

A Case of Infantile Miller Fisher Syndrome

Naoe Yamada¹, Akio Nakai^{2,3*}, Koh-ichi Nishida⁴ and Mitsufumi Mayumi¹

¹Department of Pediatrics, Faculty of Medical Sciences, University of Fukui, Japan

²Hyogo Children's Sleep and Development Medical Research Center, Japan

³Department of Child and Adolescent Psychological Medicine, University of Fukui Hospital, Japan

⁴Department of Pediatrics, Fukui CardioVascular Center, Japan

Abstract

We report a 7-month-old female infant with Miller Fisher Syndrome (MFS), presenting with external ophthalmoplegia, blepharoptosis, ataxia, and loss of deep tendon reflexes. We treated the patient with high-dose immunoglobulin therapy (400 mg/kg/day, 5 days), which yielded favorable recovery. Serum anti-Cytomegalovirus (CMV) IgM antibody was positive in the early stage of the illness; therefore, association with CMV infection was suspected. Serum tests for antibodies to gangliosides, including anti-GQ1b immunoglobulin G, were negative. Tachycardia and increased sweating, signs of autonomic dysfunction, were observed during the clinical course. Magnetic resonance imaging revealed enhancement of the cauda equina on day 13 of illness; however, this enhancement was no longer seen 4 months later. Miller Fisher Syndrome is thought to be a variant of the acute inflammatory polyneuropathies, such as Guillain-Barre Syndrome (GBS). GBS occurs widely in infants through old adults, but infantile MFS is rare, and to the best of our knowledge, our case might be the youngest reported case in the literature.

Keywords: Autonomic function; Cytomegalovirus (CMV); Guillain-Barre syndrome (GBS); Infancy; Miller Fisher Syndrome

Abbreviations: Miller Fisher Syndrome: MFS; Guillain-Barre Syndrome: GBS; Cytomegalovirus: CMV; Magnetic Resonance Imaging: MRI; Diphtheria-Pertussis-Tetanus: DPT; Deep Tendon Reflexes: DTR; Electromyogram: EMG; Motor Nerve Conduction Velocity: MCV; Compound Muscle Potential CMAP; Immunoglobulin: IG; Electrocardiographic: ECG; Coefficient of Variation of the R-R Intervals: CVR-R

***Corresponding Author:** Akio Nakai, Senior Executive Vice-Director & Director, Department of Pediatric Neurology, Department of Pediatrics, Hyogo Children's Sleep and Development Medical Research Center, Akebono-cho 1070, Nishi-ku, Kobe, 651-2181, Japan; Tel: +81-78-927-2727, Fax : +81-78-925-9203; E-Mail : anakai.kodomo@gmail.com

Introduction

Miller Fisher described 3 adult patients with ophthalmoplegia, ataxia, and areflexia, and the characteristic triad of disorders is now known as "Miller Fisher Syndrome"

(MFS) [1]. We report a 7-month-old female infant with bilateral external ophthalmoplegia and blepharoptosis. Association with Cytomegalovirus (CMV) infection was suspected; however, serum tests for antibodies to gangliosides were negative. The patient also showed autonomic dysfunction and Magnetic Resonance Imaging (MRI) changes of the cauda equina. Infantile MFS is rare, and to the best of our knowledge, our 7-month-old infant is the youngest reported case in the literature.

Case Report

A 7-month-old female infant was admitted to our hospital with external ophthalmoplegia and blepharoptosis. She was born full term, and the pregnancy, delivery, and early development were all normal. She had received Diphtheria-Pertussis-Tetanus (DPT) and BCG vaccines 12 days and 1 day, respectively, before admission. She was breastfed and had never taken honey before. Although she had had fever 4 days before admission, she was afebrile at admission. Bilateral external strabismus and right-sided blepharoptosis were observed. The pupillary light reflex was normal bilaterally. No tetraplegia or adynamia was noted. The Deep Tendon Reflexes (DTR) were

all normal. Babinski's sign was negative. There were no signs of meningeal irritation. The heart rate was 110/min. Routine blood parameters, including the total and differential White Blood Cell (WBC) counts, C-reactive protein, serum electrolytes, fasting blood sugar, and the renal and hepatic functions were normal. On day 2, the blepharoptosis became bilateral and the external strabismus worse. Cerebellar signs, such as intention tremor and ataxia, and facial nerve paralysis became apparent. Cerebrospinal fluid examination was performed on day 3: protein 14 mg/dl; no pleocytosis; IgG index 0.44; myelin basic protein and oligoclonal bands negative. On day 5, the DTRs disappeared, hypotonus of the lower extremities developed, and suckling became weak. There were, however, no fatigability of ocular symptoms and no respiratory disturbance. Brain MRI on the same day revealed no abnormalities. On day 6, Electromyogram (EMG) revealed no waning. Whereas Motor nerve Conduction Velocity (MCV) was in the normal range, F waves were not detected in the upper or lower extremities, and depression of the Compound Muscle Potential (CMAP) amplitude in the lower extremities was observed (Table 1).

