Clinical Case Report

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Combined usage of extracorporeal membrane oxygenation and double filtration plasmapheresis in amyopathic dermatomyositis patient with severe interstitial lung disease

A case report

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Abstract

Rationale: We report a man with amyopathic dermatomyositis (ADM) complicated by severe interstitial lung disease (ILD) received extracorporeal membrane oxygenation (ECMO) in combination with double filtration plasmapheresis (DFPP). This is the first report of the utility of ECMO in combination with DFPP in ADM related ILD in adults.

Patient concerns: A 48-year-old man who was previously healthy had a 2-month history of cough and shortness of breath, which aggravated in 5 days.

Diagnoses: Amyopathic dermatomyositis and complicated by severe interstitial lung disease.

Interventions: ECMO was giving when the patient suffered acute respiratory failure. Though corticosteroids was giving, primary disease was still developing with relapses of spontaneous pneumomediastinum and pneumothorax. Then, DFPP treatment was initiated.

Outcome: After the treatments above, the patient's clinical condition improved with the reduction of bilateral interstitial infiltrates and improvement of lung compliance. Unfortunately, he discontinued the treatment because of the financial problem.

Lessons: When get a rapid progressive interstitial lung disease for no apparent reason, amyopathic dermatomyositis should be considered, especially with suspected skin lesions. ECMO, in combination with DFPP, should be considered as a supportive therapy and initiated early in patients in acute respiratory failure secondary to ADM-ILD. Prompt initiation of DFPP in dermatomyositis patients with ILD might help reduce the occurrence of spontaneous pneumomediastinum or pneumothorax.

Abbreviations: ADM = amyopathic dermatomyositis, DFPP = double filtration plasmapheresis, DM = dermatomyositis, ECMO = extracorporeal membrane oxygenation, HRCT = high-resolution computerized tomography, ICU = intensive care unit, ILD = interstitial lung disease, JDM = juvenile dermatomyositis, PR-ILD = rapidly progressive interstitial lung diseases.

Keywords: acute respiratory failure, amyopathic dermatomyositis, double filtration plasmapheresis, extracorporeal membrane oxygenation, rapidly progressive interstitial lung disease

1. Introduction

Amyopathic dermatomyositis (ADM) is a unique subset of dermatomyositis (DM) with the pathognomonic skin rash of classic DM, with a little or without clinical and laboratory evidence of muscle involvement.[1] Patients with ADM have a high prevalence of interstitial lung diseases (ILD)[2]; and ILD is the potential fatal condition of ADM, especially the rapidly progressive ILDs (RP-ILD), which is refractory to immunosuppressive therapy and results in acute fatal respiratory failure. RP-ILD is the life-threatening complication and the primary cause of death in patients with ADM.[2,3] Extracorporeal membrane oxygenation (ECMO), one of the most aggressive supportive modalities available, can support gas exchange for patients who fail to conventional mechanical ventilation. It is reasonable to suppose that ECMO may be a perfect choice for patients with ADM complicated by acute fatal respiratory failure. Double filtration plasmapheresis (DFPP) can rapidly remove the pathogenetic antibodies and immune complexes efficiently, which is considered as 1B treatment and strongly recommended in inflammatory muscle diseases.[4] Here we present the case of a

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Ethics committee of Shunde Hospital of Southern Medical University approved this study.

The authors declare no conflicts of interest.

