## Title

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## Journal

Dermatology Online Journal, 30(1)

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## Publication Date

2024

## DOI

10.5070/D330163301

# Three cases of anti-MDA5-positive dermatomyositis with interstitial lung disease and pneumomediastium

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*Keywords: anti-MDA5, anti-RO52, antibody, dermatomyositis, pneumodiastinum*

To the Editor:

Dermatomyositis (DM) is an idiopathic inflammatory myopathy that may be associated with significant systemic manifestations. Most patients have myositis-specific antibodies (MSA) and also myositis-associated autoantibodies, also present in other rheumatic disorders, like anti-nuclear antibodies and anti-Ro52. Myositis-specific antibodies are correlated with specific disease phenotypes, response to treatment, and prognostic implications. For example, positive anti-melanoma differentiation-associated protein-5 (anti-MDA5)-DM is linked with the development of interstitial lung disease (ILD) and rapidly progressive-ILD (RP-ILD) which is associated with a high fatality rate. Identification of the subgroup of anti-MDA5-positive patients with higher risk of developing RP-ILD may help select patients who are good candidates for early aggressive immunosuppressive therapy, which may improve survival [1,2].

We report three cases of acute onset anti-MDA5 positive DM with severe ILD complicated with spontaneous pneumomediastinum, one with a fatal outcome (Table. 1).

Three women, ages 43, 54 and 64 years, with typical cutaneous signs of DM (heliotrope rash, erythema on the V of the neck, the holster and shawl signs, typical Gottron papules and Gottron sign, periungual erythema and cuticular hemorrhages, and signs of cutaneous vasculopathy as palmar erythema with violaceous palmar papules and ulcerations (**Figure 1**) presented to our dermatology clinic. Proximal muscle weakness and high muscle enzymes (creatine kinase and aldolase) were observed in two cases from the onset, although electromyography did not show significant changes. All cases had antibodies to MDA5 (in high titers in patients 1 and 3, and anti-Ro52 in patients 1 and 2. Chest high-resolution CT scan revealed bilateral ground glass opacities in all cases, peripheral fibrosis in patients 2 and 3, and emphysematous changes in patient 2 (**Figure 2A**), but lung function tests were initially within normal limits. Patient 2 and 3 stabilized on prednisolone 1mg/kg, hydroxychloroquine 400mg/day, and oral mycophenolate mofetil 2g/day or methotrexate 25mg/week. Patient 1, who had the highest anti-MDA5 and anti-Ro52 titers, progressed to respiratory insufficiency within one month and developed mechanic hands and erosions/ulcers on the fingers and trunk. Despite i.v. methylprednisolone pulses (1g/day), cyclophosphamide 750mg, mycophenolate mofetil

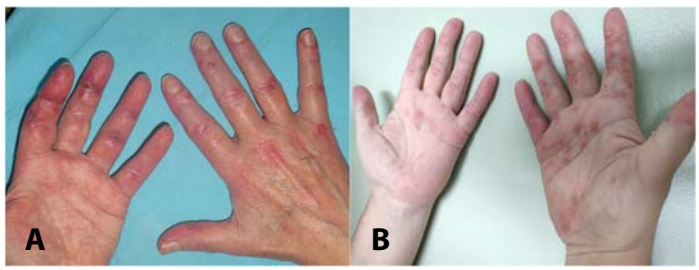


**Figure 1.** *Clinical and radiological features in anti-MDA-5-associated dermatomyositis.* ***A)*** *Ulcerative Gottron and palmar papules.* ***B)*** *Mechanic´s hands.*

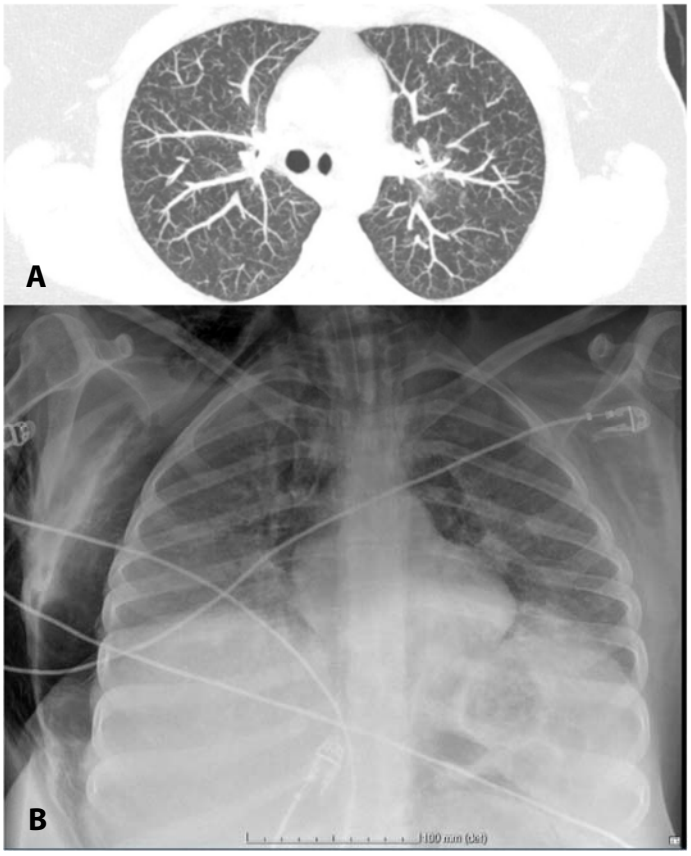


**Figure 2.** ***A)*** *CT showing scan showing bilateral ground glass opacities and emphysematous changes.* ***B)*** *Pneumomediastinum, subcutaneous emphysema and bilateral pneumothorax.*

2g/day, and i.v. immunoglobulin 2g/kg, she further developed pneumomediastinum, pneumothorax, an extensive subcutaneous emphysema (**Figure 2B**), and a nosocomial pneumonia, and died on day 32 of admission. Patients 2 and 3 also developed subcutaneous emphysema and pneumomediastinum (one week after an airplane flight in patient 2), but they resolved after immunosuppressive and conservative therapy and are stable after 8 and 4 years of follow-up, respectively.

Our three patients had the typical cutaneous signs of anti-MDA5positive DM (inverted Gottron papules and ulcerations) and interstitial lung disease complicated with pneumomediastinum. However, a good response to immunosuppressive therapy was observed in two cases whereas another patient developed rapidly progressive-interstitial lung disease with a fatal outcome despite multiple forms of immunosuppressive treatment. Pneumomediastinum is a life-threatening complication that may occur in patients with anti-MDA5-DM and interstitial lung disease. Cutaneous ulcers (ulcerated or inverted Gottron papules) are also associated with an increased risk of this complication [3]. Patients with positive anti-MDA5 and anti-Ro52 antibodies, especially in high titers as seen in case 1, have a higher risk of rapidly progressive-interstitial lung disease and a lower survival rate compared to patients with only anti-MDA5 [4-8]. Coexistence of these antibodies may help identify a subgroup of patients with severe disease, predict prognosis, and possibly guide risk-based therapy as previously shown in very few cases.

## Potential conflicts of interest

The authors declare no conflicts of interest.

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