RHEUMATOLOGY ADVANCES IN PRACTICE

Letter to the Editor (Case report)

Rheumatology Advances in Practice 2020;0:1–3
doi: 10.1093/rap/rkaa068
Advance Access Publication 17 November 2020

Complication of coronavirus disease 2019 during remission induction therapy against anti-MDA5 antibody-positive dermatomyositis

Key message

- Severe acute respiratory syndrome coronavirus 2 infection might not be exacerbated during intensive immunosuppression, but viral clearance is delayed.

Dear Editor, the coronavirus disease 2019 (COVID-19), a respiratory infection caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), originated in and spread from Wuhan city, Hubei Province, China, in December 2019. In patients with severe COVID-19, conditions similar to those of macrophage activation syndrome (MAS) and increased blood levels of inflammatory cytokines, such as IL-6 and TNF-α, have been reported [1, 2].

Anti-MDA5 antibody-positive DM is a refractory rheumatic disease, and in 50–80% of cases a severe, rapidly progressive interstitial pneumonia develops as a complication [3]. Hyperferritinaemia, a marker of MAS, is a primary pathological feature of the disease [4]. In addition to high-dose CS therapy, calcineurin inhibitor and CYC triple immunosuppression therapy was recommended in a previous report [5]. Although this treatment has been established, the 6-month survival after diagnosis is only 75% [3].

A 46-year-old woman was diagnosed with interstitial pneumonia developing as a complication of anti-MDA5 antibody-positive DM in February 2020 (Fig. 1A). Remission induction therapy with 3 days of CS pulse therapy (methylprednisolone, 500 mg/day) and post-therapy prednisolone, 50 mg/day + i.v. CYC pulse therapy + tacrolimus, 4 mg/day triple therapy was administered. Improvement of interstitial pneumonia (Fig. 1B) and decreased anti-MDA5 antibody titre was confirmed (950 → 65 INDEX; cut-off 32 INDEX), and the patient was discharged after four cycles of i.v. CYC (750 mg/dose). The patient was scheduled to undergo further i.v. CYC.

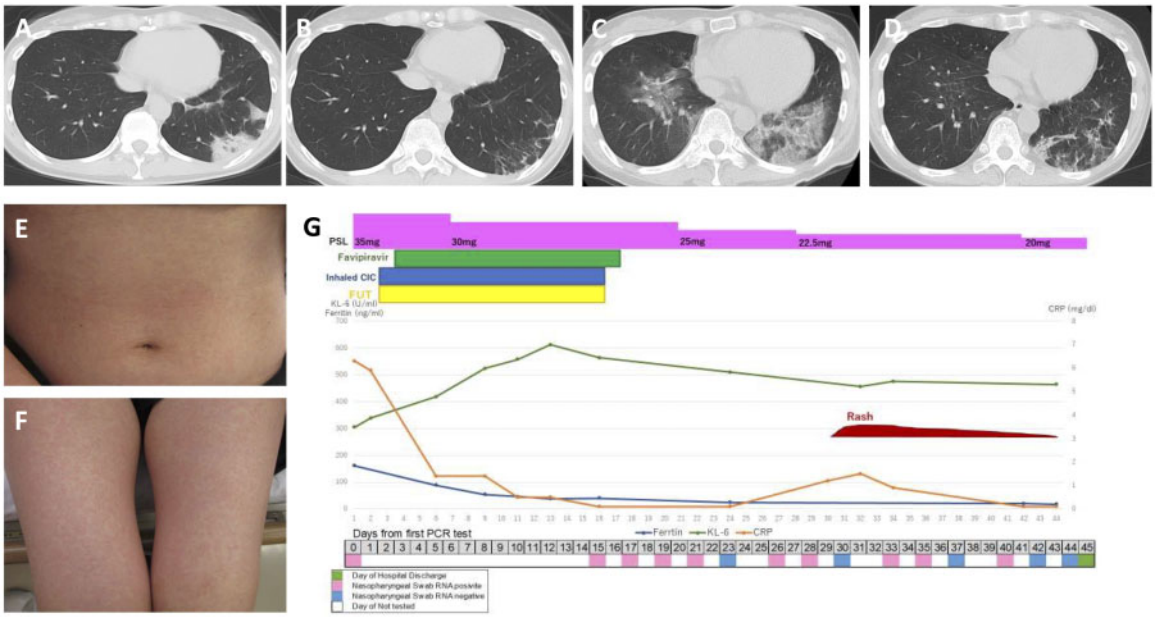
A non-productive cough was noted from 23 April, and the patient visited our hospital on 6 May. Plain chest CT showed bilateral, non-segmental, diffuse ground-glass opacity (Fig. 1C). Oxygen saturation using a 2 litre nasal cannula was 96%. Blood tests at admission revealed low lymphocyte count (299.2/μl), an inflammatory reaction (CRP, 6.3 mg/dl) and hypercoagulability (D-dimer, 2.63 μg/ml). The ferritin level was within the reference range (160.8 ng/ml) but fluctuated at ∼40 ng/ml before admission, suggesting a mild increase. Anti-MDA5 antibody titres were 37 INDEX and continued to show an improving trend.

