Successful treatment of plasma exchange for refractory systemic juvenile idiopathic arthritis complicated with macrophage activation syndrome and severe lung disease

We read with great interest the recent article by Saper et al describing high mortality of systemic juvenile idiopathic arthritis (sJIA) patients affected by parenchymal lung disease (LD). LD with sJIA has also been associated with macrophage activation syndrome (MAS). While both MAS and LD complicating sJIA are known risk factors for mortality, an effective therapeutic strategy has not been established. The present case report highlights an exacerbated LD complication in an sJIA patient treated successfully with additional plasma exchange (PE).

A 5-year-old boy was diagnosed with sJIA when presenting with arthritis, prolonged fever and a skin rash. His white cell count (WCC, 8.5×10⁹/L), C-reactive protein (CRP, 4.8 mg/dL), ferritin (467 ng/mL) and interleukin (IL)-18 (25.453 pg/mL) levels were elevated on diagnosis. Initial treatment of oral prednisolone at 18 mg/day and oral methotrexate at 6 mg/week was insufficient.

Oral cyclosporine was started followed by tocilizumab, but clinical remission was still not achieved. He had no respiratory symptoms, but slight pneumonia on chest CT (figure 1A) during biologic agent therapy change screening. He was switched to canakinumab 10 months after the onset of sJIA.

Two months after starting canakinumab, he developed new fever, arthritis and a mild cough. Vital signs were as follows: temperature, 38.2°C; respiratory rate, 20/min, pulse oximetry, 98% SpO₂; room air. A chest X-ray revealed a silhouette sign of the left diaphragm. On admission, blood tests showed a WCC of 10 000/μL with a marked raise in glutamic-pyruvic transaminase (GPT) (63 UI/L), CRP (3.7 mg/dL) and IL-18 (149 269 pg/mL). He also developed hepatosplenomegaly, suggesting progression to MAS. A third chest CT showed progression of consolidation with pleural effusion in both lower lobes, and ground-glass opacities are detected in both upper lobes. (figure 1C) Therefore, PE therapy was performed eight times. After his respiratory condition and fever improved, a progressive pancytopenia occurred. We administered granulocyte-macrophage colony stimulating factor and his neutropenia resolved. At the 2-month imaging follow-up, the chest CT showed decreased degree of peripheral septal thickening and pleural thickening on the left lower lobe (figure 1D). He has remained well, arthritis as well as respiratory condition, for 5 years, and prednisolone (PSL) dose has been reduced to 7 mg/day with infliximab.

Hypercytokinemia plays a key role in the pathogenesis not only of MAS but also LD as complications of sJIA. This case was refractory, and clinical remission could not be achieved, despite using IL-1/IL-6 inhibitors. Treatment guidelines and algorithms for MAS in sJIA still require thorough development, especially when conventional treatments are ineffective. However, after initiation of PE, the patient improved in this study. PE was effective because it rapidly decreased circulating cytokine levels, such as IL-18. The present case demonstrated that combining immunosuppression and PE can be a useful therapeutic strategy for LD and MAS complicated by hypercytokinemia in patients with sJIA.

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