Effective intravenous immunoglobulin therapy for Churg-Strauss syndrome (allergic granulomatous angiitis) complicated by neuropathy of the eighth cranial nerve: a case report

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Abstract

Introduction: We report the case of a patient with Churg-Strauss syndrome with eighth cranial nerve palsy. Vestibulocochlear nerve palsy is extremely rare in Churg-Strauss syndrome. To the best of our knowledge, only one case of complicated neuropathy of the eighth cranial nerve has been described in a previous report presenting an aggregate calculation, but no differentiation between polyarteritis nodosa and Churg-Strauss syndrome was made. High-dose immunoglobulin was administered to our patient, and her neuropathy of the eighth cranial nerve showed improvement.

Case presentation: At the age of 46, a Japanese woman developed Churg-Strauss syndrome that later became stable with low-dose prednisolone treatment. At the age of 52, she developed sudden difficulty of hearing in her left ear, persistent severe rotary vertigo, and mononeuritis multiplex. At admission, bilateral perceptive deafness of about 80dB and eosinophilia of 4123/μL in peripheral blood were found. A diagnosis of cranial neuropathy of the eighth cranial nerve associated with exacerbated Churg-Strauss syndrome was made. Although high doses of steroid therapy alleviated the inflammatory symptoms and markers, the vertigo and bilateral hearing loss remained. Addition of a high-dose immunoglobulin finally resulted in marked alleviation of the symptoms associated with neuropathy of the eighth cranial nerve.

Conclusions: A high dose of immunoglobulin therapy shows favorable effects in neuropathy of the eighth cranial nerve, but no reports regarding its efficacy in cranial neuropathy have been published.

Keywords: Churg-Strauss syndrome, Cranial neuropathy, Intravenous immunoglobulin
in CSS as coverage under the national health insurance scheme. Although IVIg shows favorable effects in neuropathy of the peripheral nerves, no reports regarding its efficacy in cranial neuropathy have been published. Here, we report a case of CSS complicated by neuropathy of the eighth cranial nerve in which IVIg was effective.

**Case presentation**

A 35-year-old Japanese woman with no notable medical or family histories developed bronchial asthma. Treatment was initiated, and the course of bronchial asthma had been favorable. After 11 years, rotary vertigo, difficulty of hearing in the right ear, and palsies of the left lower extremity and right forearm occurred. A diagnosis of CSS was made on the basis of bronchial asthma, neuropathy of the peroneal nerve and ulnar nerve, findings of angiitis by biopsy of the left sural nerve, increased eosinophil counts, and positivity for myeloperoxidase anti-neutrophil cytoplasmic antibody (MPO-ANCA). The pathological conditions were alleviated by prednisolone (PSL) treatment with a tapering schedule from a dose of 1mg/kg and methyl-prednisolone pulse therapy (mPSL). Three years later, owing to another increase in MPO-ANCA and exacerbation of peripheral nerve neuropathy during PSL treatment at a dose of 10mg/day, mPSL pulse therapy was administered again and the dose of PSL was increased to 50mg/day (1mg/kg). However, because the neuropathy was not alleviated, intravenous cyclophosphamide (IVCY) pulse therapy (750mg/body) was administered six times every four weeks. The IVCY therapy stabilized our patient’s condition. Subsequently, the dose of PSL was decreased to 10mg/dL gradually.

