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AMYOPATHIC DERMATOMYOSITIS WITH A RAPIDLY PROGRESSING INTERSTITIAL PNEUMONIA

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ABSTRACT

Background: Clinically amyopathic dermatomyositis (CADM) is a rare subtype of idiopathic inflammatory myositis often linked with the presence of autoantibodies targeting melanoma differentiation-associated protein 5 (MDA5). Patients with CADM are at increased risk of developing rapidly progressing interstitial lung disease, which significantly increases both morbidity and mortality compared to other forms of inflammatory myopathies. While there is no standardized treatment regimen, current therapeutic strategies are generally focused on combination immunosuppressive therapies. Despite early diagnosis and immunosuppressive therapy, the disease remains highly aggressive and is associated with a poor prognosis.

Case report: This report describes the case of a 63-year-old previously healthy male who developed acute interstitial pneumonia. Polymerase chain reaction testing for pneumonia pathogens and routine autoimmune antibody screening were both negative. Despite treatment with corticosteroids and broad-spectrum antibiotics, the patient's condition continued to deteriorate. A multidisciplinary team was assembled, and a myositis antibody panel was ordered, which led to the diagnosis of anti-MDA5 associated clinically amyopathic dermatomyositis. The patient was initiated on treatment with cyclophosphamide, intravenous immunoglobulin, and a calcineurin inhibitor. However, his condition remained critical, and he ultimately succumbed to respiratory failure.

Conclusion: In all cases of rapidly progressive interstitial pneumonia of unclear aetiology, anti-MDA5-associated interstitial lung disease should be considered, regardless of the presence or absence of extrapulmonary manifestations. Despite early recognition and aggressive immunosuppressive therapy, patients with anti-MDA5-associated rapidly progressive interstitial lung disease face a mortality risk of up to 80%. A multidisciplinary approach, with collaboration between specialized centres, is crucial for early diagnosis and timely initiation of treatment.

KEYWORDS

Acute interstitial pneumonia, amyopathic dermatomyositis, anti-MDA5

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LEARNING POINTS

- Anti-melanoma differentiation-associated protein 5 (anti-MDA5) associated clinically amyopathic dermatomyositis (CADM) is an extremely rare disease associated with significantly higher morbidity and mortality compared to other inflammatory myopathies.
- This report describes a unique case of a patient who presented with an acute interstitial pneumonia and rapidly progressing respiratory failure due to an undiagnosed anti-MDA5 amyopathic dermatomyositis, without any of the typical dermatomyositis symptoms or physical exam findings.
- Diagnosis of anti-MDA5 amyopathic dermatomyositis is challenging and standardized treatments for this disease have not been fully developed, which highlights the importance of multidisciplinary approach and collaboration between medical centres.

INTRODUCTION

Clinically amyopathic dermatomyositis (CADM) is a rare subtype of idiopathic inflammatory myositis, frequently associated with autoantibodies targeting melanoma differentiation-associated protein 5 (MDA5). Anti-MDA5 dermatomyositis accounts for less than 2% of all idiopathic inflammatory myopathies in Europe[1]. The disease was initially described in Japan, where it was discovered that the antigen targeted by the antibodies, MDA5, is a protein involved in the innate immune response to viral infections and is encoded by the melanoma differentiation-associated gene 5. Anti-MDA5 dermatomyositis is commonly characterized by distinctive mucocutaneous and systemic features, including skin ulcerations, palmar papules, arthritis, and interstitial lung disease. Rapidly progressing interstitial lung disease (RP-ILD) is a particularly severe complication of this condition, often associated with rapid progression and poor prognosis. In rarer cases, RP-ILD associated with anti-MDA5 may occur in the absence of both muscle and skin involvement. Currently, there are no epidemiological data on MDA5-associated RP-ILD in patients without either skin or muscle involvement.

The diagnosis of myositis-related acute interstitial pneumonia can be particularly challenging, and this challenge is especially pronounced when the hallmark skin or muscle manifestations are absent, or when there is no prior history of idiopathic inflammatory myopathies. Consequently, despite the high mortality rate, diagnosis is often delayed, highlighting the need for increased awareness of this condition.

Although the disease course is typically severe and carries a high mortality risk, there is no established standard of care. Recent studies and case reports suggest that early intervention with combined immunosuppressive therapy and corticosteroids may improve outcomes if initiated promptly after symptom onset.

This case report describes a 63-year-old previously healthy male diagnosed with anti-MDA5 amyopathic dermatomyositis and RP-ILD, in the absence of both muscle and skin involvement. It highlights the importance of early diagnosis and underscores the aggressive nature of the disease.

