Variants of Guillain-Barré Syndrome:
Miller Fisher Syndrome, Facial Diplegia
and Multiple Cranial Nerve Palsies

Ashfaq Shuaib and Werner J. Becker

ABSTRACT: We report the experience at a large teaching hospital over a 10 year period with Miller Fisher Syndrome, facial diplegia, and multiple cranial nerve palsies. In these patients, absence of drowsiness on examination, normal cranial CT scans, albumino-cytological dissociation on CSF examination and slowing of nerve conduction, all suggest that a peripheral nerve dysfunction is the underlying mechanism. Pertinent literature is reviewed, in an attempt to separate these probable variants of Guillain-Barré Syndrome from brainstem encephalitis, with which they may be confused.

METHODS

We report here our analysis of patients admitted over a ten year period with AAO, multiple cranial nerve dysfunction and facial diplegia. Our results will be compared with reports from the literature where the underlying etiology was considered to be brainstem encephalitis in an attempt to separate two distinct entities with different underlying mechanisms and prognosis.

The syndrome of ataxia, areflexia and ophthalmoplegia (AAO), initially described by Bogaert et al in 1938, became widely recognized after Miller Fisher's classic description of three patients with AAO in 1956. Often called Miller Fisher syndrome (MFS), it is considered rare and mentioned only in passing in most neurological text books.

The syndrome of multiple cranial nerve palsies, as a variant of Guillain-Barré Syndrome (GBS) was initially described by Guillain in Brussels in 1937, but has only rarely been since reported. Facial diplegia with minimal associated limb weakness or sensory deficits, another reversible neuropathy with a good prognosis has also been considered a variant of GBS.

The pathogenesis of MFS has traditionally been considered to be similar to that of GBS, as most patients have a preceding viral illness, albumino-cytological (A-C) dissociation on cerebrospinal fluid (CSF) examination, and a favorable outcome. This view has however recently been challenged by reports that consider brainstem encephalitis as the underlying cause for the AAO.
velocities were not excluded if the clinical course was typical. Drowsiness or signs of upper motor neuron involvement were not present in any of our cases. Out of a total of 60 patients, 15 met diagnostic criteria for MFS, multiple cranial nerve dysfunction or facial diplegia and are presented here. The remaining 45 patients, all with a diagnosis of GBS, will not be discussed further. These 15 patients were divided into the following three groups.

1) AAO, with minimal weakness and/or sensory symptoms (MFS).

2) Facial diplegia, ataxia and areflexia.

3) Multiple cranial nerve dysfunction, with or without associated ataxia or areflexia.

**PATIENT ANALYSIS**

1) Ataxia, Areflexia and Ophthalmoplegia

Seven patients had AAO. Clinical features are shown in Table 1A. Ataxia and ophthalmoplegia were present in all cases, but the degree of ophthalmoplegia was quite variable. One patient had bilateral ptosis only, 3 patients showed incomplete third nerve palsy, two patients had involvement of third and sixth nerves and one patient showed complete external ophthalmoplegia. Pupillary involvement was noted in two cases. In addition to ataxia, intention tremor was said to be present in one case and truncal titubation was seen in one patient. Preceding viral illness was present in six patients. Reflexes were absent in five patients and decreased in two patients. Involvement of cranial nerves other than 3, 4, & 6 was seen in only one patient. No patients had upper motor neuron signs and none of the patients were drowsy. Hospital stay was less than 15 days in all cases, and all were showing signs of recovery prior to discharge. All patients were followed for at least 2-3 months, and during this time no relapses occurred.

Results of nerve conduction studies varied widely from patient to patient. Two patients showed normal motor and sensory conduction velocities, but H reflexes were absent. Three patients showed slowed nerve conduction velocities. These ranged from very mild in some patients to motor conduction velocities as low as 27 meters per second in others. Sensory action potential amplitudes in the median and ulnar nerves were markedly reduced in several patients.

