IJD Case Report

Clinically amyopathic dermatomyositis during the COVID-19 pandemic

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We report a case of clinically amyopathic dermatomyositis (CADM) with anti-MDA5 positivity associated with rapidly progressive interstitial lung disease. The analogies between CADM-associated interstitial lung disease and coronavirus disease 2019 (COVID-19) pneumonia may hinder the diagnosis and delay the start of immunosuppressive therapy. High-resolution computed tomography revealed an evident worsening of the bilateral consolidation, interlobular septal thickening, and ground-glass opacities, highlighting the diagnosis of rapidly progressive interstitial lung disease. The radiological presentation, combined with the laboratory findings, underscored the diagnosis of CADM. In the following days, the respiratory failure progressed, and the patient required extracorporeal membrane oxygenation and lung transplantation. The typical cutaneous rash of dermatomyositis and non-pulmonary clinical differences can help the physician reach a correct diagnosis. Assessing patients with interstitial lung diseases during the COVID-19 pandemic is difficult. Through experience with systemic autoimmune diseases such as clinically amyopathic dermatomyositis, we can develop new pathophysiology models and therapeutic strategies for COVID-19.

Keywords: COVID-19, SARS-CoV-2, clinically amyopathic dermatomyositis, anti-MDA5

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INTRODUCTION

The major high-resolution computed tomography (HRCT) features of COVID-19 (coronavirus disease 2019) pneumonia resemble those observed in patients with connective tissue disease (CTD)-associated interstitial lung disease (ILD), making it sometimes

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difficult to distinguish between the two diseases. We present a clinical case of clinically amyopathic dermatomyositis (CADM) identified during the pandemic.

CASE PRESENTATION

A 43-year-old man came to our attention in September 2020, complaining of dyspnea with minimal activity, fatigue (but no muscle weakness or myalgia), arthralgia, and persistent low-grade fever. He reported that the clinical manifestations had begun eight months before, with recent worsening. Suspecting COVID-19, several SARS-CoV-2 nasopharyngeal swabs and a bronchoalveolar lavage had been performed during the previous months, all returning negative. He had been admitted twice to other hospitals and, on suspicion of bronchopneumonia, was treated with multiple courses of antibiotics. Chest auscultation revealed diminished vesicular sounds with bibasilar crackles, while the muscle strength test was negative. Respiratory rate was 22 breaths per minute, and oxygen saturation on room air was 94%. Moreover, we observed violaceous papules and plaques over the metacarpophalangeal joints (Figure 1) and elbows associated with acral edema and a purplish facial rash with a "butterfly" pattern.

The lung HRCT scan showed bilateral parenchymal distortion with consolidation areas and ground-glass opacities (GGOs) in the context of ILD (Figure 2). The blood gas analysis showed a pH of 7.46, pO_2 77 mmHg, and pCO_2 33 mmHg. The laboratory findings revealed elevated levels of C-reactive protein (2.40 mg/dl), normal creatine kinase (CK) and aldolase, antinuclear antibody (+, 1:80), anti-ENA antibody (+), p-ANCA (-), c-ANCA (-), anti-dsDNA antibody (-), myositis antibodies (+, anti-melanoma differentiation-associated gene 5). These results, associated with the histopathological examination performed on a skin biopsy (Figure 3), indicated the diagnosis of CADM. The patient was treated with methylprednisolone 1 mg/kg/day combined with intravenous immunoglobulin (0.4 g/kg/day for 5 days) and was discharged with prolonged glucocorticoid (GC) therapy after the improvement of the symptoms and laboratory parameters.

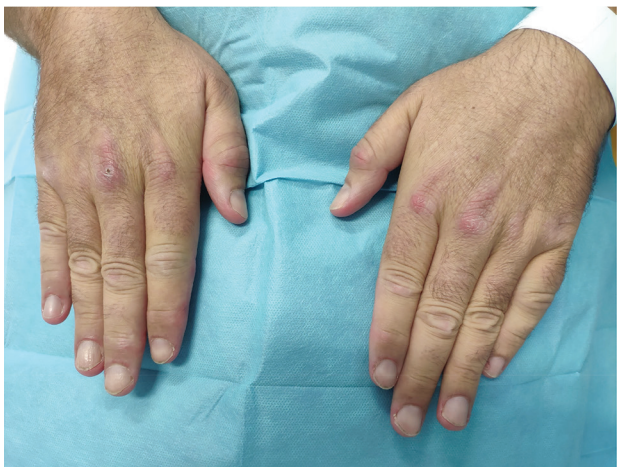

Figure 1. Violaceous papules and plaques over the metacarpophalangeal joints (Gottron's papules)

Two weeks later, the patient was admitted to the respiratory intensive care unit due to the onset of pneumomediastinum and pneumothorax. HRCT revealed an evident worsening of the bilateral consolidation, interlobular septal thickening, and GGOs of the whole lung parenchyma (Figure 2), highlighting the diagnosis of rapidly progressive ILD (RP-ILD), while the PaO_2/FiO_2 ratio was 65. In the following days, the respiratory failure progressed, and he required extracorporeal membrane oxygenation and lung transplantation. At the follow-up visit, the patient showed good clinical status during the anti-rejection therapy, with no signs of disease recurrence.

