Acute Autonomic, Sensory and Motor Neuropathy: Successful Treatment with IVIg

Akihiro Ueda, Kunihiko Asakura, Takateru Mihara, Hideo Hara, Madoka Ueda, Tadayuki Miyashita and Tatsuro Mutoh

Abstract

Acute autonomic, sensory and motor neuropathy (AASMN) is a rare peripheral nerve disorder characterized by prominent dysautonomia with somatic sensory and motor impairment. Dysautonomia in AASMN is intractable even with corticosteroid therapy or plasmapheresis. Here we report a case of AASMN with severe orthostatic hypotension. Although the effectiveness of corticosteroid was insufficient, high dose intravenous immunoglobulin therapy (IVIg) was effective for not only sensorimotor symptoms but also autonomic symptoms. This is the first case of AASMN showing favorable responses to IVIg treatment, suggesting that IVIg should be considered when corticosteroid therapy or plasmapheresis is ineffective or insufficient.

Key words: dysautonomia, intravenous immunoglobulin, peripheral neuropathy, corticosteroid

(Inter Med 48: 843-846, 2009)
(DOI: 10.2169/internalmedicine.48.1848)

Introduction

Acute autonomic, sensory and motor neuropathy (AASMN) is a rare disease characterized by prominent dysautonomia with severe somatic sensory and motor impairments. It has been considered to be a variant form of acute idiopathic autonomic neuropathy (1). The cause of AASMN is still unknown though some of the cases have been reported in association with viral infection (2). The effects of the treatments, e.g., corticosteroid administration and plasmapheresis, were unsatisfactory in most of the reported cases in particular, autonomic symptoms were usually intractable (1-7). Here we report a case of AASMN showing good response to high dose intravenous immunoglobulin therapy (IVIg).

Case Report

A 60-year-old man had acute fever without abdominal symptoms including diarrhea. His fever continued over the next few days and he developed mild weakness and numbness in the lower extremities. He also noticed decreased sweating in the lower part of the body. Weakness and sensory disturbances were gradually progressed and he became unable to walk and was hospitalized in the local hospital at 25 days after the onset. Urinary disturbance and fecal incontinence were also noted. He became bed ridden because of severe orthostatic hypotension and moderate weakness. At 53 days after the onset, he was transferred to our hospital for further investigation and treatment. On admission, he did not have a headache and his consciousness was alert. Cranial nerves including pupillary function were not involved. Bilateral calf muscle atrophy was observed and there was moderate loss of all modalities of sensations except joint position sense in extremities (legs more than arms) with distal dominancy. Muscle strength testing revealed 3/5 strength in the proximal part of lower extremities and 1/5 or 2/5 strength in the distal part of lower extremities. Ataxia in lower extremities was not evaluated because of muscle weakness. Weakness and ataxia were not observed in upper extremities. The deep tendon reflexes were reduced in his arms and absent in the lower extremities. The blood pressure at the supine position was 100/70 mmHg, while sitting, 70/50 mmHg without responsive tachycardia. Cerebrospinal fluid examination revealed monocytic pleocytosis (28/mm³, all of the cells were mononuclear lymphocytes) with mildly elevated protein (78 mg/dL; normal range, 10-40 mg/dL).

Department of Neurology, Fujita Health University School of Medicine, Toyoake
Received for publication November 7, 2008; Accepted for publication January 7, 2009
Correspondence to Dr. Kunihiko Asakura, kasakura@fujita-hu.ac.jp
and IgG concentrations (13 mg/dL; normal range, <4 mg/dL). Serological and PCR examinations for viral infection were negative including herpes simplex viruses, human herpes virus-6 and -7, cytomegalovirus, and Epstein Barr virus. Anti-nuclear antibodies, anti-DNA antibodies, anti-SS-A and anti-SS-B antibodies, and anti-p-ANCA and c-ANCA antibodies were all negative. Anti-ganglioside antibodies were negative. Nerve conduction study revealed that the compound muscle action potentials (CMAPs) were decreased in tibial nerves and sensory nerve action potentials (SNAPs) were decreased in median, ulnar, and sural nerves. F wave latency was elongated in tibial nerve. Needle electromyograph revealed mild to moderate neurogenic changes including fibrillation, polyphasic wave, and decreased motor units in the lower extremities. The left sural nerve was biopsied at 56 days after the onset. The histological study showed a mild decrease of both large and small myelinated fibers as shown in Fig. 1. Myelinated fiber density was 6,117/mm². Unmyelinated fibers seemed to be unaffected under light microscopic examination, although endoneurial edema was observed. Mononuclear cell infiltration was not observed.

