Successful treatment with tocilizumab in a patient with rapidly progressive interstitial lung disease with positive anti-melanoma differentiation-associated gene-5 antibody

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To the Editor: Anti-melanoma differentiation-associated gene 5 (MDA-5) positive interstitial lung disease (ILD) is featured by rapidly progressing respiratory failure and limited hospital survival. No standard therapy has been established or proven to be beneficial. Herein, we report a case of a rapidly progressing patient diagnosed of ILD with positive anti-MDA-5 antibody receiving tocilizumab treatment.

A 63-year-old lady with past medical history of hypertension presented with dry cough and dyspnea. Fever, rashes, arthralgia, muscle weakness or myalgia was denied. She presented with normal blood routine test and normal serum high sensitivity C reactive protein (hsCRP). Chest computed tomography (CT) scan revealed bilateral ground-glass opacity. Lung needle biopsy demonstrated organizing pneumonia [Figure 1A]. She was instructed to receive oral methylprednisolone of 40 mg/d for two weeks and tapered by 4 mg each week. However, she was transferred to emergency room for worsening hypoxemia. Laboratory tests of blood routine test, urinalysis, liver and kidney function, and creatine kinases were normal [Supplementary Table 1, http://links.lww.com/CM9/A389]. She had positive antinuclear antibody at titer of 1:80 with homogeneous pattern, positive anti-MDA-5 antibody and anti-Ro52 antibody.

The patient was diagnosed of ILD and received high-dose intravenous methylprednisolone (160 mg/d for 2 weeks) as well as intravenous immunoglobulin (20 g/d for 5 days) at ICU admission. However, her conditions deteriorated and she required invasive ventilation 3 days later. Intravenous tocilizumab was administrated at a single dose of 8 mg/kg at Day 7, Day 13 and Day 19 with glucocorticoids treatment. Intravenous cyclophosphamide (CTX, 0.2 g every 2 days) was additionally given at Day 7.

The patient was extubated after 14 days of invasive mechanical ventilation support and two doses of tocilizumab, with the third dose given after extubation [Figure 1B]. Glucocorticoids was tapered and switch to oral methylprednisolone. Oral tacrolimus was administrated 4 weeks later. Repeated chest CT scan revealed remarkably ameliorated bilateral pulmonary lesions [Figure 1C]. The patient was discharged after 54 days of hospitalization, with nasal cannula ventilation, oral methylprednisolone of 44 mg/d, oral CTX 50 mg every 2 days, and oral tacrolimus 3 mg/d.

Anti-MDA-5 antibody is a myositis autoantibody associated with rapidly progressive ILD, with 94% in-hospital mortality according to Vuillard and his colleagues,¹⁰ requiring early medical intervention as well as intensive immunosuppressive treatment. Though high-dose glucocorticoids remain the first choice for physicians, no standard treatment for anti-MDA-5 positive ILD is elucidated nor has been proven to be beneficial for refractory respiratory failure.

Tocilizumab is a monoclonal antibody targeting IgG1 subclass of IL-6 receptor, and it is widely used in
autoimmune diseases and cancers. To our knowledge, this is a rare case report of anti-MDA-5 positive ILD presenting with dramatically improved hypoxemia after tocilizumab administration at 8 mg/kg per week for 3 weeks in combination with high-dose glucocorticoids, CTX and tacrolimus. A fluctuation of serum IL-6 was observed before and after tocilizumab administration as previously reported,[2] which could be explained by the release of IL-6 after the blockage of IL-6/IL-6 receptor complex. Rapid decline to normal level in hsCRP after immunosuppressive therapy was also illustrated. However, the relationships between serum IL-6 or hsCRP and disease activity and outcome remain controversial.[2,3] Although further investigations are required to confirm the effect of tocilizumab in ILD with positive anti-MDA-5, in which hospital mortality was almost 100% with the treatment of glucocorticoids and CTX, our study suggested that tocilizumab might be a salvage therapy in treating fatal ILD with positive anti-MDA-5 antibody. Moreover, further studies are needed to investigate the prognostic value of serum IL-6 level.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

Conflicts of interest
None.

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