

Dear Editor

Step by Step Improvement of Peripheral Polyneuropathy Associated with Churg-Strauss Syndrome by Six Courses of High-Dose Intravenous Immunoglobulin Therapy

Churg-Strauss syndrome (CSS) is a systemic vasculitis, developing with peripheral blood eosinophilia under a background of an upper respiratory disease. It involves multiorgan systems.¹ Most of the Japanese CSS patients develop the peripheral nervous system, that frequently leaves residual damage as a major clinical problem, although corticosteroids and cyclophosphamide are efficacious.²

Since a good response to high-dose intravenous immunoglobulin (IVIg) therapy was first reported in CSS in 1991, several studies have confirmed its efficacy, particularly for peripheral neuropathy.³⁻⁵ However, the optimal number of courses for the satisfactory treatment has not yet been known.

We treated a case of CSS with severe polyneuropathy successfully by six sequential courses of IVIg.

A 61-year-old female, having suffered from bronchial asthma for 4 years, felt progressive numbness of her extremities, developed drop hands and feet, and became not able to walk at all 3 months before visiting our hospital. On admission to a previous hospital, she had neither fever, skin eruption, nor chest and abdominal abnormalities, but a nerve conduction test of her lower extremities showed reduced amplitudes of action potentials in distal compound muscle and sensory nerves. She was diagnosed as having mononeuritis multiplex. The findings of the manual muscle strength test (MMT) as defined by the Medical Research Council scale are listed in Figure 1. Laboratory data were: peripheral blood white blood cell count, 32,900/ μ L; peripheral blood eosinophil count, 25,470/ μ L; serum C-reactive protein level, 1.0 mg/dL; serum IgE level, 2,327 IU/mL; rheumatoid factor level, 631 U/mL; and negativity for both the myeloperoxidase-specific and proteinase-3-specific anti-neutrophil cytoplasmic antibody, and anti-nuclear antibody. Analysis of bone marrow aspirates revealed reactive eosinophilia. These findings and a history of asthma fulfilled the diagnostic criteria for CSS. Three courses of pulsed methylprednisolone 1 g for 3 consecutive days, followed by oral prednisolone at 1 mg/kg/day and IVIg (S-sulfonated gammaglobulin, Venilon®; Teijin, Tokyo, Japan) at 400 mg/kg/day for 5 days were administered. Her eosinophil count decreased to less than 50/ μ L, IgE level did to 127 IU/mL, and her neurological symptoms stopped progressing further after having extended from the pe-

ripheries to above the elbows and knees, but there was no further improvement and she was transferred to our hospital.

When she was transferred, she had pain, burning sensation, and numbness of her extremities. She had paralyzes most severely in the bilateral common peroneal and radial nerves. MMT findings are listed in Figure 1. Her score in the modified Rankin Scale (mRS), which measures the degree of disability or dependence in daily activities, was 4, which means a moderately severe disability and inability to walk without assistance, although a little improvement from before the first IVIg might be suspected. She had five additional courses of IVIg approximately every 6 weeks, whereas oral prednisolone was tapered from 1 month after its start. During the courses of IVIg, her mRS score improved incrementally course by course. After the second course of IVIg, which was the first in our hospital, she could keep standing just enough by herself. After the third, she was able to walk using foot orthoses and to go to the washroom by herself. After the fourth, she was able to use chopsticks. After the fifth, she was able to walk for 200 meters at a time. After the sixth, she was able to go abroad to take care of her grandchild. Her mRS score became 2, which means slight disability and ability to look after own personal needs without assistance. Her sensory nerve symptoms became less and less severe, localized only to the peripheries of her fingers and toes.

After the sixth course, prednisolone was tapered to 10 mg/day, and her disease activity was still controlled well with the eosinophil count being below 50/ μ L.

Peripheral neuropathy develops in 66-95% of patients with CSS, the most common feature of which being mononeuritis multiplex.⁴ It disrupts patients' activities of daily living, although CSS seldom has a fatal outcome.

Recently, IVIg has been shown to be beneficial for the treatment of CSS-associated neuropathy and cardiopathy.⁴ IVIg is an immunoglobulin preparation fractionated from pooled plasma from healthy volunteers, and is considered relatively safe, even in an infectious condition or during pregnancy.⁶

IVIg does not directly decrease peripheral blood eosinophil count. Some case reports show that the temperature of the extremities measured by thermography increases immediately after IVIg administration.⁵ The improvement of blood flow may contribute to that of CSS-associated neuropathy. Furthermore, IVIg down-regulates transforming growth factor- β and interleukin-4 in mice, which results in the blockage of fibrosis and may suppress the progression of fibrinoid degeneration particularly in small vessels.⁷