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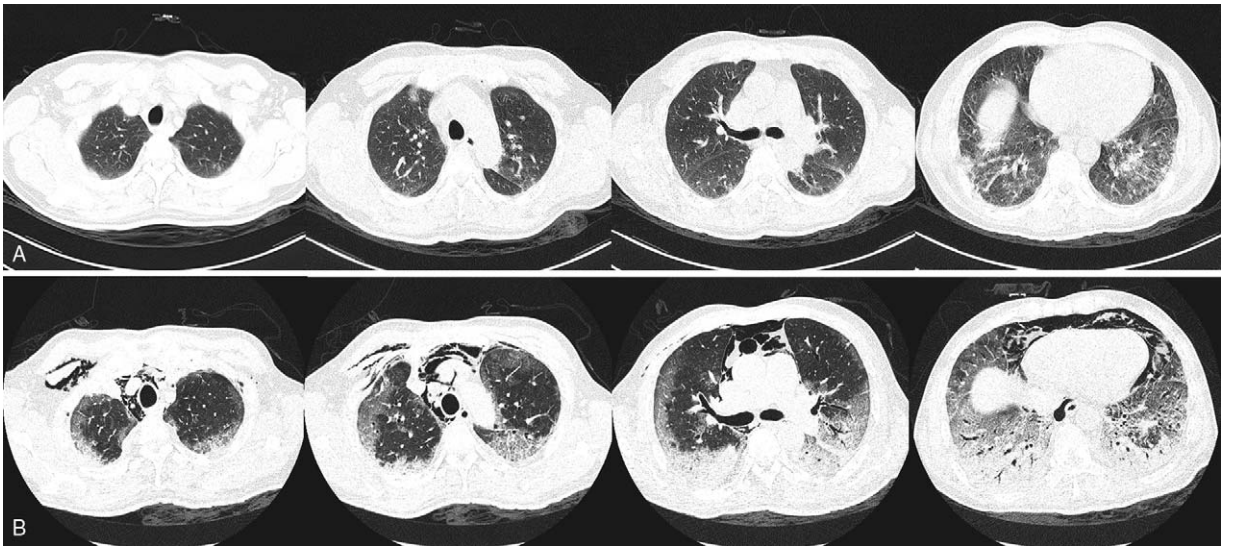

Figure 1. A, Chest HRCT 5 days before admission showing bilateral patchy infiltrations, mainly of the lower lung area, with mild pleural effusion. B, Chest HRCT 6 days after admission showing extensive bilateral ground glass opacities, reticular opacities, consolidation, pneumomediastinum, and subcutaneous emphysema in the right. HRCT = high-resolution computerized tomography.

man with ADM complicated by severe PR-ILD treated with ECMO and DFPP.

2. Case report

A previously healthy 48-year-old man was admitted to the respiratory department of our hospital on August 10, 2015 with a 2-month history of cough and shortness of breath, which aggravated in 5 days. On physical examination, suspicious heliotrope rash on both upper eyelids as well as, unremarkable Gottron's papules over interphalangeal, metacarpophalangeal, and elbow joints were detected; however, he has no manifestation in muscle weakness and myalgia. Laboratory investigations on admission showed: white blood cell count 7.03×10^9/L, hemoglobin 129 g/L, platelets 192×10^9/L, C-reactive protein 40.46 mg/L, procalcitonin 0.5 ng/mL, erythrocyte sedimentation rate 50 mm/h, creatine kinase 45u/L, and creatine kinase isoenzyme MB 20 u/L. Antibodies against Jo-1, ANA, dsDNA, SSA/Ro, SSB/La, ANCA, and U1-snRNP were negative. Arterial blood gas analysis on admission showed pH 7.41, $PaCO_2$ 35.8 mmHg, PaO_2 75.6 mmHg, FiO_2 21%, and PO_2/FiO_2 360 mmHg. Five days before hospitalization, a chest high-resolution computed tomography (HRCT) scan showed bilateral pneumonia, as well as mild bilateral pleural effusion (Fig. 1A).

On the basis of clinical symptoms, laboratory data, and chest HRCT findings, the diagnosis of community-acquired pneumonia and suspected ADM were considered. Treatment with methylprednisolone and antibiotic therapy was initiated. However, the patient's respiratory status exacerbated continuously with an increased dyspnea and hypoxemia that required noninvasive mechanical ventilation on day 5. The chest HRCT scan on day 6 showed an increasing bilateral interstitial infiltrates and pleural effusion, as well as pneumomediastinum and subcutaneous emphysema (Fig. 1B). Thus, he was transferred to the intensive care unit (ICU).