Ethical statement

This clinical picture respects ethical standards. No funding was involved. The patient's anonymity has been protected.

DISCUSSION

Clinically amyopathic dermatomyositis CADM is a form of highly aggressive dermatomyositis with mild or no muscle weakness or muscle enzyme elevation. Up to 70% of patients with CADM are characterized by a specific antibody known as anti-MDA5 [1] and often affected by RP-ILD [2]. Studies show a six-month survival rate of 28–66% [3–5] due to both rapid progression of lung involvement and frequent drug failure. First-line therapy consists of long-term, high-dose GCs, followed by second-line immunosuppressants: azathioprine, cyclosporine, cyclophosphamide, mycophenolate mofetil, and tacrolimus (often associated with GCs). Intravenous immunoglobulin and immunoadsorption apheresis should also be considered [6].

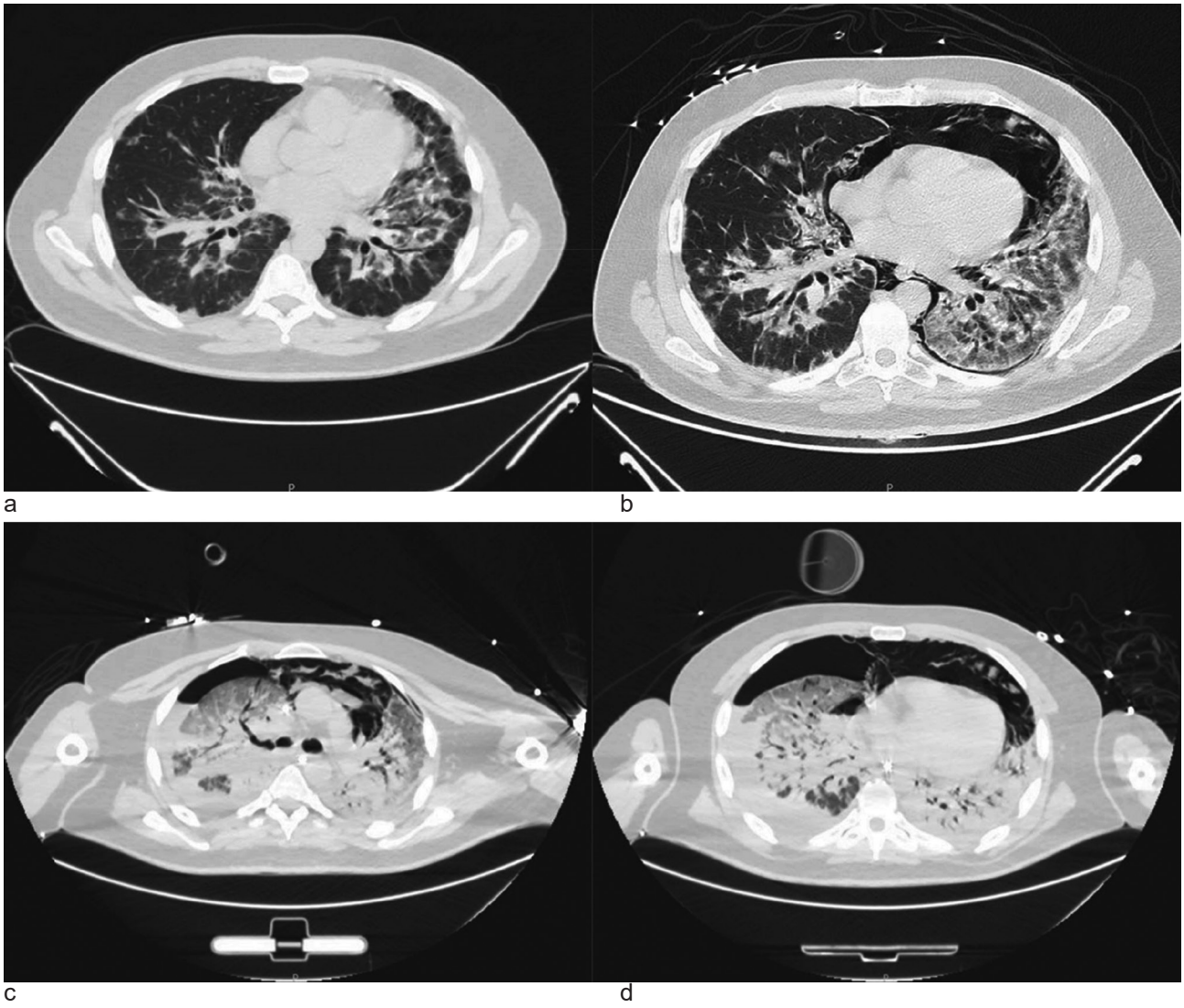

Figure 2. Time course of HRCT images. a) On admission: bilateral parenchymal distortion with consolidation areas and ground-glass opacity, in the context of interstitial lung disease; b) Second admission to RICU: pneumomediastinum with worsening of the bilateral consolidation, interlobular septal thickening and ground-glass opacities; c, d) One week after the second admission: upper and lower lobes, further worsening of the rapidly progressive interstitial lung disease.