CASE DESCRIPTION

A 63-year-old previously healthy male was admitted to hospital on January 21, 2024, complaining of progressive shortness of breath, weakness and a fever reaching 39°C over the past 4 weeks. His symptoms began in late December initially presenting as general malaise, which progressively worsened. During this period the patient had an unintentional weight loss of approximately 6 kg. He had no known comorbidities and was not on any medications. He was an ex-smoker (5-6 pack-years) who had quit smoking some years ago.

On January 9 an outpatient chest X-ray (CXR) revealed bilateral basal bronchopneumonia, and he was started on antibacterial therapy without improvement. Upon admission the patient reported continued weakness and shortness of breath. On physical examination bilateral basal dry crackles were heard on chest auscultation. His oxygen

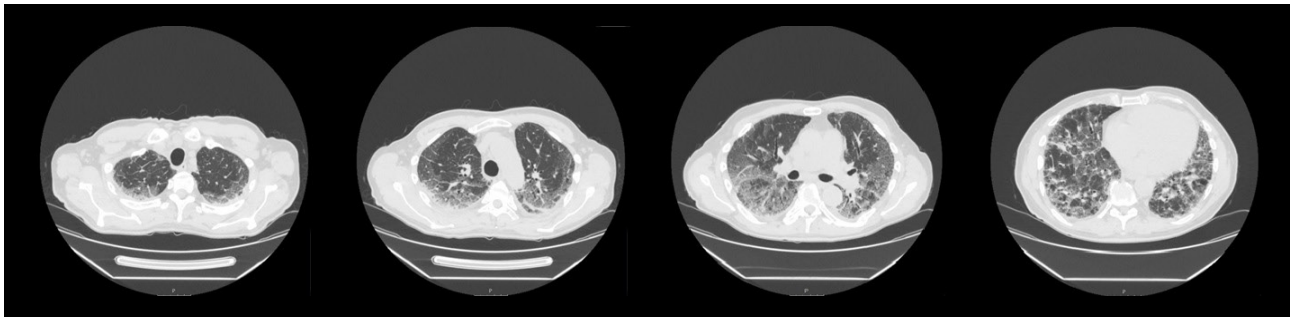

Figure 1. Computed tomography scan of the patient's lungs showing ground-glass opacities predominantly in the peripheral lung regions, with associated thickening of the pulmonary interstitium. Gas trapping is observed in the basal lung areas.

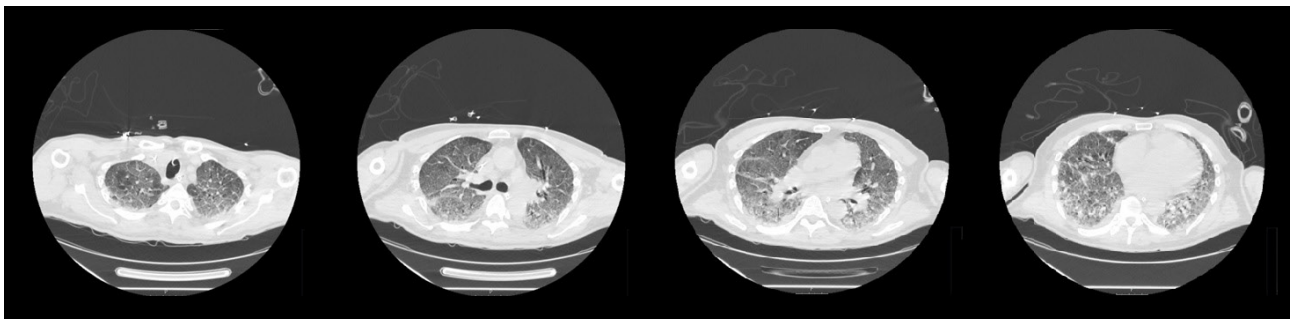

Figure 2. Repeat computed tomography scan of the patient's lungs shows progressive worsening of pulmonary changes, both in intensity and extent, now diffuse in nature. Evidence of pulmonary artery thromboembolism is seen in multiple branches of the pulmonary arteries.

saturation was 95% on a high-concentration oxygen mask. He denied any history of animal exposure, medication use or a family history of a chronic lung disease. The patient had no signs of skin rashes or any musculoskeletal symptoms. A computed tomography (CT) scan was performed, showing signs of interstitial lung disease *(Fig. 1)*. Laboratory tests revealed elevated C-reactive protein levels (93 mg/l), though leucocytosis was absent. The patient was started on therapy with intravenous methylprednisolone 250 mg daily, piperacillin/tazobactam 4.5 g every 6 hours, and oral clarithromycin 500 mg twice daily. Polymerase chain reaction (PCR) for pneumonia pathogens and routine autoimmune antibody screening were negative. Blood tests showed no significant changes, but respiratory failure worsened, prompting the initiation of high-flow nasal cannula therapy. A multidisciplinary team convened, and an extended autoantibody screening *(Table 1)*, including a myositis antibody panel *(Table 2)*, was ordered.