More than three years later (when our patient was 52 years old), she was hospitalized again because of the recurrence of bilateral hearing difficulty and rotary vertigo. At admission, physical findings included a body temperature of 36.2°C, a blood pressure of 132/74mmHg, a pulse of 66 beats per minute, and a respiratory rate of 18 per minute. No abnormal cardiac sounds were noted, and mild wheezing sounds were present in the lung field. Spontaneous leftward horizontally rotary mixed nystagmus was present, and owing to strong vertigo our patient had difficulty being in a sitting position. A hearing test revealed average hearing thresholds of 86.2dB in the right ear and 78.8dB in the left ear, which indicated severe perceptive deafness (sensorineural hearing impairment). She did not have tinnitus or recruitment phenomenon. Neurological findings included neuropathies of the right ulnar, left peroneal, and right tibial nerves, and left foot drop. Chest radiography and head magnetic resonance imaging did not show any abnormalities, and examination findings included a leukocyte count of 13,300/μL, an eosinophil count of 31.0% (4123/μL), a C-reactive protein (CRP) level of 6.408mg/dL, and an MPO-ANCA of 226EU (Table 1). The results of serum cytokine measurements by the cytometric bead array method were as follows: interleukin-4 (IL-4) of 3.3pg/mL (normal is less than 1.4), IL-5 of 11pg/mL (normal is less than 1.1), IL-6 of 3.0-9.0, CRP of 6.408mg/dL (normal is less than 0.3), IgG of 883mg/dL (normal is 870-1700), IgA of 112mg/dL (normal is 110-410), IgM of 82mg/dL (normal is 46-260), IgE of 421IU/mL (normal is <320), MPO-ANCA of 226EU (normal is <20), PR3-ANCA of 0IU/mL (normal is <3.5), Rheumatoid factor of 5IU/mL (normal is <20), and Anti-nuclear antibody of 20x (normal is <40).

**Table 1 Laboratory findings of the patient on admission**

| Parameter                          | Value     | Normal range |
|------------------------------------|-----------|--------------|
| White blood cell count, ×102/μL    | 133       | 35-85        |
| Neutrophil, percentage             | 63.0      | 42.0-77.0    |
| Basophil, percentage               | 0.5       | 0.1-2.0      |
| Eosinophil, percentage             | 31.0      | 0.5-6.0      |
| Lymphocyte, percentage             | 3.5       | 18.0-49      |
| Monocyte, percentage               | 2.0       | 3.0-9.0      |
| Red blood cell count, ×104/μL      | 413       | 370-510      |
| Hemoglobin, g/dL                   | 14.5      | 11.3-15.4    |
| Hematocrit, percentage             | 41.9      | 34-46        |
| Platelet, 104/μL                   | 18.1      | 14-34        |
| Glucose, mg/dL                     | 98        | 60-100       |
| Hemoglobin A1c, percentage         | 5.7       | 4.0-6.0      |
| Sodium, mEq/L                      | 144       | 138-146      |
| Potassium, mEq/L                   | 3.7       | 3.5-5.0      |
| Chloride, mEq/L                    | 102       | 100-110      |
| Blood urea nitrogen, mg/dL         | 8         | 8-20         |
| Creatinine, mg/dL                  | 0.55      | 0.4-0.8      |
| Uric acid, mg/dL                   | 3.1       | 2.5-5.5      |
| Calcium, mg/dL                     | 8.8       | 8.5-10.3     |
| Total protein, g/dL                | 6.2       | 6.5-8.2      |
| Albumin, g/dL                      | 3.9       | 3.8-5.0      |
| Aspartate aminotransferase, U/L    | 17        | 13-35        |
| Alanine aminotransferase, U/L      | 5         | 5-35         |
| Total bilirubin, mg/dL             | 0.6       | 0.2-1.2      |
| Alkaline phosphatase, U/L          | 115       | 107-340      |
| γ-Glutamyl transpeptidase, U/L     | 36        | 8-45         |
| Lactate dehydrogenase, U/L         | 226       | 112-230      |
| Creatine kinase, U/L               | 36        | 45-165       |
| Amylase, U/L                       | 61        | 37-125       |
| C-reactive protein, mg/dL          | 6.408     | <0.3         |
| IgG, mg/dL                         | 883       | 870-1700     |
| IgA, mg/dL                         | 112       | 110-410      |
| IgM, mg/dL                         | 82        | 46-260       |
| IgE, IU/mL                         | 421       | <320         |
| MPO-ANCA, EU                       | 226       | <20          |
| PR3-ANCA, U/mL                     | 0         | <3.5         |
| Rheumatoid factor, IU/mL           | 5         | <20          |
| Anti-nuclear antibody               | ×20       | <×40         |

Ig: immunoglobulin; MPO-ANCA: myeloperoxidase anti-neutrophil cytoplasmic antibody; PR3-ANCA: proteinase 3 anti-neutrophil cytoplasmic antibody.
of 6.9pg/mL (normal is less than 1.6), IL-10 of 4.9pg/mL (normal is less than 0.13), IL-13 of 7.4pg/mL (normal is less than 0.6), and interferon-gamma (IFNγ) of 0.1pg/mL (normal is less than 1.8).