On ICU admission, the patient's arterial gasometry showed: pH 7.44, $PaCO_2$ 36.0 mmHg, PaO_2 62 mmHg, FiO_2 60%, and PO_2/FiO_2 103 mmHg with an EPAP of 8 cmH2O. On day 8, hypoxemia deteriorated further and he was shifted to invasive mechanical ventilation (plateau pressure 35 cmH_2O, rate 25 breaths/min, PEEP 15 cmH_2O, FiO_2 100%, and inspiratory pressure 15 cmH_2O generating a tidal volume between 380 and 420 mL). Prone-position ventilation was also given to ameliorate hypoxia. However, repeated blood gas analysis revealed acute respiratory acidosis and severe hypoxia (pH 7.26, PaO_2 45 mmHg, $PaCO_2$ 63 mmHg, and PaO_2/FIO_2 45). Despite the treatment of lung-protective ventilation, muscle relaxant and prone-position ventilation, the PaO_2/FiO_2 was unable to increase above 60 mmHg. Besides, chest radiography found a new pneumothorax on the left with lung tissue compressed by 30% (Fig. 2A). For the reason above, we decided to support the patient with percutaneous puncture veno-venous ECMO via right internal jugular vein and right femoral vein.

After 10 hours of ECMO support the patient's clinical condition improved considerably. Blood gas analysis showed pH 7.45, PaO_2 71 mmHg, $PaCO_2$ 40 mmHg, FiO_2 60%, and PaO_2/FiO_2 118. Because of the atypical DM rashes and absence of muscle damage, the diagnosis of ADM was not very informative.[5] So we decided to perform the biopsy in patient's left rectus femoris and skin on day 10, which revealed leukocyte infiltration in dermis and muscle bundles, hyperplasia, and focal degeneration of fibrofatty tissue in muscle bundles. A definitive diagnosis of ADM with PR-ILD was made by pathologic consultants from Guangzhou institute of inspiratory disease on the basis of the clinical symptoms, laboratory data, radiologic finds of the lungs, and the biopsy specimens. Treatment with methylprednisolone pulse therapy (500 mg per day) for 3 days was given, and then tapered to 40 mg per day for maintenance. Beside chest radiography showed a complete resorption of pneumothorax and subcutaneous emphysema (Fig. 2B). On day 16, however, the pneumothorax occurred again with the right lung tissue compressed by 85% (Fig. 2C). We considered that might be a manifestation of exacerbation of the primary disease. Immediately, pleural drainage was performed on the right thoracic cavity (Fig. 2D). Simultaneously, he received DFPP treatment to help remove the molecules responsible for ADM on

