities.skin ulcersskin ulcers

The complete blood count revealed normocytic normochromic anemia (hemoglobin, 96 g/L; hematocrit, 29.9%). The white blood cell count was within the normal range, but the neutrophil percentage was markedly elevated (90.9%), and the platelet count was normal. The erythrocyte sedimentation rate was 22 mm/hour, and the C-reactive protein level was 19.54 mg/L. The procalcitonin level was 0.087 ng/mL. Interleukin-6 was elevated to 64.5 pg/mL. The creatine kinase (CK) level was 157 U/L (normal range [NR], <200), but lactate dehydrogenase (LDH) was elevated (375 U/L, NR 120–250), as were aspartate aminotransferase levels (59 U/L, NR 13–35). During hospitalization, the patient experienced persistent fever, with a maximum temperature of 38.9°C. Blood and urine cultures showed no growth. Ferritin was markedly elevated (787.3

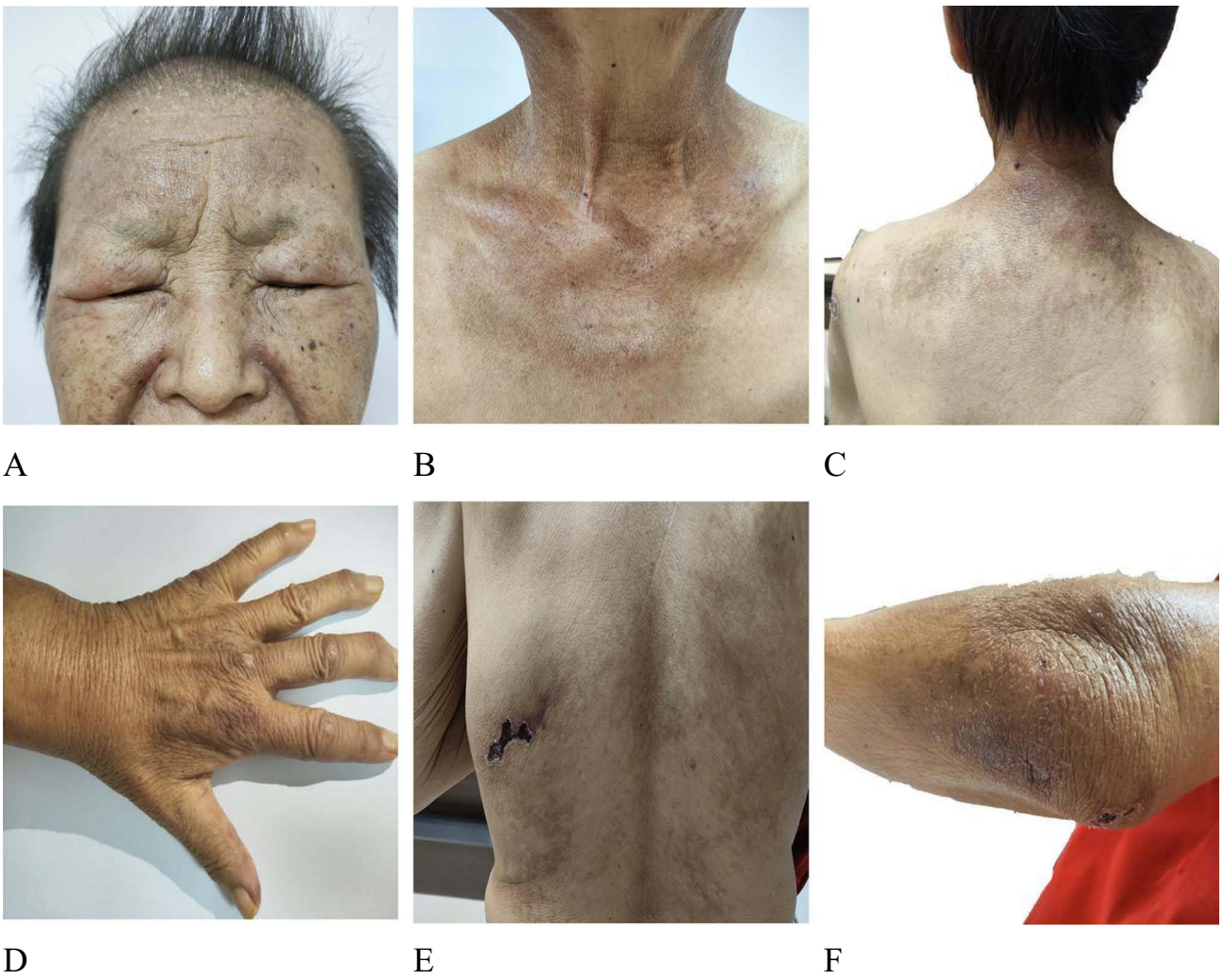

Figure 1 (**A**) The patient presented with periorbital edema and heliotrope rash on the eyelids. (**B**) Poikiloderma of the upper chest, consistent with findings of the V-neck sign. (**C**) Hyperpigmented patches on the posterior aspect of the shoulder, consistent with findings of the shawl sign. (**D**) The patient presented with hyperpigmented, erythematous papules overlying the metacarpophalangeal and interphalangeal joints, consistent with Gottron's papules. (**E**) The patient developed skin ulceration and necrosis on the posterior aspect of the back, which has now become crusted. (**F**) The patient presented with psoriasiform changes and crusted lesions on the extensor surfaces.