Test	Result	Normal range
Complement		
C3c (g/l)	1.13	0.9-1.8
C4 (g/l)	0.32	0.1-0.4
Antibodies against cell antigens		
ANA screening in HEp-2 cells (IFA)	Negative	Negative
ENA	Negative	Negative
Antibodies against dsDNA (IU/ml)	< 9.8	0-26.9
ANCA		
P-ANCA	Negative	Negative
C-ANCA	Negative	Negative
Atypical ANCA	Negative	Negative
Antibodies against MPO (IU/ml)	< 0.96	0-5.9
Antibodies against PR3 (IU/ml)	< 0.6	0-4.9
Antibodies against phospholipids		
Antibodies against cardiolipins screening (U/ml)	5.75	0-10
Rheumatoid arthritis antibodies		
Antibodies against CCP IgG (U/ml)	< 0.5	0-5
Rheumatoid factor, IgA (U/ml)	9.2	0-19.9

Abbreviations: C3c, complement component 3c; C4, complement component 4; ANA, antinuclear antibody; IFA, indirect immunofluorescence assay; ENA, extractable nuclear antigen antibodies; dsDNA, double stranded deoxyribonucleic acid; ANCA, antineutrophil cytoplasmic antibodies; P-ANCA, perinuclear antineutrophil cytoplasmic antibodies; C-ANCA, cytoplasmic antineutrophil cytoplasmic antibodies; MPO, myeloperoxidase; PR3, proteinase 3; CCP, cyclic citrullinated peptide.

Table 1. Extended autoantibody screening.

On January 24 the patient's condition deteriorated rapidly with increasing respiratory failure requiring invasive mechanical ventilation. CT scan revealed acute respiratory distress and pulmonary artery thromboembolism *(Fig. 2)*. The extended myositis antibody panel returned strongly positive for antibodies against melanoma differentiation-associated protein 5 (MDA5) *(Table 2)* leading to diagnosis of anti-MDA5-associated amyopathic dermatomyositis with RP-ILD (the diagnosis was established within 48 hours of the patient's admission). Treatment with cyclophosphamide and intravenous immunoglobulin was started.

Despite the therapy, the patient's condition continued to deteriorate with worsening of respiratory failure. On January 30th a multidisciplinary team was convened again and based on available studies, literature reviews and recommendations from other major centres, it was decided to add the calcineurin inhibitor tacrolimus to the treatment regimen. Despite all therapeutic interventions, the patient's condition continued to deteriorate with progressive respiratory failure. On February 4th the patient ultimately succumbed to his illness.

DISCUSSION

The diagnosis of CADM-associated acute interstitial pneumonia is extremely challenging, especially in cases when a patient does not have characteristic skin or muscle manifestations or a history of idiopathic inflammatory myopathy. Interstitial lung disease is the most important systemic complication in anti-MDA5 dermatomyositis because it may have a rapidly progressive and fatal course[2]. This case highlights the rapid and aggressive progression

Test	Result
Antibodies against Mi-2 alpha	Negative
Antibodies against Mi-2 beta	Negative
Antibodies against TIF1g	Negative
Antibodies against MDA5	**Strongly positive**
Antibodies against NXP2	Negative
Antibodies against SAE1	Negative
Antibodies against Ku	Negative
Antibodies against PM-Scl100	Negative
Antibodies against PM-Scl75	Negative
Antibodies against Jo-1	Negative
Antibodies against SRP	Negative
Antibodies against PL-7	Negative
Antibodies against PL-12	Negative
Antibodies against EJ	Negative
Antibodies against OJ	Negative
Antibodies against Ro-52	**Weakly positive**
Antibodies against cN-1A	Negative

Table 2. Extended myositis antibody panel.

of the disease despite intensive immunosuppressive therapy and highlights the importance of early recognition. Standardized treatments for patients with RP-ILD have yet to be fully established and are mainly based on case reports and retrospective studies. A combination of high-dose glucocorticoids and calcineurin inhibitors with or without cyclophosphamide is typically the first-line treatment[3]. Even with early disease detection and high levels of immunosuppression the risk of mortality is up to 80%[4]. A multidisciplinary approach, with collaboration between specialized centres, is crucial for early diagnosis and timely initiation of treatment.

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