

Dear Editors,

My colleagues and I are pleased to learn that you are interested in reviewing a revised version of our manuscript (NO: 85673), entitled **“Anti-MDA5 and anti-Ro52 antibody-dual positive dermatomyositis complicated with interstitial lung disease: report of three cases and literature review”**. We modified the paper according to the reviewers' comments. Each comment has been answered accordingly in the manuscript. We appreciate the reviewers' comments, and hope that the revised version will fulfill the requirements for publication in World Journal of Clinical Cases.

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors:

1. Indicate that anti-Ro52 are also named anti-TRIM21 -Table 1 : indicate normal values for each biological parameter-

Response: According to the suggestion of the reviewer, we added normal values for each biological parameter in Table 1

For ANA screening, indicate the pattern of fluorescence observed when positive. This is important because it has been shown recently that a specific MDA5 pattern was associated with a higher risk to develop interstitial lung disease (Coutant F et al: Monoclonal antibodies from B cells of patients with anti-MDA5 antibody-positive dermatomyositis directly stimulate interferon gamma production. J Autoimmun. 2022; PMID: 35436746). This point should be discussed in this manuscript (for instance in the section Discussion: “In clinical, multiple inflammatory indicators such as ferritin IL-18, IL-6, albumin, anti-MDA5 antibody titer, KL-6 and anti-Ro52 antibody, were associated with patient prognosis”). If the MDA5 specific pattern has not been observed with the sera of the 3 patients, then you should discussed why: different ANA technique, etc.

Response : Thank your for your suggestions. We added the pattern of fluorescence observed when positive. Additionally, according to the study of Coutant F et al, we discussed that a specific MDA5 pattern was associated

with a higher risk to develop interstitial lung disease.

In the Discussion section: “However, several particular cutaneous manifestations, such as cutaneous ulceration, painful palmar papules and panniculitis, were thought to be secondary to the development of interstitial lung, especially in the early stage of the disease.” The authors should detail this aspect which is interesting and which is not or little known. -

Response: Thank you for your comments. The clinical manifestations of anti-MDA5 DM differs substantially from the other forms of DM, with three distinct clinical phenotypes, according to the predominance of pulmonary, skin or vascular symptoms, however, the pathogenesis of these three forms of anti-MDA5 DM is largely unknown

In the Discussion section: “Moreover, a recent study showed that the incidence of anti-MDA5 antibody positive was 48.2% in COVID-19 patients[17]. I think that these results should be taken with caution. Indeed, although the titers of anti-MDA5 Abs are statistically higher in the non-survivals infected SARS-CoV-2 patients versus the survivals, the orders of magnitude are very low (5.95 ± 5.16 U/mL vs 8.22 ± 6.64 U/mL, $P = 0.030$). For this aspect, please read the following review: Nombel et al, Dermatomyositis With Anti-MDA5 Antibodies: Bioclinical Features, Pathogenesis and Emerging Therapies. Front Immunol, 2021. PMID: 34745149

Response: thank you for your suggestions. According to the point of Nombel et al, Indeed, although the titers of anti-MDA5 Abs are statistically higher in the non-survivals infected SARS-CoV-2 patients versus the survivals, the orders of magnitude are very low (5.95 ± 5.16 U/mL vs 8.22 ± 6.64 U/mL, $P = 0.030$). anti-MDA5-associated DM have a more higher titers of anti-MDA5 Abs than in COVID-19 patients.

Typos: - Table 1: change "Procalcitonin" - Section Discussion "panniculitis » -
In the following sentence : "It is vital for clinicians to the recognize those
unique cutaneous rashes", delete "the"

Response: thank you for your comments. We have revised above mistakes.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors:

1. Please change the title of the article to reflect the current study's goal(s).

Response: Thank your for your suggestions. We decided to change a new
title: Anti-MDA5 and anti-Ro52 antibody-dual positive clinically
amyopathic dermatomyositis accompanied by rapidly interstitial lung
disease: A case series and literature review.

2. I couldn't find a line in the discussion section that explained the present
study's strengths and flaws. What are the present study's future directions?
I'm hoping to discover satisfactory answers to these three inquiries.

Response: Thank you for your comment. We have added the following
content.

Hererin, the case series first described that the anti-MDA5 and anti-Ro52
antibody-dual positive DM patient should receive accurate and early

diagnosis and aggressive treatment. Moreover, the current study noted that early recognition of CADM cutaneous eruptions, especially anti-MDA5 antibody-associated DM, should be considered. However, several limitations exist. First, due to the small sample size, researchers cannot develop a strong conclusion that is applicable to the general population. Additionally, more detailed data such as clinical features, family history, laboratory results, and long-term outcomes are unavailable. The cases are expected to increase awareness on the rising number of cutaneous eruptions related to anti-MDA5 and anti-Ro52 antibody-dual positive DM, however, to explore characteristic cutaneous lesions and effective treatment, it is necessary to expand the sample size of CAMD patients.

3. The study conclusion should be updated such that it shows if the research problem was handled or whether the current study attained its objectives.

Response: Thank you for your suggestions, we have updated the conclusion.

The case indicates that anti-MDA5 antibody-associated DM patients should receive accurate and early diagnosis and aggressive treatment. Dermatologists should consider monitoring MDA5 and Ro52 Abs while they monitor characteristic cutaneous lesions.

4. Some of the research citations are out of date and should be updated. Please

update out-of-date references with those that are less than five years old as of 2023.

Response: Thank you for your comments. We have updated out-of-date references.

5. I have a question: are the radiological images used in the present study the author(s)' own work, or were they come from somewhere else? Please respect the property rights of other parties if derived from other sources.

Response: Thank your for your suggestions. Radiological images used in the present study are our own work, and the patients or family member in this case have given written informed consent. Additionally, we can provide the original radiological images.