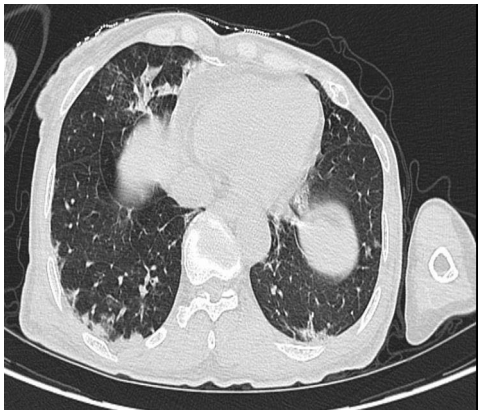

Figure 2 The patient's chest CT scan reveals interstitial changes.

ng/mL, NR 13–150), and the anti-cyclic citrullinated peptide antibody titer was significantly elevated (193.3 U/mL, NR 0–17). An evaluation for malignancy, including tumor markers and abdominal and pelvic computed tomography (CT), revealed no evidence of malignancy. Chest CT revealed bilateral inflammatory changes with interstitial fibrosis (Figure 2). Color Doppler ultrasonography of the knees showed small amounts of joint effusion and significant synovial thickening bilaterally, indicative of severe synovitis. Plain radiographs of the hands demonstrated narrowing of multiple interphalangeal joint spaces and subchondral sclerosis, consistent with rheumatoid arthritis. Given her unusual presentation, and negative ANA and anti-Jo1 autoantibodies, further screening for other dermatomyositis autoantibodies was performed. Double immunofluorescence staining conducted at an external clinical immunology laboratory detected the presence of anti-MDA5 and anti-Ro52 antibodies. Electromyography revealed mildly impaired peripheral nerve motor conduction (peroneal, tibial, and superficial peroneal nerves) and slightly reduced recruitment potentials. The absence of typical myopathic changes on electromyography, such as spontaneous activity or small-amplitude, short-duration motor unit potentials, was consistent with CADM, supporting the diagnosis in a patient with characteristic skin manifestations but minimal muscle involvement. A skin biopsy was not performed due to financial constraints. Based on these findings, the patient was diagnosed with anti-MDA5- and anti-Ro52-positive dermatomyositis overlapping with rheumatoid arthritis and interstitial lung disease.

The patient was initiated on prednisone 25mg daily and mycophenolate mofetil 0.75g per dose twice daily, with adjunctive therapies for gastroprotection and osteoporosis prevention. Following this treatment regimen, the patient demonstrated gradual clinical improvement with reduced fatigue, improved appetite, and no development of new rashes. Due to the patient's return to her distant rural hometown, face-to-face follow-up visits were not feasible. However, telephone consultations with the patient's husband at one month post-discharge revealed sustained clinical improvements, including weight gain and improved appetite. Laboratory tests performed at the local hospital demonstrated notable improvements: hemoglobin increased to 111 g/L, hematocrit to 35.7%, LDH decreased to 283 U/L, and ferritin to 276 ng/mL. The patient remained clinically stable at 6-month follow-up with no evidence of disease recurrence.

Discussion

This case highlights the rare coexistence of anti-MDA5 positive DM and rheumatoid arthritis, a combination that has been scarcely reported in the literature. This overlap syndrome presents unique diagnostic and therapeutic challenges, particularly given the poor prognosis associated with anti-MDA5-positive DM and its frequent association with RP-ILD.

The progression of this patient's symptoms provides significant insights into the interplay between these autoimmune diseases. The patient was previously healthy, with RA as the initial diagnosis, characterized by symmetrical polyarthritis with inflammation and joint deformities. Due to irregular use of RA medications, the disease progressed, and features of DM subsequently emerged, including heliotrope rash, Gottron's papules, and skin ulcerations. Laboratory investigations revealed markedly elevated anti-MDA5 and anti-Ro52 antibodies, along with a high titer of anti-cyclic citrullinated peptide (ACPA) antibodies, establishing the diagnosis of RA-DM overlap syndrome. However, our study has certain

limitations. A skin biopsy was not performed due to financial constraints, which could have provided valuable histopathological evidence to support the dermatomyositis diagnosis.

