Improvement of Cytomegalovirus-Related Guillain-Barré Syndrome after High Doses of Intravenous Methylprednisolone Pulses

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Dear Sir,

Guillain-Barré syndrome (GBS) is an acute polyradiculoneuropathy, preceded by a cytomegalovirus (CMV) infection in about 10–15% of cases [1, 2]. Randomized therapeutic trials on GBS patients have shown that intravenous immunoglobulin (IVIg) and plasma exchange are equally effective [3, 4]. Despite some rare favourable results in open studies [5, 6], controlled trials did not prove that oral or intravenous corticoids modify the long-term outcome when given alone in this condition [7].

Here we describe the case of a young woman with GBS preceded by CMV infection who dramatically improved after steroid pulse therapy.

Case Report

A 24-year-old woman had experienced headache, distal paraesthesiae and progressive muscle weakness of the limbs for a week when she was admitted to hospital. Clinical examination revealed a moderate muscle weakness predominant in the lower limbs and the absence of deep tendon reflexes. The weakness extended rapidly in a few days, with bulbar dysfunction, left facial palsy and difficulty in breathing (fig. 1).

Routine laboratory studies showed hepatic cytolytic and cholestatic abnormali-

Fig. 1. Clinical and therapeutic data over 5 months.

ties. Cerebrospinal fluid (CSF) examination revealed protein 1.8 g/l and a normal leucocyte count. Tests for antiganglioside antibodies and serological studies were negative, except antibodies against CMV (IgM: 6.6 IU/ml, normal value <1.2 IU/ml; negative IgG).

Nerve conduction studies showed prolonged distal motor latencies, absence of F waves, reduction of nerve conduction ve-

locities and multiple motor nerve conduction blocks (table 1). GBS was diagnosed based on the above-mentioned findings, and the patient received IVIg at a dose of 0.4 mg/kg of body weight per day for 5 days. She slightly improved but the weakness in the upper and lower limbs persisted. Seven weeks after the onset her neurological condition was exacerbated with severe tetraparesis predominant in the lower

Table 1. Time course of electrophysiological results (right/left)

	ENMG 1 day 8	ENMG 2 month 2	ENMG 3 month 5	Normal limit
Median CMAP				
DL, ms	5.7/5.9	30/26.2	13/11	<4
NCV, m/s	32/41	11/13	24/29	>50
Dist. amp., mV	3.1/3.8	0.3/0.8	1/1.8	>3.5
Prox. amp., mV	0.8/2.4	0.07/0.08	1/1.5	>3.5
Ulnar CMAP				
DL, ms	ND/ND	0/ND	5.6/6.4	<3
NCV, m/s	ND/ND	NR/ND	7/21	>50
Dist. amp., mV	ND/ND	0.04/ND	0.5/0.6	>2.8
Prox. amp., mV	ND/ND	NR/ND	0.3/0.6	>2.8
Peroneal CMAP				
DL, ms	5.7/5.5	NR/NR	9.1/14.8	<5.5
NCV, m/s	29/23	NR/NR	15/14	>40
Dist. amp., mV	2.4/3	NR/NR	1.6/1.9	>2.5
Prox. amp., mV	0.8/0.4	NR/NR	1.2/1.6	>2.5
Sural SNAP				
NCV, m/s	45/12	NR/NR	NR/NR	>40
Amp., μ V	40/20.5	NR/NR	NR/NR	>8
Ulnar SNAP				
NCV, m/s	NR/50	NR/NR	NR/NR	>45
Amp., μ V	NR/1.5	NR/NR	NR/NR	>5
Median SNAP				
NCV, m/s	NR/43	NR/NR	NR/NR	>45
Amp., μ V	NR/1.8	NR/NR	NR/NR	>5

ENMG = Electroneuromyography; NR = no response; ND = not done; CMAP = compound motor action potential; DL = distal latency; NCV = nerve conduction velocity; amp. = amplitude (negative peak); SNAP = sensory nerve action potential; dist. = distal; prox. = proximal.

limbs, bilateral facial palsy, diffuse hypoesthesia and bladder dysfunction (fig. 1). At this time, electroneuromyography displayed persisting conduction blocks and severe axonal loss (table 1). CSF protein was 5.6 g/l with 14 leucocytes. Cerebral MRI was normal. Serum IgM and IgG CMV antibodies were increased (IgG: 2.63 IU/ml, normal value <0.4 IU/ml; IgM: 2 IU/ml). Neither a second dose of IVIg nor foscarnet were effective. Three weeks after the exacerbation, she received 1 g/day of methylprednisolone intravenously for 5 days and rapidly improved within a week (fig. 1). The recovery started in the pelvic and scapular girdles. Electroneuromyography 3 months later was also notably improved but still showed distal

axonal loss predominant in the lower limbs (table 1). The outcome after 1 year was excellent: the patient only retained some paraesthesiae in the extremities and suffered no relapse 32 months later.

Discussion

The first presentation of our patient fulfilled the clinical, electrophysiological and CSF criteria for acute GBS [8]. However, despite initial improvement after IVIg, her condition worsened 7 weeks after onset. Since the time to reach the nadir in GBS is normally within 4 weeks, this case could be considered as acute chronic inflammatory demyelinating polyneuropathy (acute CIDP) or subacute inflammatory demyelinating polyneuropathy

(SIDP). However, several arguments contradict either hypothesis: (1) according to the study of Ruts et al. [9], the diagnosis of acute CIDP should be considered when the deterioration occurs after 9 weeks from onset; (2) our patient had a rapid severe course within 2 weeks, which is not consistent with cases of SIDP reported by Oh et al. [10]; (3) she had no relapse on a follow-up longer than 2 years. So, this patient may rather be diagnosed as a case of GBS with treatment-related fluctuations [9]. Moreover, she had the characteristic clinical and electrophysiological pattern of CMV-related GBS described by Visser et al. [2] and Ogawara et al. [11] in that she was young and experienced a severe course, with sensory and motor pattern of four limbs, cranial nerve involvement, respiratory insufficiency and demyelination on nerve conduction studies. Benefits of antiviral treatment have been reported in this condition [12]. We cannot exclude a delayed effect of foscarnet in our patient, but she continued to worsen 2 weeks after initiating this treatment. A second dose of IVIg was ineffective as well. In fact, a clear improvement was only observed after steroid pulse therapy. Two open studies actually suggested a beneficial effect of intravenous methylprednisolone in GBS patients [5, 6] but none of the published controlled trials supported its use [3, 7, 13, 14]. Nevertheless, a recent paper described a favourable outcome in a case of CMV-related GBS after steroid pulse therapy as was the case with our patient [15]. Such cases may sustain the hypothesis that pathogenic mechanisms in CMV-related GBS are in part distinct from classical GBS. Indeed, other factors could explain the efficiency of corticoids such as the timing of their administration. They should be more efficient in the first stage of the disease because of the presence of inflammation. In our patient, the initial recovery in limb girdle muscles was probably due to the persisting inflammatory process and the release of proximal conduction blocks.

In conclusion, high doses of intravenous steroid pulses should be tried in CMV-related GBS when other treatments are ineffective or when clinical worsening occurs after initial improvement or stabilization.

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