Unveiling the Complexities: A Case Report on Anti-MDA5 Amyopathic Dermatomyositis and Its Clinical Implications and Therapeutic Challenges.

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Background

Dermatomyositis, an inflammatory myopathy, typically unveils itself through a characteristic rash that often accompanies or precedes muscle weakness.[1] Among its variations is Anti-melanoma differentiation-associated gene 5 (MDA5) dermatomyositis (DM), a subtype recognized relatively recently in a 2005 study involving a Japanese cohort. MDA5 antibodies play a pivotal role in the antiviral mechanism of innate immunity, leading to speculation that viral infections may serve as a trigger for the autoimmune response seen in this particular subtype.[2]

Clinical features of MDA5 DM differ from the conventional dermatomyositis presentation, adding complexity to its diagnosis. Alongside typical dermatomyositis symptoms, patients may present with palmar papules, panniculitis, arthritis, mucocutaneous ulceration, and nonscarring alopecia.[3] Classified as amyopathic dermatomyositis, this subtype rarely involves muscle symptoms but carries a markedly increased risk of rapidly progressive interstitial lung disease, which significantly impacts mortality rates. Given the high mortality rate, timely diagnosis and intervention are imperative to optimize patient outcomes.

Case Presentation

A 44-year-old woman with a prior history of contact dermatitis, unspecified allergies, and undifferentiated inflammatory arthritis presented for evaluation of acute respiratory symptoms. She had been seen in our office several times over the past year for what was thought to be a contact dermatitis, environmental allergies, and diffuse joint pain. She was referred to Rheumatology and an extensive outpatient evaluation was inconclusive. Treatment for an undifferentiated inflammatory arthritis was initiated and initially her symptoms were well controlled on hydroxychloroquine and adalimumab. She was also seen by an Allergist who started her on dupilumab. Upon presentation, she reported a non-productive cough with fevers starting a few days prior. On physical exam, vital signs were stable, she was afebrile, lungs were clear to auscultation bilaterally. She had a diffuse erythematous rash present on her face, chest, and extremities, with associated alopecia. The rash was painless and nonpruritic.

The diffuse rash was suspected to be secondary to adverse effects from her dupilumab, and she had follow-up appointment scheduled with her Allergist. Addressing her acute concerns, an outpatient chest x-ray and lab work were completed. X-ray revealed diffuse interstitial opacities and bronchial wall thickening, suggesting an atypical or viral pneumonia. With her X-ray findings and continued worsening respiratory status, she presented to the Emergency Department for further evaluation.

Initial work up in the ER included a CT scan of the chest which ruled out a pulmonary embolism, but it did reveal nonspecific diffuse ground glass opacities throughout the lung fields and enlarged mediastinal and bilateral axillary lymph nodes. Intravenous antibiotics were initiated to cover a suspected atypical pneumonia. Subsequent sputum cultures and PCR testing were positive for Pseudomonas fluorescens and Pneumocystis jirovecii. Despite adjustments to antibiotic therapy for more targeted treatment, her symptoms worsened. Drug-induced pneumonitis was considered, but adalimumab is rarely associated, and dupilumab was typically linked with eosinophilic disease which the patient did not exhibit. Further lab work revealed a positive ANA which led to initiation of high-dose intravenous steroid therapy and the completion of an interstitial lung disease (ILD) panel. Testing revealed elevated MDA5 antibody titers suggestive of amyopathic dermatomyositis with rapidly progressive ILD.

Despite aggressive treatment with methylprednisolone, cyclophosphamide, tacrolimus, and baricitinib, alongside plasmapheresis, her respiratory status continued to decline, necessitating intubation. Subsequently, she underwent a tracheostomy for long-term ventilation. Evaluation for lung transplantation was initiated, but her limited functional capacity deemed her ineligible. Opting for palliative care, she eventually succumbed to the disease.

Results

Workup For Suspected Dermatomyositis Associated Interstitial Lung Disease		Patient's Values
Muscle Enzymes	CK/Aldolase	33-75
ANA	Autoimmune condition	**Positive**
Anti-Jo-1	Inflammatory myopathy such as DM or PM	Negative
Anti PL-7 Anti PL-12 MDA5	Myositis-specific autoantibodies associated with ILD	Negative Negative **Positive**
Ferritin	Elevated level suggestive of poor prognosis	**592-1418**

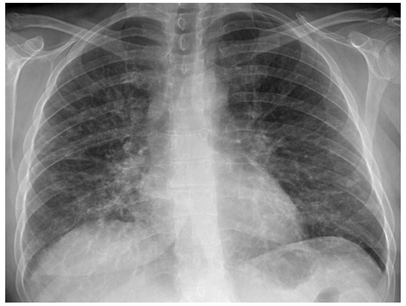

Image A: Pre-admission CXR in the outpatient setting with ground glass opacities.