Table 1: Nerve conduction studies

	6th day	18th day	53rd day	137th day	Normal range (7 month)
Median nerve MCV (m/s)	38	44	42	43	42.5 ± 4.7
Median nerve CMAP (mV)	3.3	4.0	4.3	7.5	2.9 ± 1.2
Median nerve F wave	-	+	+	+	
Median nerve distal latency (ms)	2.3	2.4	2.2	2.2	2.1 ± 0.3
Tibial nerve MCV (m/s)	31	30	34	44	35.0 ± 2.1
Tibial nerve CMAP (mV)	0.8	3.2	7.4	6.7	6.8 ± 2.7
Tibial nerve F wave	-	-	+	+	
Tibial nerve distal latency (ms)	3.9	3.7	3.4	2.9	2.6 ± 0.7

MCV: Motor Nerve Conduction Velocity, CMAP: Compound Muscle Action Potential

The Tensilon test was negative and serum acetylcholine receptor antibody was also negative. We made the diagnosis of MFS and started the infant on high-dose Immunoglobulin (IG) therapy (400 mg/kg/day, 5 days) on day 6. Improvement of blepharoptosis became apparent immediately after the start of the IG therapy, and the DTRs and hypotonus of the upper extremities improved by the end of the therapy. On day 13, spinal MRI showed enhancement and thickening of the cauda equina (Figure 1A). On day 24, the infant could stand by holding on to the bed railing.

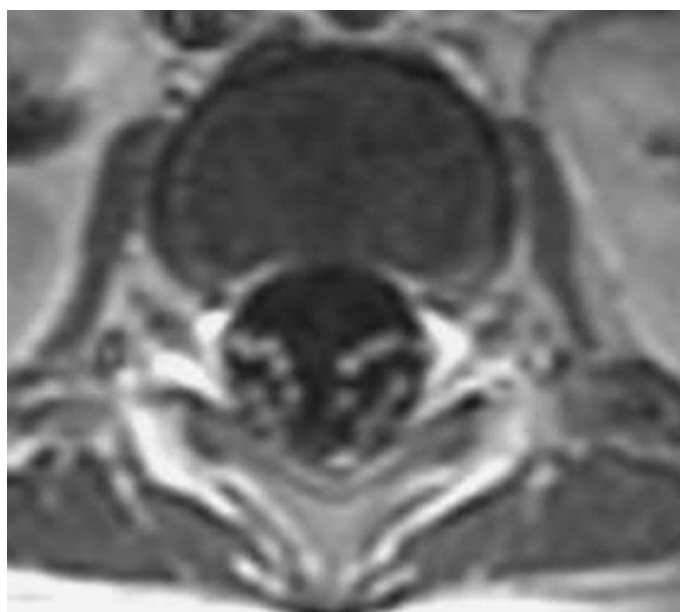


Figure: 1A: Spinal MRI axial image showed enhancement and thickening of the cauda equina.

(GE Signa 1.5 T; TR 383 ms, TE 14 ms)

During the clinical course, tachycardia (140-190/min) and increased sweating were noted. To evaluate the autonomic nervous activity, 24-hr ambulatory Holter Electrocardiographic (ECG) recording was undertaken on days 11, 25, and 53. In the domain analysis, the %RR50 and the Coefficient of Variation of the R-R Intervals (CVR-R) were depressed on day 11, but improved gradually thereafter. In the frequency domain analysis, the mean HF power was low on day 11, but increased on days 25 and 53. The cardiovascular autonomic dysregulation was no longer noted when the infant was discharged on day 28.

In the nerve conduction study on day 18, the F wave appeared in the upper limbs and the CMAP amplitude improved in the lower limbs, and on day 53, they were almost normal. Spinal MRI, performed 4 months later, no longer showed cauda equina enhancement (Figure 1B).

