SHORT REPORT

Development of facial palsy during immunoadsorption plasmapheresis in Miller Fisher syndrome: a clinical report of two cases

Keiji Chida, Sadao Takase, Yasuto Itoyama

Abstract

Immunoadsorption plasmapheresis (IAP) using a tryptophan linked gel column has been shown to effectively remove serum IgG anti-GQ1b antibody which may contribute to the pathogenesis of Miller Fisher syndrome. Two patients are reported on with Miller Fisher syndrome, who developed bilateral facial palsy during IAP using a tryptophan column, while ophthalmoplegia, ataxia, and, areflexia were improving. In these patients, the titre of anti-GQ1b antibodies was reduced. The IAP using a tryptophan column has a beneficial effect on Miller Fisher syndrome but may not inhibit the development of facial palsy. The mechanism of such a dissociated effect of IAP on Miller Fisher syndrome is discussed.

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Miller Fisher syndrome is an acute self limiting disorder characterised by ophthalmoplegia, ataxia, and areflexia,¹ and facial and bulbar palsy often occur.² Recent studies have shown an association of IgG anti-GQ1b antibody with the pathogenesis of Miller Fisher syndrome.^{3–5} Furthermore, immunoadsorption plasmapheresis (IAP) using a tryptophan linked gel column, a new plasmapheresis procedure, has been reported to effectively remove serum IgG anti-GQ1b antibody⁶ and to have a beneficial effect on Miller Fisher syndrome.⁷ We describe here, however, two patients with Miller Fisher syndrome in whom facial palsy developed during IAP treatment when other neurological symptoms and signs were improving.

Case reports

PATIENT 1

A 65 year old man noticed diplopia 12 days after a cough, sputum, and low grade fever. The next day diplopia increased, then paraesthesia developed in his hands and general unsteadiness was noted. On day 4 he noticed a nasal voice. He was admitted to hospital on day

8, when he had external ophthalmoplegia (complete in the vertical movement and pronounced in the horizontal movement), blepharoptosis, soft palate palsy, moderate limb and truncal ataxia, and diffuse areflexia. Facial motor functions were normal. He had dysaesthesia and reduced vibration in the upper limbs but no limb weakness and no Babinski's sign. IgG anti-GQ1b antibody was detected in the serum by enzyme linked immunosorbent assay,⁶ but IgM anti-GQ1b antibody and IgG and IgM antibodies against other gangliosides (GM3, GM2, GM1, GD3, GD2, GD1a, GalNAc-GD1a, GD1b, and GT1b) were not detected. Cerebrospinal fluid was acellular with a protein concentration of 27 mg/dl on day 8 and 41 mg/dl on day 21.

The patient underwent five sessions of IAP (on days 10, 13, 15, 17, and 20). In the IAP procedure, blood taken from the cannulated femoral vein was moved by roller pump through a membrane type plasma separator (Plasmaflo 0P-08, Asahi Medical, Tokyo, Japan). The separated plasma was passed through a tryptophan linked polyvinyl alcohol gel column (TR-350, Asahi Medical, Tokyo, Japan) which adsorbs large plasma proteins including immunoglobulins. The perfused plasma was mixed with the cell components and returned to the patient. Plasma flow rate was 20–25 ml/min, and plasma volume treated in each session was 2000 ml. Plasma samples were taken before and after each session and were frozen. All samples were simultaneously tested to determine the antibody titres.⁶

There were no complications related to the therapy. On day 14, ataxia and ophthalmoplegia started to improve. The titre of IgG anti-GQ1b antibody was reduced; 1:100×2⁸ before the first session, 1:100×25 after the third session, and 1:100×23 after the fifth session. However, bilateral facial weakness developed on day 17. There was no remarkable weakness of limb muscles and no deterioration in the cardinal neurological signs of Miller Fisher syndrome. Facial palsy started improving on day 27 and disappeared on day 45. Ataxia and diplopia disappeared on day 45 and day 85 respectively.

Department of
Neurology, Kohnan
Hospital, Sendai,
Japan

K Chida
S Takase

Department of
Neurology, Tohoku
University School of
Medicine, Sendai,
Japan

Y Itoyama

Correspondence to:
Dr K Chida, Department of
Neurology, Kohnan Hospital,
4–20–1 Nagamachi-minami,
Taihaku-ku, Sendai 982,
Japan.

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Clinical courses of the two patients. Refer to text and table for clinical scores. Ab = antibody; IAP = immunoadsorption plasmapheresis; EOP = external ophthalmoplegia.

PATIENT 2

A previously well 60 year old man awoke with diplopia one morning. The next day his diplopia worsened, he staggered when walking, and acroparaesthesiae were noted. On day 4, examination showed complete external ophthalmoplegia, mild blepharoptosis, mydriasis, soft palate palsy, limb and truncal ataxia, and diffuse areflexia. Facial muscle power was normal. Vibration sensation was moderately reduced in the upper limbs. There was no limb weakness and no Babinski's sign. In serum, IgG and IgM anti-GQ1b antibodies were detected, but IgG and IgM antibodies against other gangliosides (GM2, GM1, GD1a, GD1b, and GT1b) were not. Cerebrospinal fluid was acellular with a protein concentration of 120 mg/dl on day 18.