Anti-MDA5 antibodies play a central role in the pathogenesis of dermatomyositis through multiple mechanisms, including endothelial cell injury, immune complex deposition, and activation of type I interferon pathways, culminating in cutaneous and muscle inflammation and ILD development.[8,9] The presence of these antibodies defines a distinct subset of DM, characterized by minimal or absent muscle involvement while being closely associated with hallmark mucocutaneous features, such as Gottron's sign, mechanic's hands, and ulcerative lesions, as well as a significantly heightened risk of RP-ILD.[10,11] Clinical heterogeneity within anti-MDA5+ dermatomyositis has been demonstrated through an unsupervised analysis of a French nationwide multicenter retrospective cohort,[12] revealing three distinct phenotypes: the "rheumatoid phenotype", characterized by predominant arthritis and cutaneous manifestations, female preponderance, low incidence of RP-ILD, and favorable prognosis; the "vasculopathic phenotype" marked by male predominance, severe vasculopathy (manifesting as Raynaud's phenomenon, skin ulcers, and necrosis), classical dermatomyositis rashes, and intermediate RP-ILD prevalence (22.7%) with moderate prognosis; and the "RP-ILD phenotype", distinguished by poor clinical outcomes, frequent ICU admissions, and high mortality associated with severe RP-ILD. Based on the clinical presentation and disease course, our patient clearly represents the "rheumatoid phenotype" of anti-MDA5+ dermatomyositis. This classification is supported by several key characteristics: female sex, predominant arthritic manifestations with established rheumatoid arthritis and markedly elevated anti-CCP antibodies, classic dermatomyositis cutaneous features, and favorable treatment response with good prognosis. Although interstitial lung disease was present, it did not manifest as rapidly progressive ILD, which distinguishes this case from the RP-ILD phenotype. The presence of skin ulcers might suggest some vasculopathic features; however, the overall clinical picture, including the female predominance and dominant rheumatoid arthritis presentation, aligns most closely with the rheumatoid phenotype. This phenotypic classification helps contextualize the case within the current understanding of anti-MDA5+ dermatomyositis heterogeneity and may guide clinicians in recognizing similar presentations. Beyond their diagnostic significance, anti-MDA5 antibodies serve as dynamic indicators of disease activity, with elevated levels typically signaling disease progression, particularly in relation to ILD severity.[13] Notably, decreasing antibody titers correlate strongly with disease remission and improved pulmonary function, establishing their utility as a crucial biomarker for monitoring therapeutic response.

The clinical presentation in our patient was further complicated by the coexistence of RA, which presents multiple diagnostic and therapeutic challenges. The polyarticular manifestations and RA-associated joint damage may obscure classic dermatomyositis symptoms, while the intersection of inflammatory and immune pathways in these two conditions may modify the natural history and treatment response of CADM. The concurrent presence of RA significantly influences therapeutic decision-making, particularly regarding the combined use of biological agents and immunosuppressants. This requires careful balance between managing joint and pulmonary pathology while avoiding excessive immunosuppression and its associated infectious complications. Moreover, the inflammatory burden of RA may potentially accelerate ILD progression through synergistic inflammatory mechanisms. These complex interactions underscore the necessity of a comprehensive approach to patient management, integrating systematic assessments of articular manifestations, cutaneous involvement, ILD risk, and systemic immune status into therapeutic decision-making.

The treatment of anti-MDA5-positive DM overlapping with RA requires an individualized approach encompassing both systemic inflammation and ILD. While disease-modifying antirheumatic drugs (DMARDs) remain the cornerstone of RA management, the presence of anti-MDA5 antibodies and ILD necessitates more aggressive immunosuppressive therapy.[14] In this case, combination treatment with prednisone and mycophenolate mofetil (MMF) led to significant clinical improvement, aligning with existing evidence supporting MMF's efficacy in managing DM-associated ILD.[15]

Conclusion

This article presents a rare case of anti-MDA5 positive DM overlapping with RA, emphasizing the critical importance of early recognition and individualized treatment in improving patient outcomes. The patient experienced clinical improvement after treatment with prednisone and mycophenolate mofetil, suggesting the efficacy of this regimen. However, the management of anti-MDA5-positive DM with concurrent RA remains challenging due to disease heterogeneity and an

increased risk of infection, compounded by the limited availability of high-quality evidence to guide optimal therapeutic strategies. Therefore, prospective studies are needed to refine treatment strategies and enhance patient outcomes.

Consent to Publish Statement

Written informed consent was obtained from the patient for the publication of this case report and any accompanying images. The Medical Ethics Committee of Shenzhen Longgang Central Hospital has authorized the publication of this case report.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest in this work.

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