On day 2 of hospitalization, the patient was confirmed to be SARS-CoV-2 positive after a PCR test (nasopharyngeal swab sample) and was diagnosed with COVID-19. Treatment was initiated with favipiravir, nafamostat and inhaled ciclesonide, and continued for 14 days. On day 5 of hospitalization, oxygen therapy was discontinued. On day 16 of hospitalization, plain chest CT showed reduced findings of pneumonia (Fig. 1D). On the same day, PCR tests were initiated and performed every alternate day. According to the hospital protocol at that time, two consecutive negative nasopharyngeal swab PCR test results were necessary for discharge, because there had been two instances of the PCR test showing a positive result after a negative result, twice during the hospital stay (on hospital days 24 and 29). On day 29 of hospitalization, erythematous papules appeared on the trunk and limbs (Fig. 1E and F). Various virus antibody tests for CMV, EBV, HSV and herpes zoster virus showed negative results, suggesting that the eruptions were caused by COVID-19. Subsequently, the eruptions improved spontaneously. On day 43 of hospitalization, the second consecutive PCR test was negative, and the patient was discharged on day 46 (Fig. 1G).

In this patient, after the onset of DM in February 2020, remission induction therapy was initiated in the early phase (the only symptoms were skin lesions and slight arthralgia); hence, the symptoms of respiratory failure, CT findings of pneumonia, and serum ferritin levels were more prominent at the time of onset of COVID-19 (Fig. 1A and C). In a lot of reports, anti-MDA5 antibody-positive DM and severe COVID-19 have much in common at the point of rapid progressive respiratory failure and hyperferritinaemia, suggestive of MAS. Although the infection developed under intense immunosuppression, the patient's condition improved while the symptoms were still mild. A recent study showed that dexamethasone therapy for severe COVID-19 infection reduced the mortality rate [6]. Hence, similarities between the pathologies of severe COVID-19 that involves MAS and severe rheumatic diseases, including anti-MDA5 antibody-positive DM, were suggested. Furthermore, immunosuppressants could be protective against secondary antibody-mediated organ damage in SARS-CoV-1 (a form of coronavirus close to the one responsible for COVID-19) [7]. This indicates the rationale of using immunosuppressive therapies in COVID-19 that are used in anti-MDA5 antibody-positive DM.

With respect to CS administration, a retrospective observational study on Middle East Respiratory Syndrome

Fig 1. CT images and post-admission course in 2020 (coronavirus disease 2019)



(**A**) CT at admission in February 2020 (DM): showing infiltrative shadow in the left lower lobe. (**B**) CT at discharge in April 2020. (**C**) CT at admission in May 2020 (coronavirus disease 2019), showing diffuse non-segmental ground-glass opacity in the right middle lobe and lower lobe and left upper and lower lobes. (**D**) CT on day 16 of hospitalization. Compared with CT findings at admission, CT findings of pneumonia were reduced. (**E**, **F**) Erythematous papules on the trunk and limbs. (**G**) Post-admission course. CIC: ciclesonide; FUT: nafamostat mesylate; PSL: prednisolone.

(MERS) showed a relationship with delayed clearance of the viral RNA from airway secretions [8]. In our patient also, there was a delay of 42 days for the PCR test result to turn negative.

We treated a patient with anti-MDA5 antibody-positive DM complicated with COVID-19 pneumonia during remission therapy. The patient followed a good course, without signs of exacerbation of the rheumatic disease during intense immunosuppression therapy; however, the PCR results turned negative after a prolonged duration.

Acknowledgements

We are grateful to Ms Kazumi Goto for secretarial assistance.

Funding: No specific funding was received from any funding agency in the public, commercial or not-for-profit sectors to carry out the work described in this manuscript.

Disclosure statement: The authors have declared no conflicts of interest.

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