Among the 6 types of immunoglobulin preparation

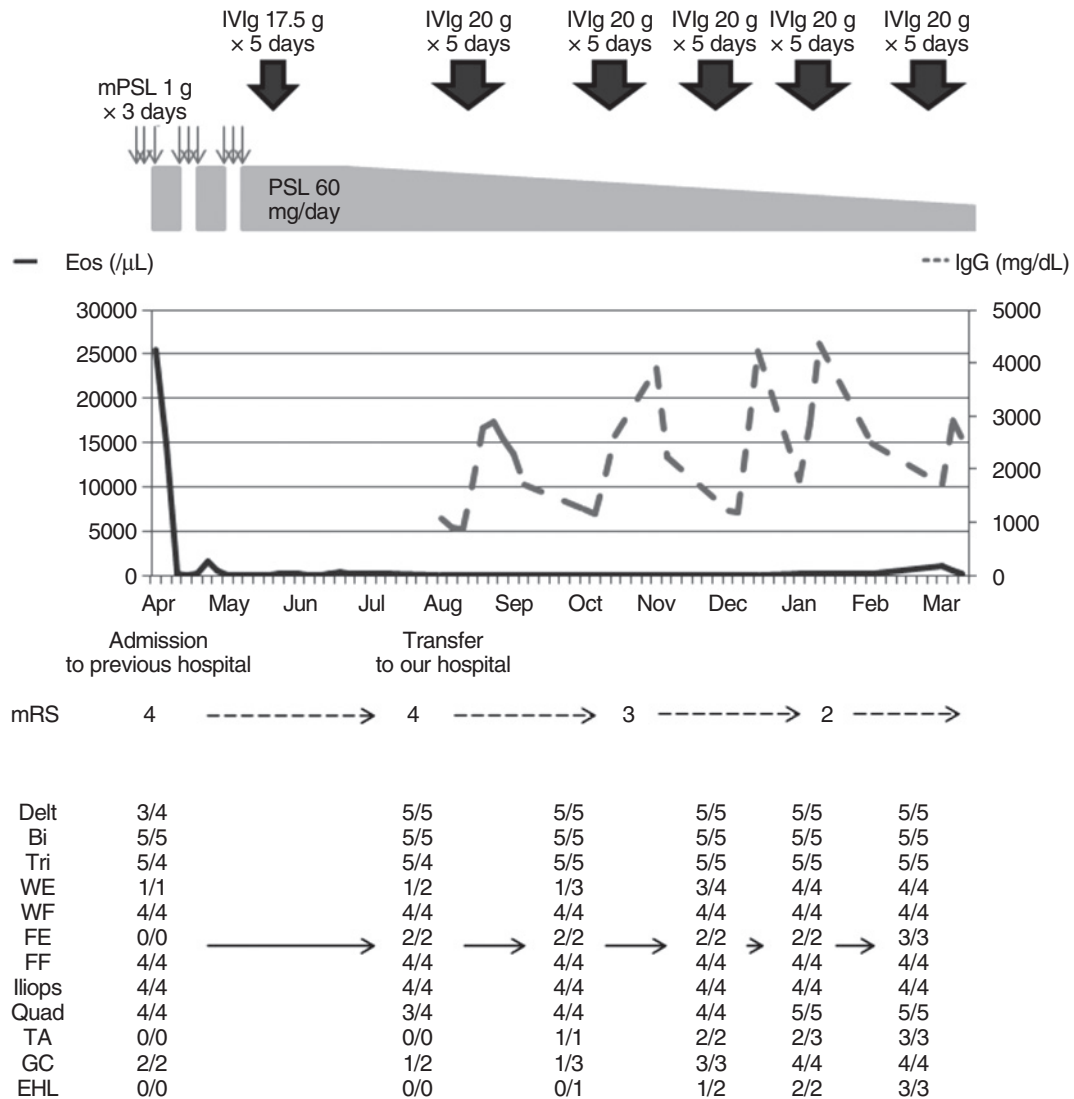


Fig. 1 The progress report of her disease. IVIg, intravenous high-dose immunoglobulin; mPSL, methylprednisolone; PSL, prednisolone; Eos, peripheral blood eosinophil count; IgG, immunoglobulin G; mRS, modified Rankin Scale; Delt, deltoid; Bi, biceps brachii; Tri, triceps brachii; WE, wrist extensors; WF, wrist flexors; FE, finger extensors; FF, finger flexors; Iliops, iliopsoas; Quad, quadriceps; TA, tibialis anterior; GC, gastrocnemius; EHL, extensor hallucis longus.

available in Japan, S-sulfonated gammaglobulin contains IgG dimers the most and is the only preparation for on-label use for CSS. Dimeric IgG is reported to be efficacious for treating idiopathic thrombocytopenic purpura in comparison with monomeric IgG through the blockade of the Fcγ receptor.⁸ The blockade would control autoantibody-mediated pathogenesis. As autoantibodies are also involved in CSS, dimeric IgG-rich preparations could be related to the recovery from CSS-associated neuropathy.

In Kawasaki disease, some reports state that the extent of increase in IgG level from immediately before to after IVIg therapy might be an indicator for evaluating its effect.⁹ In our patient, the IgG level in-

creased linearly after each course of IVIg (Fig. 1). Measurement of this change would be better conducted and compared in relation to the improvement of neuropathy.

In this case, a course by course incremental effect of IVIg on CSS-associated polyneuropathy was clearly observed even in its late phase. Although the underlying mechanism have yet to be determined, repeated administrations of IVIg, even if expensive at present, would be quite effective for CSS-associated neuropathy.

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