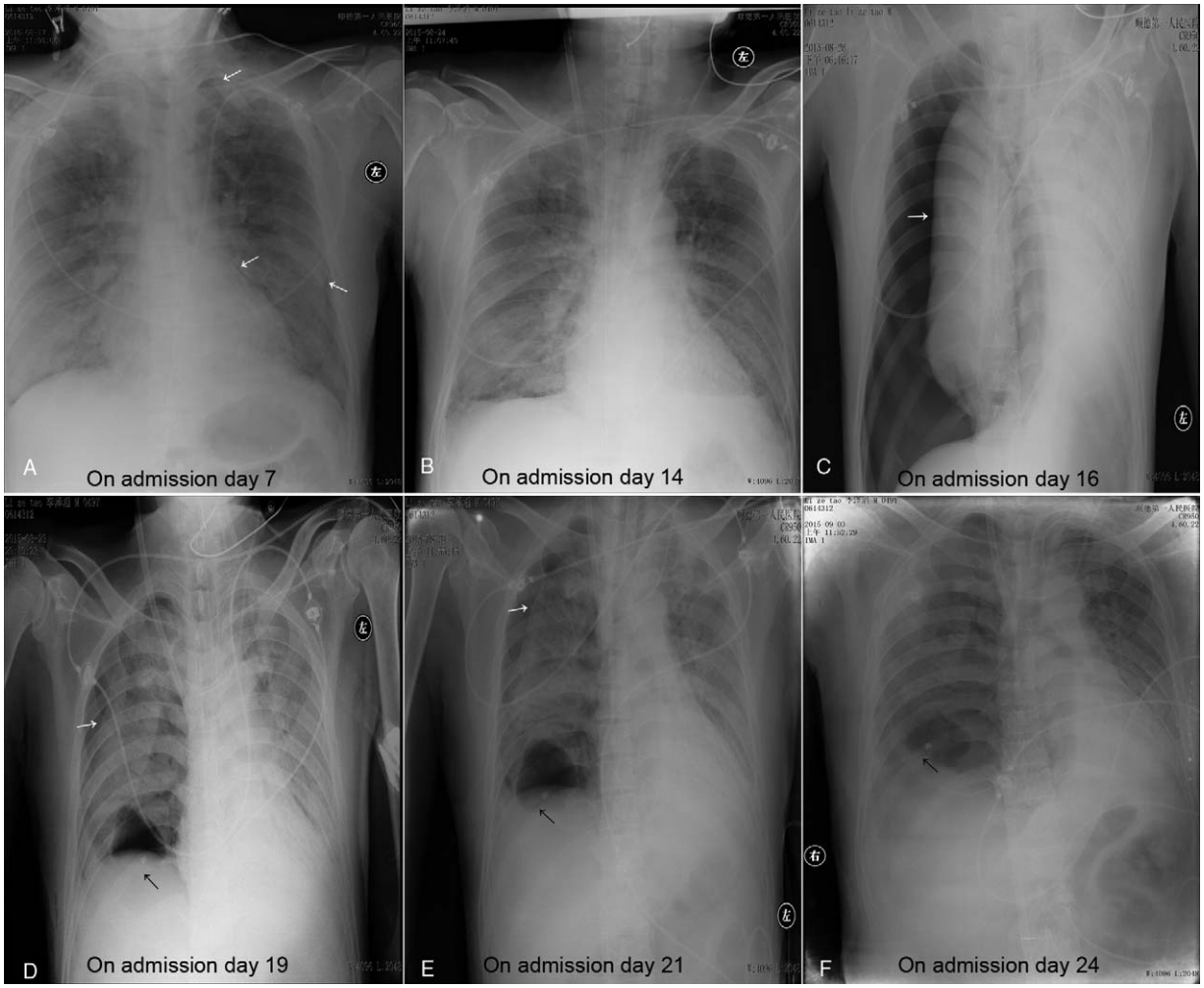

Figure 2. Chest x-rays showing the evolution of the lung changes after admission to ICU, with a reduction of bilateral interstitial infiltrates and a complete resolution of pneumothorax after ECMO and DFPP treatment (B–F). Chest x-ray before initiating the ECMO and DFPP (A). The white arrows indicate pneumothorax, the yellow arrow indicates pneumomediastinum, and the black arrows indicate pleural drainage. DFPP = double filtration plasmapheresis, ECMO = extracorporeal membrane oxygenation, ICU = intensive care unit.

day 20 and 22, respectively. The catheter placement of DFPP was inserted to the ECMO circuit that the arterial side was anterior to oxygenator while the venous side was posterior to it. His clinical condition got ameliorated again (Fig. 2E). On September 3, 2015 (day 24), the chest x-ray showed a reduction of bilateral interstitial infiltrates and a complete resolution of pneumothorax on the right (Fig. 2F) and the lung compliance improved from 23 to 45 mL/cmH_2O. Unfortunately, the patient gave up due to the high costs of treatment on day 25. The patient in our case did not suffer any ECMO-related complications despite he was being supported by V-V ECMO for 396 hours (Fig. 3).

3. Discussion

ADM is a rare, idiopathic, connective tissue disease that presents with characteristic cutaneous manifestations of classic dermatomyositis without muscle involvement.[1] Patients with ADM-ILD show a rapidly progressive course, which is resistant to conventional therapy and frequently fatal within months, especially in East Asia.[6,7] In a recent published retrospective study of 41 Chinese Han patients, the prevalence of acute/subacute ILD in clinically ADM patients was 26.83%; however, the 6-month mortality was up to 55.50%.[8] Another retrospective cohort study even showed a 6-month mortality of 59.2% in 37 ADM patients with PR-ILD.[3] The mortality rate of ADM patients with PR-ILD is high due to an acute fatal respiratory failure, Therefore, more aggressive therapy or temporary life support technology may be required in rapid progressive course in ADM-ILD patients.