Large dose intravenous administration of methylprednisolone (1 g/day over 3 days) followed by oral administration (1 mg/kg) was performed at 60 days after the onset. The corticosteroid therapy, however, resulted in a limited improvement in sensory and motor disturbances from 1/5 to 2/5 strength in lower extremities and no effect on autonomic dysfunctions. The patient was still unable to stand up because of severe orthostatic hypotension although joint position sense was relatively preserved in lower extremities and therefore urinary catheterization was needed. Then, we tried IVIg treatment (0.4 g/kg over 5 days) at 79 days after the onset. Soon after the IVIg treatment, severe orthostatic hypotension was apparently ameliorated. Before IVIg treatment, he felt faintness by 45° head-up tilt though he did not lose consciousness. However, at 30 days after IVIg treatment, he had no symptoms during head-up tilt test as shown in the Fig. 2. Intriguingly, basal levels of plasma renin and norepinephrine concentrations were drastically increased at thirty days after IVIg treatment as shown in Fig. 3. The prompt increases of plasma renin and norepinephrine levels with a 45° head-up tilt position were also observed after IVIg treatment (Fig. 3). Moreover, he was able to void urine immediately after the start of IVIg treatment. Other autonomic symptoms including fecal incontinence and hypohydration were also improved. The sensory, motor and autonomic impairments were further improved and finally he could walk by himself after the second IVIg treatment. His muscle strength was improved up to 4/5 strength in proximal part of lower extremities and 3/5-4/5 strength in the distal part of lower extremities. The deep tendon reflexes remained reduced in his arms and was absent in his lower extremities. In the laboratory examinations, the CSF protein and IgG

![Figure 1.](image)

**Figure 1.** Transverse section of biopsied sural nerve. Toluidine blue staining (×80). Endoneurial edema was observed but not inflammatory cell infiltration. Both large and small myelinated fibers were mildly decreased.

![Figure 2.](image)

**Figure 2.** Head-up tilt test (45°) before (at 25 days after admission) and at 30 days after IVIg treatment. (A) Both systolic and diastolic pressures dropped right after 45° head-up tilt without reactive tachycardia before IVIg treatment. The patient did not lose consciousness but felt faintness. (B) After IVIg treatment orthostatic hypotension was markedly improved.
concentrations were normalized when he was discharged. Nerve conduction velocities and F wave latencies were not changed.

Discussion

The clinical pictures of autonomic impairment with symmetrical sensory and motor neuropathy found in this patient were compatible with those of AASMN. AASMN is a rare peripheral neuropathy and its pathogenesis still remains to be elucidated. In this case, neurological symptoms appeared within a few days after initial fever and CSF analysis showed mild pleocytosis that are quite similar to one of the two cases reported by Yokota et al (1). The present case did not have meningeal symptoms or signs and the histological study of biopsied sural nerve did not show any inflammatory cell infiltration or inclusion body. Therefore, it is considered that direct viral invasion to the peripheral nerves was unlikely. Some of the clinical features of AASMN and Guillain-Barré syndrome with prominent dysautonomia overlap. Pleocytosis in the CSF is uncommon in Guillain-Barré syndrome, however, mild pleocytosis in the CSF was occasionally reported in AASMN (1, 5, 6). Guillain-Barré syndrome can occur in all races. In contrast, most of the reported cases of AASMN are Japanese, which might suggest the possibility that there are underlying genetic susceptibilities or environmental factors (1, 2, 4-7). Most of the cases in the literature were treated with corticosteroid and/or plasmapheresis with unsatisfactory improvement (1-7). Some cases were treated with IVIg and it has been reported that IVIg treatment induced improvement of sensory and motor symptoms but not autonomic dysfunction (6, 7). In contrast, IVIg treatment in the present case was considered to be very effective not only for sensory and motor symptoms but also autonomic symptoms despite the long-standing course of illness, although partial effectiveness of corticosteroid therapy was observed as seen in other patients reported previously.

It has been proposed that dysautonomia in AASMN is divided based on the lesions of sympathetic efferent pathways into two groups: postganglionic axonopathic type and preganglionic demyelinating type (1). The sympathetic efferent pathways in the peripheral nerve consist of preganglionic myelinated and postganglionic unmyelinated fibers. Dysautonomia caused by the sympathetic postganglionic lesions are considered to be intractable because of direct axonal damages. In contrast, the recovery from dysautonomia produced by preganglionic sympathetic lesions seems better than that produced by postganglionic lesions (1). In the present case, the basal level of plasma catecholamine concentration recovered promptly after IVIg treatment as shown in Fig. 2. This finding was compatible with the result of sural nerve biopsy, i.e., relatively mild nerve damage in comparison with other reported cases, and also supports the speculation that the involvement of postganglionic fibers is relatively mild in this patient (8).

Two cases of AASMN have been treated with IVIg (6, 7), one of which was accompanied by central nervous system disturbances (7), but both cases did not show satisfactory recovery of autonomic function (6, 7). To our knowledge, the present case seems to be the first case of AASMN showing a good response to IVIg. Despite the long course of illness, there might exist some surviving neurons in the present case, which can respond to IVIg treatment. Recently it has been reported that IVIg is effective for dysautonomia in Sjögren’s syndrome (9) or acute idiopathic autonomic neuropathy (10). Therefore, IVIg treatment can be a possible therapeutic strategy in similar cases when other treatments are ineffective and insufficient. The precise underlying pharmacological mechanism of IVIg effectiveness in the present patient remains unknown. We must wait for a definite an-
swer on this issue until a case-control study is performed, although the number of AASMN patients is very limited and therefore such studies can not easily be performed. Nevertheless, the results of IVIg treatment in the present case strongly suggest that repetitive IVIg treatment should be considered for severe autonomic disturbances when corticosteroid therapy or plasmapheresis is ineffective or insufficient in patients with AASMN.

Acknowledgement

We thank Drs. Haruki Koike (Nagoya University School of Medicine) and Hiroshi Koga (Fujita Health University School of Medicine) for their helpful comments on sural nerve analyses.

References