The diagnosis was neuropathy of the eighth cranial nerve associated with exacerbation of allergic granulomatous angiitis, and mPSL pulse therapy and subsequent oral PSL at a dose of 55mg/day (1mg/kg per day) were begun. This treatment resulted in gradual alleviation of bronchial asthma, eosinophilia, CRP level, and mononeuropathy multiplex but not of the foot drop. Also, the hearing difficulty and vertigo were not alleviated. Although reinforced treatment by IVCY was planned initially, our patient refused because of the severe nausea that occurred in the previous IVCY treatment. Therefore, IVIg (400mg/kg per day for five days) was combined from day 14. From around day 20, the hearing ability and foot drop began to improve gradually. On day 42, a hearing test revealed average hearing thresholds of 70.0 and 61.7dB in the right and left ears, respectively, and the vertigo had disappeared. After our patient was discharged from the hospital, the dose of PSL was decreased to 10mg/day and her condition is currently stable.

Discussion
Because the vertigo continued for a long period of time and recruitment phenomenon and tinnitus were not present, we ruled out atypical sudden deafness in our patient. Since auditory brain-stem response was not performed, the cause of her hearing loss was not identified. Her vertigo and deafness were likely the results of CSS exacerbation or late flare-up, which was evidenced by rising titers of MPO-ANCA and inflammatory markers. Thus, the presumptive diagnosis of CSS-associated cranial neuropathy involving the eighth cranial nerve was made, and the condition subsequently resolved with immunoglobulin therapy.

Conclusions
CSS accompanying cranial neuropathy is relatively rare. Guillevin et al. [9] reported that only four out of 96 CSS cases were complicated by cranial neuropathy. In the present case, the perceptive deafness with vertigo corresponded to pathological conditions of CSS, such as increased MPO-ANCA and some inflammatory markers and exacerbated neuropathy of the peripheral nerves. With regard to serum cytokine concentrations in CSS, increases in Th2 cytokines IL-4 [10], IL-5 [11], IL-10 [12], and IL-13 [10,13] have been reported, although there are reports showing no apparent increases in IL-4 [13], IL-5, and IL-10 [10]. In the present case, increases in serum level of inflammatory cytokine IL-6 and IL-4, IL-5, IL-10, and IL-13, but not Th1 cytokine IFNγ, were found.

As a disease complicated by angiitis and perceptive deafness, Cogan syndrome in aortitis syndrome is well known. However, the pathogenesis of perceptive deafness with Cogan syndrome remains unclear. Meanwhile, the etiology of neuropathies in CSS has been suggested to be involved in damage by feeding vessels of the peripheral nerves. It is speculated that the effect of IVIg is due to the blockade of Fc receptors, adjustment of complement activities with idiootype network [14], or inhibition of damage to myelin or axons as an antigen [15]. In the present case, as for mononeuritis multiplex of the sensory nerves, mPSL pulse therapy was effective. The foot drop as a neuropathy of the motor nerve and the neuropathy of the eighth cranial nerve were resistant to the mPSL pulse therapy but were alleviated after administration of IVIg. We inferred that the effects of steroids were enhanced through some active mechanisms of IVIg as speculated above. Given our present case, IVIg could possibly be a useful treatment for cranial neuropathy associated with CSS and should be taken into consideration for cases in which the effects of mPSL pulse therapy are insufficient or administration of immunosuppressants is difficult.

Consent
Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Abbreviations
CRP: C-reactive protein; CSS: Churg-Strauss syndrome; IFNγ: interferon-gamma; IL: interleukin; IVCY: intravenous cyclophosphamide; IVIg: intravenous immunoglobulin; MPO-ANCA: myeloperoxidase anti-neutrophil cytoplasmic antibody; mPSL: methyl-prednisolone pulse therapy; PSL: prednisolone.

Competing interests
The authors declare that they have no competing interests.

Authors' contributions
YO wrote the paper. SN helped to write and revise the paper. KS and TI performed the cytokine analysis. YS, HA, and AT took responsibility for the clinical management of our patient. All authors read and approved the final manuscript.