ECMO is a direct extension of cardiopulmonary bypass. It's provides a temporary life support in patients with severe but potentially reversible cardiac and/or respiratory failure unresponsive to maximal conventional management.[9] With improved technology and experience over the years, it has undergone substantial changes in its indications. In the past, the presence of a chronic systemic disease was considered a contraindication to ECMO. However, more series of cases showed that ECMO was successfully used in the treatment of acute respiratory failure secondary to systemic lupus erythematosus, systemic vasculitis, or polyangiitis.[10–12] The case reported by Francesco et al[13] found that a 3-year-old girl with severe juvenile DM (JDM) was successfully managed with 5-week ECMO support after developing acute respiratory failure secondary to severe ILD. The girl did not suffer any ECMO-related complications and her pulmonary as

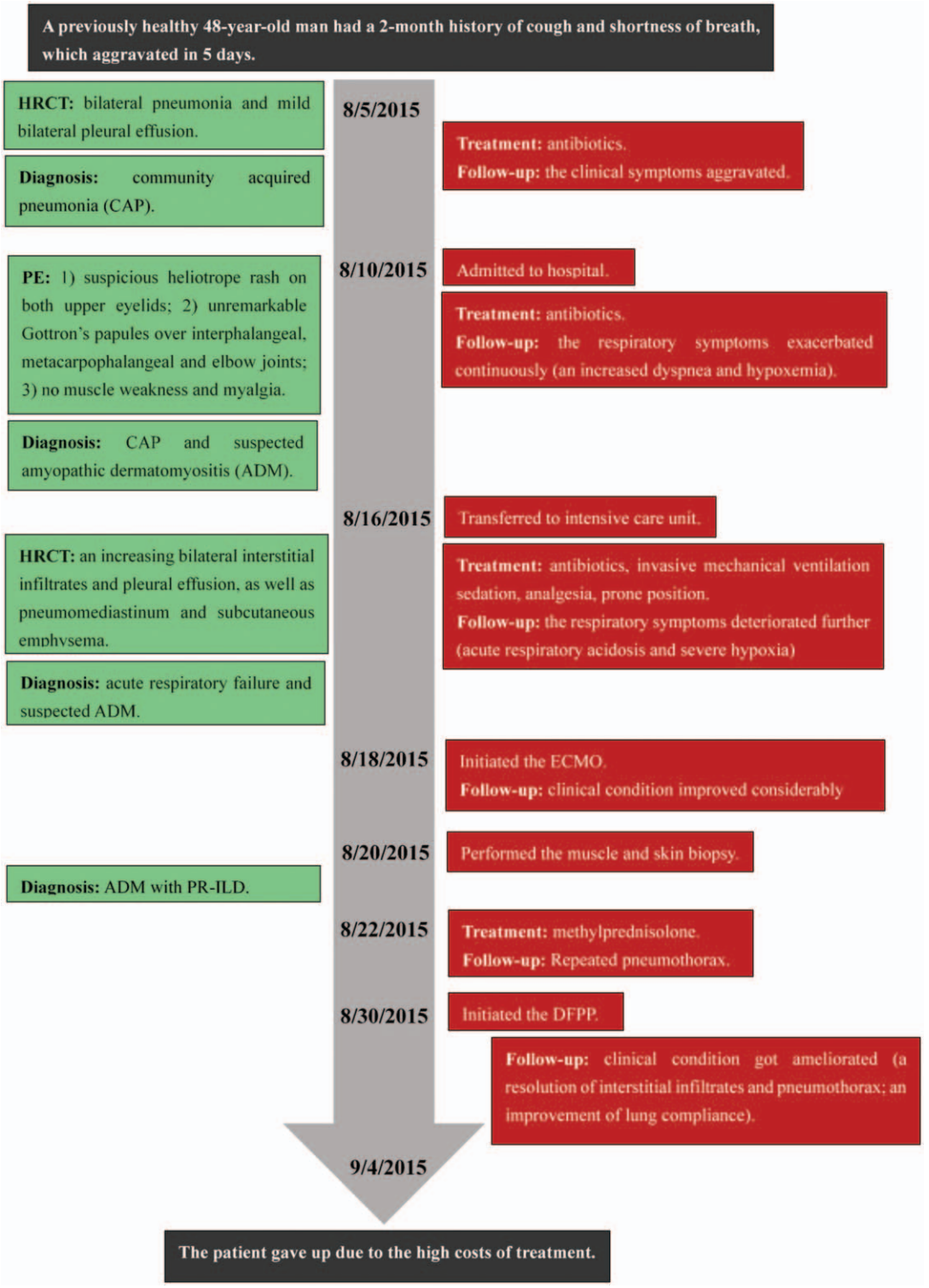

Figure 3. Timeline of the whole clinical diagnosis and treatment process from admission to discharge.

well as neurological function showed normal during her 5-year follow-up. This was the first report of a child with severe JDM related ILD successfully treated with ECMO so far.

In our present case, because of the absence of traditional muscle findings and atypical skin lesions of DM, the diagnosis of ADM can be a challenge. The patient presented firstly with interstitial pneumonia initially, and then developed refractory respiratory failure very quickly. Despite a maximum respiratory support and the corresponding treatment the patient's condition aggravated continuously with a life-threatening hypoxemia. Prompt initiation of ECMO support reversed the severe, life-threatening respiratory complication, and provided an opportunity to perform a muscle biopsy, which helped this patient get a further diagnosis and treatment.

There is no current consensus on the first-line treatment for ADM for that is an inflammatory disease of unclear etiology. Treatments with corticosteroids plus immunosuppressants, antimalarials, or intravenous immunoglobulin have shown to be effective. But usually effects of mention above do not appear as quickly as we expected, especially in an emergent condition. DFPP, an apheresis technique, is an emergency intervention that can be effective and selective to remove a large amount of pathogenetic antibodies and immune complexes. Importantly, it is completely autologous and it saves time till immunosuppression become effective.