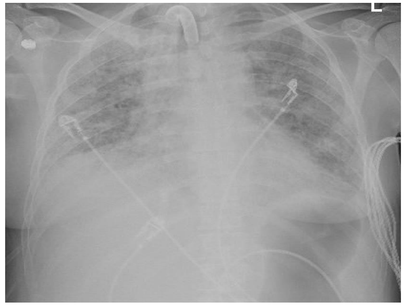

Image B: CXR after admission with evidence of interstitial lung disease.

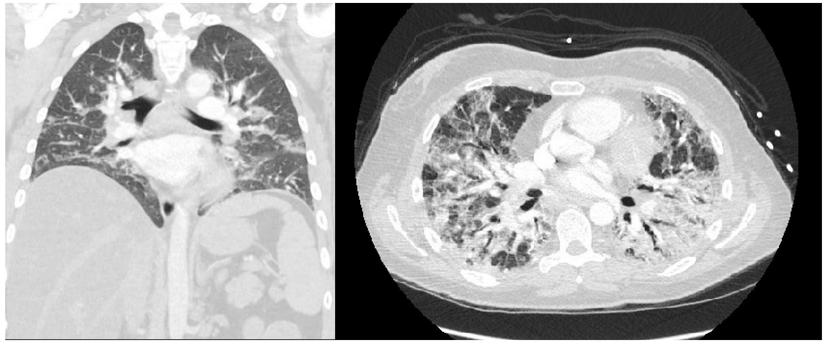

Image C/D: CTA chest on admission with diffuse ground glass opacities consistent with rapidly progressive interstitial lung disease.

Discussion

Anti-MDA5+ dermatomyositis (DM) is a rare autoimmune condition primarily documented in East Asia. Characterized as an amyopathic dermatomyositis, its distinctive presentation includes DM-specific rashes such as the heliotrope rash and Gottron's papules, along with amyopathic or hypomyopathic muscle involvement. Notably, it poses a significant challenge as it is often associated with rapidly progressive interstitial lung disease, leading to markedly high mortality rates. It was only through an ILD panel that Anti-MDA5 was detected, eventually leading to the diagnosis of amyopathic DM with associated rapidly progressive ILD. Additional supportive findings included a positive ANA titer alongside normal levels of muscle enzymes with the absence of muscle weakness.[5] The patient also exhibited characteristic features such as an erythematous rash, alopecia, and arthritis, which were thought to be related to a drug reaction and inflammatory arthritis. DM was not initially suspected due to the atypical presentation of this disease process. Her elevated ferritin levels further underscored the severity of the condition, as high ferritin levels are strongly associated with a poor prognosis.

Current treatment approaches for this disease primarily rely on empirical methods, commonly employing a "triple therapy" of immunosuppressive treatments. This regimen typically includes high-dose glucocorticoids, tacrolimus, intravenous cyclophosphamide, and JAK inhibitor-based therapy.[4] However, despite these efforts, the disease often proves refractory, with continued progression. Ongoing dedicated research is essential to determine the most efficacious treatment regimen, particularly for patients with advanced stages of anti-MDA5 dermatomyositis ILD. Recent studies have shown slightly improved outcomes in cases where successful lung transplantation was performed.[7] Despite treatment, mortality rates remain stubbornly high. Thus, early recognition and consideration of this disease are paramount. Prompt diagnosis and initiation of treatment are crucial for optimizing patient outcomes.

Conclusion

Our patient received a diagnosis of anti-MDA5 dermatomyositis. While individuals with this subtype may exhibit typical dermatomyositis presentations, they occasionally lack the characteristic muscle weakness, complicating diagnosis and potentially delaying treatment. Due to the strong correlation with rapidly progressive interstitial lung disease (ILD), which significantly increases mortality rates, heightened awareness is crucial for prompt diagnosis and intervention. Early recognition and treatment may lead to improved outcomes for patients.

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