He received IAP by the same procedure as patient 1, but only three sessions (on days 4, 6, and 8) were performed because nausea and hypotension occurred at the end of each session. The titre of IgG anti-GQ1b antibody was decreased from more than 1:100×215 (before the first session) to 1:100×212 (after the third session). IgM anti-GQ1b antibody

titre also decreased from 1:100×2⁵ to 1:100×2³. Ataxia and areflexia had started to improve so that he could walk without assistance on day 10, then facial muscles became weak and complete paralysis developed by day 12. Limb muscle power was normal. A high dose of methylprednisolone (1000 mg/day for three days) was given. Facial palsy started to improve on day 22 and disappeared on day 36. Improvement of eye movement began on day 15 and rapidly progressed during the first half of the second month. Diplopia disappeared on day 126.

CLINICAL COURSE

The figure shows the clinical course of the two patients. The assessment of the severity of the cardinal neurological signs of Miller Fisher syndrome was based on grading scores described elsewhere⁷ with minor modifications (table).

Discussion

It is of an advantage not to need to replace plasma protein during IAP treatment because IAP does not remove albumin from patients.

Impairment scores of the cardinal neurological signs in Miller Fisher syndrome

EOP:	
Score	Adduction or abduction: 4=cannot rotate, 3=can rotate 10°, 2=can rotate 20°, 1=can rotate 30°, 0=can rotate 40° or more. Supraduction or infraduction: 3=cannot rotate, 2=can rotate 10°, 1=can rotate 20°, 0=can rotate 30° or more.
Total score	Sum or impairment scores of each duction +n. (n=2(diplopia on forward gaze), 1 (diplopia only on lateral gaze), or 0 (no diplopia)).
Ataxia:	
Score	Upper limbs: 3=severe, 2=moderate, 1=mild, 0=normal. Lower limbs: 3=severe, 2=moderate, 1=mild, 0=normal. Gait: 4=cannot maintain a broad based standing position, 3=can maintain a standing position but cannot walk independently, 2=can walk independently but positive Mann's test, 1=negative Mann's test but not normal, 0=normal.
Total score	Sum of impairment scores of upper limbs, lower limbs, and gait ataxia.
Areflexia:	
Score	Biceps, triceps, quadriceps, and Achilles tendon reflexed in both sides: 2=absent, 1=diminished, 0=normal.
Total score	Sum of impairment scores of each deep tendon reflex.

EOP = external ophthalmoplegia. The total scores range from 0 to 30 for EOP, from 0 to 10 for ataxia, and from 0 to 16 for areflexia.

The tryptophan linked gel column has been shown to effectively remove the IgG anti-GQ1b antibody⁶ which may contribute to the pathogenesis of Miller Fisher syndrome.³⁻⁵ Therefore, IAP using a tryptophan column is often employed to treat patients with Miller Fisher syndrome in Japan. Some beneficial effects of IAP on Miller Fisher syndrome have also been reported,⁷ although no randomised controlled trials have been conducted yet.

In this paper, we presented two patients with Miller Fisher syndrome in whom IAP performed in the early stage successfully stopped the progression of disease. Especially in patient 1, ophthalmoplegia and ataxia started to improve. Limb power was normal and plasma anti-GQ1b antibodies were reduced significantly in both patients. However, facial palsy developed after the third session of IAP. Although relapses have been reported in cases with Guillain-Barré syndrome treated with plasmapheresis,⁸ we think that our patients did not have a relapse because neurological signs of Miller Fisher syndrome other than facial palsy did not develop or become worse.

The facial nerve is the most frequent cranial nerve affected in Guillain-Barré syndrome and is usually affected when limb weakness is severe.⁹ In Miller Fisher syndrome, which is characterised by ophthalmoplegia, ataxia, and areflexia and is considered a variant of Guillain-Barré syndrome, facial palsy also occurs often (in about 50%)² but occurs independently of limb weakness. Therefore, facial palsy and the cardinal neurological signs in Miller Fisher syndrome may result from a similar pathomechanism.

The reason IAP was not effective in preventing the development of facial palsy is unclear. One possibility is that the effect of IAP may depend on stages of the disease process of Miller Fisher syndrome. Various pathomechanisms are probably involved in different disease stages in Miller Fisher syndrome, as in Guillain-Barré syndrome.⁹ Although it is reported that plasma exchange has a prophylactic effect on experimental allergic neuritis¹⁰ which is considered to be an animal model of Guillain-Barré syndrome, whether IAP has such a prophylactic effect has not yet been

examined. IAP may not be effective in the presymptomatic early stage of Miller Fisher syndrome.

Alternatively, the pathomechanism of facial palsy in our patients may be different from those of the cardinal neurological signs of Miller Fisher syndrome. Immunohistochemical study with the anti-GQ1b monoclonal antibody has shown prominent staining in the three ocular motor nerves, but not in the other nerves including the facial nerve.³ This evidence suggests that unknown factors other than the anti-GQ1b antibody may contribute to the pathogenesis of facial palsy in Miller Fisher syndrome. The tryptophan gel column removes IgG anti-ganglioside antibodies effectively but does not remove IgM anti-ganglioside antibodies so well.⁶ In our patients, IAP treatment may not have removed the factors contributing to the pathogenesis of facial palsy so effectively as to prevent the development of facial palsy.

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