[4] A previous case reported by Duygu et al[14] shown that a patient in anti-synthetase syndrome with pulmonary involvement who is refractory to immunosuppressive therapy successfully treated with DFPP during the activation period. In our case, the patient occurred relapses of spontaneous pneumomediastinum and pneumothorax with the development of ADM and the ADM-associated ILD, though corticosteroids was giving. Thereby DFPP treatment was initiated. The patient didn't receive immunosuppressants for a consideration of the increasing risk of infection.

To our knowledge, this is the first report of the utility of ECMO in combination with DFPP in ADM related ILD in adults. Our case indicated ECMO has shown to be a valid rescue therapy in acute respiratory failure secondary to ADM-ILD and made further diagnosis and treatment be possible. Although this patient didn't recover his health completely at the end, ECMO made accurate diagnosis and DFPP intervention successfully performed. DFPP is effective and safe to autoimmune diseases, especially in the activation period of the disease. Prompt initiation of DFPP in DM patients with ILD might help reduce the occurrence of spontaneous pneumomediastinum or pneumothorax.

In conclusion, when patients get a RP-ILD for no apparent reason, ADM should be considered, especially with suspected skin lesions. ECMO, in combination with application of DFPP, should be considered as a supportive therapy and initiated early in patients in acute respiratory failure secondary to ADM-ILD, since it could make a true opportunity to improve survival for such rare disease and its potentially deadly complication. The results of our case are promising, but more experience and further studies are needed to evaluate the true value of this method.

Author contributions

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Supervision: Jingcheng Lin, Jianhai Lu, Shuchao Wen, Liuer Zuo.
Writing – original draft: Jiequn Huang, Changzhi Liu.
Writing – review & editing: Liuer Zuo.

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