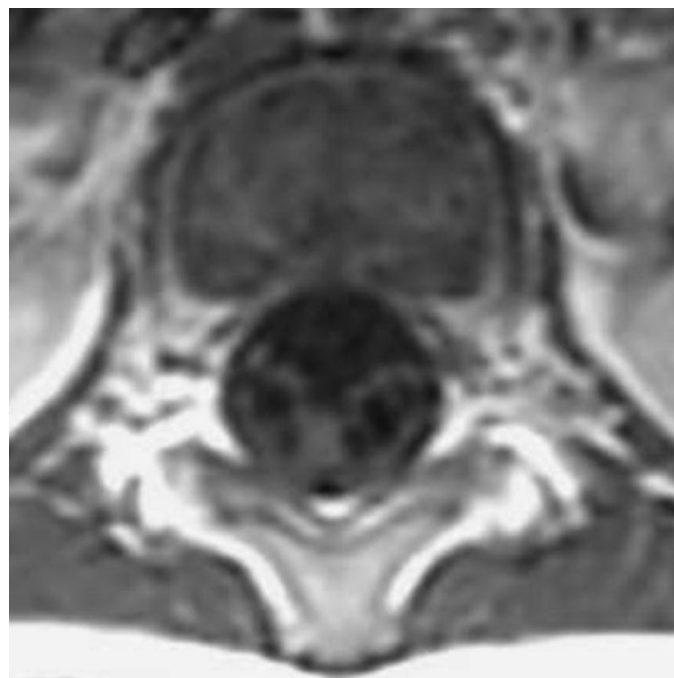


Figure: 1B: 4 months later, the cauda equina was not enhanced.

The anti-CMV antibody profile (Enzyme Immunoassay; EIA) was as follows: IgM 4.10, IgG 8.4 on day 6; IgM 3.98, IgG 23.2 on day 17; CMV antigen negative on day 17. These data indicate antecedent CMV infection. Other serological examinations for Epstein-Barr virus, *Campylobacter jejuni*, *Haemophilus influenza*, and *Mycoplasma pneumoniae* were all negative. Tests for anti-ganglioside antibodies, including anti-GM2 IgM antibody and anti-GQ1b IgG antibody, were also negative.

Discussion

Miller Fisher Syndrome (MFS) is characterized by ophthalmoplegia, severe ataxia, and loss of DTR [1], and is thought to be a variant of Guillain-Barre Syndrome (GBS) [2]. GBS occurs widely in infants through old adults, but infantile MFS is rare [3-6], and the investigation of acute ptosis in

children can be challenging [7]. To the best of our knowledge, our 7-month-old patient might be the youngest reported case in the literature.

Controversy still exists concerning whether MFS is the result of a predominantly axonal or demyelinating polyneuropathy [8]. In our case, MCV was not depressed in the upper limbs and was depressed only slightly in the inferior limbs initially. No F waves were detected in either the upper or inferior limb, and depression of the CMAP amplitude was noted in the inferior limbs; however, prolongation of the latency time was not detected. The F wave appeared and the CMAP amplitude improved, with recovery. Thus, we considered this case as predominantly showing axonal damage. F-waves could be abnormal in up to 92% cases of GBS; the most frequent abnormalities are complete absence or prolongation of minimum and mean latency [7]. Scelsa SN and Herskovitz S also reported that MFS typically represents a predominantly axonal, sensory demyelinating polyneuropathy [8].

Our case also showed transient autonomic dysfunction. Quantitative cardiovascular autonomic function tests showed that the parasympathetic nerve activity was preferentially depressed in the early stage of the disease. Both parasympathetic and sympathetic autonomic abnormalities have been reported in MFS, and could arise from a brainstem abnormality alone or brainstem abnormality in combination with peripheral nerve pathology [9].

In our case, detection of anti-CMV IgM antibodies and CMV IgG antibodies in the serum suggested antecedent CMV infection. CMV infection-associated MFS is much rarer than CMV-associated GBS [10]. Although anti-GQ1b IgG antibody is highly specific for MFS [10], it was negative in our case; a 2-year-old female without IgG anti-GQ1b antibodies has been reported in the literature [11]. While, there might be the possibility of DPT and BCG vaccines causing MFS, in this case.

In conclusion, we report a rare case of infantile MFS with transient autonomic dysfunction. While association with CMV

infection was suspected, serum anti-GQ1b IgG was negative. High-dose IG therapy proved highly effective.

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