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【 CASE REPORT 】

Additional Steroid Therapy for Delayed Facial Palsy in Miller Fisher Syndrome

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Abstract:
Miller Fisher syndrome (MFS) is a variant of Guillain-Barré syndrome. Delayed facial palsy (DFP) is a symptom that occurs after other neurological symptoms begin to recover within four weeks from the onset of MFS. As there have been few detailed reports about DFP in MFS cases treated with additional immunotherapy, we investigated three cases of DFP in MFS treated with additional steroid therapies. The duration of facial palsy in our cases was 12-24 days. No severe adverse effects were observed. Although adverse side effects should be carefully monitored, additional steroid therapy might be a treatment option for MFS-DFP.

Key words: additional immunotherapy, anti-GQ1b antibody, delayed facial palsy, Miller Fisher Syndrome, steroid

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Introduction

The acute autoimmune disorder Miller Fisher syndrome (MFS) is a variant of Guillain-Barré syndrome (GBS) characterized by the clinical triad of ophthalmoplegia, ataxia, and areflexia/hyporeflexia (1). Although approximately 20% of MFS patients are reported to have facial weakness (2), a few patients developed delayed facial palsy (DFP), which occurs after other neurological symptoms start to recover, within 4 weeks of the MFS onset (1, 3, 4).

One previous study reported that DFP occurred in 12 of 195 GBS patients (6%) and 4 of 68 MFS patients (6%) (3). The clinical characteristics and prognosis of DFP have not been reported to differ between GBS and MFS (3, 5). Because DFP cases often improve spontaneously, previous reports have claimed that it was unnecessary to perform additional immunotherapy (3, 5). However, DFP persisted in some patients for more than 50 days without additional immunotherapy (4).

There have been few reports of MFS accompanied by DFP (MFS-DFP) treated with additional immunotherapies (6, 7), and the effects of additional immunotherapies for DFP have not been fully investigated. We herein report three MFS-DFP cases treated with additional steroid therapies.

Case Report

Methods

We retrospectively investigated the medical records of 55 patients diagnosed with MFS at Hyogo College of Medicine Hospital between 2000 and 2020. The diagnosis of MFS was confirmed according to published criteria (8). We found six patients who developed DFP, four of whom were treated with additional steroid therapy. We excluded one patient whose medical information concerning the clinical course of DFP was insufficient to allow further investigation. As a result, we investigated three MFS-DFP patients treated with additional steroid therapy. We then reviewed previously reported MFS-DFP cases treated with additional steroid therapy for DFP.

This study was approved by the ethics committee of the Hyogo College of Medicine (approval number: 3293).

• Case 1

A 35-year-old man presented with diplopia and unsteadiness a few days after upper respiratory tract infection. He

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was admitted to our institution on day 6, and a neurological examination revealed bilateral external ophthalmoplegia, dilated pupils that were unreactive to light, ataxia, and areflexia. No facial weakness was observed on admission. A cerebrospinal fluid analysis on day 6 showed a normal cell count (1/μL) and an elevated protein level (55 mg/dL, normal <40 mg/dL). Serum IgG antibodies against gangliosides GQ1b and GT1a were positive. We diagnosed him with MFS and started immunoadsorption plasmapheresis (IAP) on day 6.

He completed five sessions. On day 11 (after the third IAP session was completed), his neurological signs (ataxia, external ophthalmoplegia, and light reflex of pupils) started to improve. However, on day 12, the patient developed right facial muscle weakness. Other neurological signs showed no deterioration. In addition to IAP, he was treated with methylprednisolone pulse therapy (500 mg/day for 3 days) from day 14 followed by oral prednisolone therapy (30 mg/day) with gradual tapering. His ataxia, external ophthalmoplegia, and lack of pupillary light reflex resolved completely by day 18. His facial palsy started to improve on day 21, and he completely recovered by day 24.

• Case 2

A 46-year-old woman developed diplopia and gait disturbance 1 week after an upper respiratory tract infection. She was admitted to our institution on day 3, and a neurological examination revealed bilateral external ophthalmoplegia, dilated pupils with sluggish response to light, bilateral ptosis, ataxia, and areflexia. No facial weakness was observed on admission. A cerebrospinal fluid analysis on day 3 showed a normal cell count (1/μL) and a slightly elevated protein level (44 mg/dL). Serum IgG antibody against GQ1b was positive. The patient was therefore diagnosed with MFS.

She was treated with IVIg (400 mg/kg/day for 5 days) from day 4. On day 5, her external ophthalmoplegia and pupil reactivity to light started to improve. Her dilated pupils with sluggish response to light resolved and ptosis started to improve on day 7. However, on day 9, she developed left facial muscle weakness. Other neurological signs showed no deterioration. She was treated with methylprednisolone pulse therapy (1,000 mg/day for 3 days) from day 10 followed by oral prednisolone therapy (30 mg/day) with gradual tapering. Her facial palsy started to improve on day 20, and she ultimately recovered and became able to close her left eyes completely on day 31. Her ataxia resolved by day 39, and her external ophthalmoplegia and areflexia resolved by day 162.

• Case 3

A 21-year-old woman developed numbness around her mouth a week after experiencing diarrhea, followed by nasal voice and dysphagia. She was admitted to our institution on day 3, and a neurological examination revealed bilateral external ophthalmoplegia and areflexia. The patient was not ataxic, and both pupils were reactive to light. She also complained of hand and foot numbness, but no objective sensory abnormalities were detected. No facial weakness was observed on admission.