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References
1. Masi AT, Hunder GG, Lie JT, Michel BA, Bloch DA, Arend WP, Calabrese LH, Edworthy SM, Fauci AS, Leavitt RY: The American College of Rheumatology 1990 criteria for the classification of Churg-Strauss syndrome (allergic granulomatosis and angiitis). Arthritis Rheum 1990, 33:1094–1100.
2. Sehgal M, Swanson JW, DeRemee RA, Colby TV. Neurologic manifestations of Churg-Strauss syndrome. Mayo Clin Proc 1995, 70:337–341.

3. Hattori N, Ichimura M, Nagamatsu M, Li M, Yamamoto K, Kumazawa K, Mitsuma T, Sobue G. Clinicopathological features of Churg-Strauss syndrome-associated neuropathy. Brain 1999, 122:427–439.

4. Cattaneo L, Chierici E, Pavone L, Graselli C, Manganelli P, Buzio C, Pavesi G. Peripheral neuropathy in Wegener’s granulomatosis, Churg-Strauss syndrome and microscopic polyangiitis. J Neurol Neurosurg Psychiatry 2007, 78:1119–1123.

5. Hattori N, Mori K, Misu K, Koike H, Ichimura M, Sobue G. Mortality and morbidity in peripheral neuropathy associated Churg-Strauss syndrome and microscopic polyangiitis. J Rheumatol 2002, 29:1406–1414.

6. Gullemin L, Le Thi Huong D, Godeau P, Jais P, Wechsler B. Clinical findings and prognosis of polyarteritis nodosa and Churg-Strauss angiitis: a study in 165 patients. Br J Rheumatol 1988, 27:258–264.

7. Danieli MG, Cappelli M, Malcangi G, Logullo F, Salvi A, Danieli G. Long term effectiveness of intravenous immunoglobulin in Churg-Strauss syndrome. Ann Rheum Dis 2004, 63:1649–1654.

8. Hot A, Perard L, Coppere B, Simon M, Bouhour F, Ninet J. Marked improvement of Churg-Strauss vasculitis with intravenous gamma globulins during pregnancy. Clin Rheumatol 2007, 26:2149–2151.

9. Gullemin L, Cohen P, Gayraud M, Lhote F, Jarrousse B, Casassus P. Churg-Strauss syndrome. Clinical study and long-term follow-up of 96 patients. Medicine (Baltimore) 1999, 78:26–37.

10. Kiene M, Csernok E, Metzler C, Trabandt A, Gross WL. Elevated interleukin-4 and interleukin-13 production by T cell lines from patients with Churg-Strauss syndrome. Arthritis Rheum 2001, 44:469–473.

11. Tsukadaira A, Okubo Y, Kitano H, Horie S, Momose T, Takashi S, Suzuki J, Ise M, Sekiguchi M. Eosinophil active cytokines and surface analysis of eosinophils in Churg-Strauss syndrome. Allergy Asthma Proc 1999, 20:39–44.

12. Schönnermarck U, Csernok E, Trabandt A, Hansen H, Gross WL. Circulating cytokines and soluble CD23, CD26 and CD30 in ANCA-associated vasculitides. Clin Exp Rheumatol 2000, 18:457–463.

13. Kurosawa M, Nakagami R, Morioka J, Inamura H, Mizushima Y, Sugawara N, Yamashita T, Yokoseki T, Kimura S, Ohara Y, Shibata M, Chihara J. Interleukins in Churg-Strauss syndrome. Allergy 2000, 55:765–787.

14. Levy Y, Sheer Y, George J, Langevitz P, Ahmed A, Bar-Dayan Y, Fabbrizzi F, Ternberg J, Peter J, Shoorenfeld Y. Serologic and clinical response to treatment of systemic vasculitis and associated autoimmune disease with intravenous immunoglobulin. Int Arch Allergy Immunol 1999, 119:231–238.

15. Dalkas MC. Mechanisms of action of IVIg and therapeutic considerations in the treatment of acute and chronic demyelinating neuropathies. Neurology 2002, 59(Suppl 6):S13–S21.

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