# A Case of Miller-Fisher Syndrome Demonstrating a Significant Decrease in Anti-Ganglioside Antibodies with Immunoadsorbent Therapy

Norihiro Takahashi, Minoru Kihara, Hiroshi Fujioka, Koichi Uchida, Tetsuo Shoji, Tohru Sumikura, Kazushi Deguchi\*, Nobuhiro Yuki\*\*, and Shigekazu Yuasa

Second Department of Internal Medicine, and \*Third Department of Internal Medicine, Kagawa Medical School, Kagawa 761-07, Japan, and \*\*Department of Biochemistry, Faculty of Medicine, Tokyo Medical and Dental University, Bunkyo-ku, Tokyo 113, Japan

Key words: Miller-Fisher syndrome, anti-ganglioside antibody, IgG anti-GQ1b antibody, immunoadsorbent therapy, tryptophan column

It has been recognized that Miller-Fisher syndrome (MFS) is caused by immune abnormalities and that immunoadsorbent (IA) therapy improves the neurogenic involvement in MFS.<sup>1)</sup> However, few studies have assessed the usefulness of IA therapy in view of the ability to remove anti-ganglioside antibody, IgG anti-GQ1b antibody, which may play a role in the development of MFS.<sup>2,3)</sup> This paper reports a patient with MFS who demonstrated a significant decrease in anti-ganglioside antibodies by IA therapy with a tryptophan column in association with clinical improvement.

# **Patient and Methods**

The patient was a 28-year-old female. Symptoms at onset were diplopia and giddiness following fever and diarrhea. She was administered prednisolone by a local physician, but did not respond to drug therapy. She was then admitted to our hospital for evaluation and treatment of MFS. Neurologic examination revealed moderate bilateral oculomotor paralysis and complete bilateral abducens paralysis. She had areflexia, numbness of the middle and ring fingers on the left hand, and mild ataxic gait. The CSF protein level was 37 mg/dl with a normal cell count. Nerve conduction velocities and compound muscle action potentials were normal. The brain CT and MRI were normal. Serum levels of IgG anti-GQ1b antibody measured by the ELISA method were very high.

Prior to the initiation of IA therapy, we examined the adsorption rates of immunoglobulins and anti-ganglioside antibodies on a polyvinyl alcohol gel, PH-350, and TR-350 by the bathwise adsorption method (in vitro).

IA therapy was carried out 4 times. As the IA column, a tryptophan-linked polyvinyl alcohol gel (TR-350) was used 3 times, and a phenylalanine-linked

polyvinyl alcohol gel (PH-350) once.

### Results

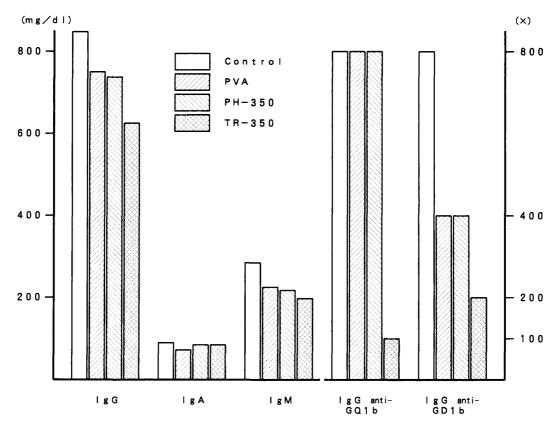
The results of immunoglobulin and anti-ganglioside antibody removal by the bathwise adsorption method are shown in Fig. 1. Both TR-350 and PH-350 adsorbed the immunoglobulins. The anti-ganglioside antibodies could be adsorbed by TR-350 but not by polyvinyl alcohol gel and PH-350.

The changes in plasma protein fractions before and after IA therapy were as follows. Using TR-350, the mean values for plasma albumin before and after therapy were 3.1 and 2.7 g/dl; IgG, 683.3 and 540.0 mg/dl; IgA, 63.3 and 56.3 mg/dl; and IgM, 161.0 and 126.7 mg/dl, respectively. Using PH-350, the values for plasma albumin before and after therapy were 3.0 and 3.0 g/dl; IgG, 600.0 and 580.0 mg/dl; IgA, 58.0 and 59.0 mg/dl; and IgM, 120.0 and 117.0 mg/dl, respectively. There was little loss of albumin as compared with immunoglobulins during IA therapy with the use of both TR-350 and PH-350.

Figure 2 shows changes in the plasma level of anti-GQ1b antibody during IA therapy. With the use of TR-350 3 times, the antibody titer decreased significantly. The titer values for anti-GQ1b antibody before and after therapy were  $\times 800$  and 200 at the first,  $\times$  400 and 100 at the second, and  $\times 200$  and 100 at the third session, respectively. On the other hand, with the use of PH-350, antibody titers were not decreased. After IA therapy, the patient's complaints, of the numbness, ataxia, and diplopia, disappeared.

## **Discussion**

We carried out IA therapy for a total of 4 times in a patient with MFS and studied the clinical effectiveness and ability to remove anti-ganglioside antibodies. In general, TR-350 and PH-350 are applicable as the IA



**Fig. 1** Evaluation of ability to remove immunoglobulins and anti-ganglioside antibodies by the bathwise adsorption method (*in vitro*). Control, patient's plasma; PVA, polyvinyl alcohol gel; PH-350, phenylalanine-linked PVA; TR-350, tryptophan-linked PVA.

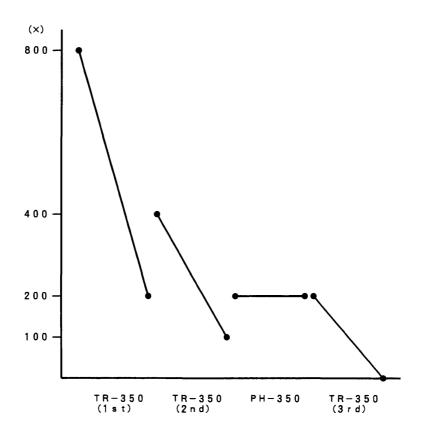


Fig. 2 Changes in plasma IgG anti-GQ1b antibody levels before and after IA therapy.

Jpn J Apheresis Vol 15 No 1 (1996)

column. Our *in vitro* study results had suggested that anti-GQ1b antibody could be removed only by TR-350. These results are consistent with the clinical findings demonstrating decreases in the serum level of autoantibodies by IA therapy only with TR-350. Furthermore, clinical improvement has been observed in association with the decrease in antibody titers. From these results it is suggested that TR-350 should be used in IA therapy of MFS.

### References

- Koh CS, Shinoda T, Shimada K, et al: Immunoadsorption plasmapheresis and plasma exchange in Miller Fisher syndrome. Therapeutic Plasmapheresis XII: 557-560, 1993
- 2) Chiba A, Kusunoki S, Shimizu T, et al: Serum IgG antibody to ganglioside GQ1b is a possible marker of Miller Fisher syndrome. Ann Neurol 31: 677-679, 1992
- 3) Yuki N, Sato S, Tsuji S, et al: Frequent presence of anti-GQ1b antibody in Fisher's syndrome. Neurology 43: 414-417, 1993