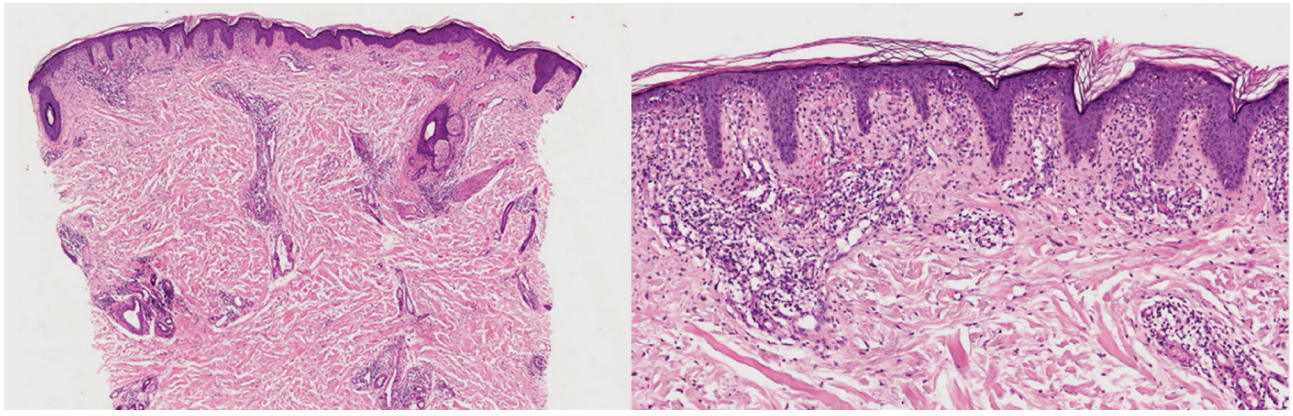

Figure 3. Vacuolar interface dermatitis with thickened basement membrane, papillary dermal edema, perivascular lymphocytic inflammatory cell infiltrate, and mucin deposits in the papillary and middle dermis.

Regarding our patient, an aggressive immunosuppressive triple therapy (GCs, tacrolimus, and cyclophosphamide) was considered, as suggested by several authors [2,5,7]. Unfortunately, it was too late for a medical approach, and a lung transplantation was necessary. In the previous months, the analogies between CADM-associated ILD and COVID-19 pneumonia had hindered the diagnosis, delaying the start of immunosuppressive therapy. In fact, they show many similarities regarding the clinical picture, radiological presentation, and some physiopathological aspects. In particular, besides the well-known similar symptoms, HRCT of COVID-19 patients shows a bilateral, multifocal distribution of GGOs associated with subpleural patchy consolidations, predominantly involving the lower lung lobes [8], analogous to those found in CTD-associated ILD. Moreover, it is believed that they share most of the cytokines involved: abnormally high titers of these cytokines result in an uncontrolled innate and adaptive response, which is key to the development of both CADM-associated ILD and COVID-19 pneumonia [9].

Shahidi Dadras *et al.* suggested strong similarities in the pathogenesis of dermatomyositis and COVID-19, including the role of type I interferons (IFN-1) in causing myofiber and severe organ damage [10]. Therefore, IFN-1 should be considered a sensitive marker for both dermatomyositis disease activity and COVID-19. This evidence may be confirmed through the use of baricitinib, a Janus kinase (JAK) inhibitor that is promising in the treatment of patients with severe systemic involvement due to COVID-19, in addition to the use of tofacitinib for the treatment of dermatomyositis.

In clinical practice, discerning COVID-19 pneumonia and autoimmune ILD has proven difficult. First, we believe repeated nasopharyngeal swabs for polymerase chain reaction tests are necessary. Furthermore, the typical cutaneous rash of dermatomyositis, non-pulmonary clinical differences, and immunological tests can help the physician reach a correct diagnosis. Classic signs of infection, marked lymphopenia, and anosmia point towards COVID-19, while conspicuous elevation of CK and difficulties in swallowing may indicate worsening CADM.

CONCLUSION

We would like to highlight the importance and the difficulties of carefully assessing patients with CTD-associated ILD during the COVID-19 pandemic: delays can compromise survival through the progressive lung damage that affects this subset of patients.

Authors contributions

Fusconi and Muratori participated in the case report conception and design whild Raone and Viviani participated in data collection and draft manuscript preparation. All authors reviewed the results and approved the final version of the manuscript.

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Conflict of Interest: None declared.

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