Repeated nerve conduction studies of the limbs were normal. A cerebrospinal fluid analysis on day 3 showed a normal cell count (2/μL) and an elevated protein level (58 mg/dL). Serum IgG antibodies against GQ1b, GD1a, GalNac-GD1a, GT1b, and GD1b were positive. The patient was then diagnosed with incomplete MFS according to the diagnostic criteria (8).

She was treated with IVIg (400 mg/kg/day for 5 days) from day 3. Her nasal voice and dysphagia began to improve on day 5. Subsequently, her external ophthalmoplegia and numbness also began to improve. On day 8, her nasal voice resolved, and she became able to eat orally. However, on day 9, the patient developed left facial muscle weakness. Other neurological signs showed no deterioration. She was treated with methylprednisolone pulse therapy (1,000 mg/day for 3 days) from day 9, and her facial muscle weakness started to improve on day 10. Her external ophthalmoplegia and numbness of her limbs completely resolved by day 17. Her facial palsy completely resolved on day 33.

Results

The initial neurological signs (ophthalmoplegia and/or ataxia) in our patients started to improve 5-11 days after the disease onset, and DFP appeared on days 9-12. All of the patients developed unilateral DFP. The duration of facial palsy in the patients was 12-24 days. None of the patients experienced serious adverse side effects of steroids.

In addition, we reviewed previous reports of MFS-DFP with additional steroid therapy. Table summarizes the clinical features of the patients included in this study.

Discussion

In this study, we presented three cases of MFS-DFP treated with additional steroid therapy. Because DFP often developed when other neurological symptoms were improving after IVIg or plasmapheresis treatments, the typical immunotherapies for GBS were thought to be ineffective (9, 10). In our case series, DFP in all patients recovered within 24 days, and there were no serious adverse side effects.

Although the precise mechanism underlying MFS-DFP remains unclear, previous studies have suggested that proximal conduction block of facial nerves is subclinical at first and ultimately progresses to clinically apparent facial palsy (4), so MFS-DFP may be part of the disease progression of MFS (3). Because previous studies defined DFP as the development of facial weakness after the neurological signs have reached their nadir or started to improve, those studies included MFS-DFP cases in which other neurological symptoms had reached their nadir but had not yet started to improve. While it does seem plausible that DFP may be part of the disease progression of MFS if facial weakness occurs

Table. Clinical Features of Delayed Facial Palsy in Miller Fisher Syndrome with Additional Steroid Therapy.

	Our Cases			Reference [6]	Reference [7]
	Case 1	Case 2	Case 3	Case 1	Case 1
Age/gender	35/M	46/F	21/F	60/M	40/M
Antecedent illness	URTI	URTI	Diarrhea	-	URTI
Initial immunotherapy	IAP	IVIG	IVIG	IAP	IVIG
Beginning of initial immunotherapy (days)	6	4	3	4	6
Nadir of other neurological signs (days)	10	4	3	4	NA
Started improvement of other neurological signs (days)	11	5	5	10	9
Appearance of facial palsy (days)	12	9	9	12	10
Resolution of facial palsy (days)	24	31	33	36	33
Duration of facial palsy (days)	12	22	24	24	23
Additional immunotherapy	MP, oPSL[§]	MP, oPSL	MP	MP	MP

[§]Initial immunotherapy was continued.

IAP: immunoadsorption plasmapheresis, IVIG: intravenous immunoglobulin, MP: methylprednisolone, NA: not available, oPSL: oral prednisolone, URTI: upper respiratory tract infection

before other neurological symptoms of MFS start to improve, it seems strange to regard DFP as part of the disease progression of MFS when facial weakness occurs after the start of improvement in other neurological symptoms of MFS. To strictly investigate the mechanism of MFS-DFP, it might be best to exclude MFS-DFP cases in which other neurological symptoms have reached their nadir but not yet started to improve.

Furthermore, facial palsy in half of DFP patients with GBS or MFS was reported to be unilateral (3), although facial palsy is typically bilateral in GBS (11). Therefore, we cannot exclude the possibility that the etiology of DFP may differ from that of the usual MFS or GBS symptoms. For example, Bell's palsy is the most common peripheral paralysis of the facial nerve, and early steroid administration is recommended to improve symptoms and facilitate recovery (12). The therapeutic mechanism underlying the effects of steroids is thought to involve modulation of the immune response or direct reduction of edema of the facial nerve in the facial canal (13). Although steroid therapy alone is not considered beneficial for GBS (14, 15), additional steroid therapy may be suitable if a different mechanism is involved in the occurrence of MFS-DFP.

Several limitations associated with the present study warrant mention. First, we did not perform electrophysiological studies for facial nerve palsy (e.g. nerve conduction studies or blink reflex) or magnetic resonance imaging (MRI) of the facial nerve. The findings of electrophysiological studies and MRI in DFP have been presented in some Japanese case reports (16, 17). The findings of consecutive electrophysiological studies (blink reflex tests) in DFP were similar to those in idiopathic peripheral partial facial paresis (16, 18), although the gadolinium enhancement pattern of the facial nerve on MRI in DFP seemed to differ from that in Bell's palsy (17, 19). More studies concerning the volume and quality will be necessary to elucidate the pathophysiology of DFP. Second, we investigated a small number of MFS-DFP cases in this study and therefore could not conclude that additional steroid therapy is effective at decreasing the duration of facial muscle weakness in MFS-DFP. Furthermore, adverse side effects of steroids should be carefully investigated. A double-blind trial of additional steroid therapy in a larger number of patients with MFS-DFP will be necessary.

In conclusion, not all MFS-DFP cases promptly improve without additional therapies, and additional steroid therapies might be effective in improving the time to recovery from DFP.

The authors state that they have no Conflict of Interest (COI).

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