Cranial computed tomography (CT) was done in five patients and was normal in all. CSF examination (Table 1B) showed only minimal white blood cell count elevations, but CSF protein was increased in five patients. An EEG was done in only one patient, and was normal.

2) Ataxia Areflexia and Facial Diplegia

There were three patients in this group (Table 2A). Preceding viral illness was present in only one patient. Ataxia and areflexia or hyporeflexia were present in all patients. The reason for neurological consultation was facial diplegia in two cases and ataxia in the third. Symptoms developed over three days in two patients and ten days in the third. In the only case where the facial diplegia was not symmetrical, paralysis began first in the more severely involved side followed by facial weakness on the opposite side three days later. Facial weakness was of lower motor neuron type in all cases and taste was affected bilaterally in one patient. Reflexes were absent in one patient, and markedly reduced in the other two. Muscle strength was normal in all patients on admission, but two patients later developed mild hip flexor weakness. Distal lower limb numbness was present in one patient and this patient also showed decreased position and vibration sense in the feet. Romberg’s sign was absent in all patients. Limb ataxia was absent in two patients, and present to a very mild degree in the third.

Hospital stay was less than ten days in all cases, with some recovery by the time of discharge. Two patients had returned to normal within 12 weeks, while the third patient required bilateral blepharoplasty for persistent facial palsy one year later. CSF protein (Table 2B) was increased markedly in all three patients, and CSF white blood cell counts were not increased. Nerve conduction studies were done during the acute illness in

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**Table 1A: Patients with Ataxia, Areflexia and Ophthalmoplegia: Clinical Features**

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Preceding Viral Illness</th>
<th>Ophthalmoplegia</th>
<th>Other Cranial Nerve Involvement</th>
<th>Gait</th>
<th>Ataxia</th>
<th>Deep Tendon Reflexes Absent</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>URTI</td>
<td>+</td>
<td>—</td>
<td>+</td>
<td></td>
<td>Hyporeflexia</td>
</tr>
<tr>
<td>2.</td>
<td>—</td>
<td>+</td>
<td>—</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>URTI</td>
<td>+</td>
<td>—</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>URTI</td>
<td>+</td>
<td>7, 9, 10</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>URTI</td>
<td>+</td>
<td>—</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>URTI</td>
<td>+</td>
<td>—</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td>URTI</td>
<td>+</td>
<td>—</td>
<td>+</td>
<td></td>
<td>Hyporeflexia</td>
</tr>
</tbody>
</table>

URTI (Upper Respiratory Tract Infection)  
(—) (Absent)

**Table 1B: Laboratory Investigations**

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>CSF Protein (GMS/L)</th>
<th>CSF WBCs (Cells/mm³)</th>
<th>CT</th>
<th>EEG</th>
<th>Nerve Conduction Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>1.40</td>
<td>5</td>
<td>Normal</td>
<td>—</td>
<td>Absent H-Reflex</td>
</tr>
<tr>
<td>2.</td>
<td>.69</td>
<td>0</td>
<td>Normal</td>
<td>—</td>
<td>Slowed-Conduction</td>
</tr>
<tr>
<td>3.</td>
<td>1.80</td>
<td>9</td>
<td>Normal</td>
<td>—</td>
<td>Slowed-Conduction</td>
</tr>
<tr>
<td>4.</td>
<td>.42</td>
<td>1</td>
<td>—</td>
<td>—</td>
<td>Slowed-Conduction</td>
</tr>
<tr>
<td>5.</td>
<td>2.25</td>
<td>2</td>
<td>—</td>
<td>—</td>
<td>Normal</td>
</tr>
<tr>
<td>6.</td>
<td>.28</td>
<td>0</td>
<td>Normal</td>
<td>—</td>
<td>Absent H-Reflex</td>
</tr>
<tr>
<td>7.</td>
<td>2.00</td>
<td>0</td>
<td>Normal</td>
<td>—</td>
<td>Absent H-Reflex</td>
</tr>
</tbody>
</table>

(—) Not done
two patients, and these patients both showed absent or markedly reduced sensory action potential amplitudes in the median and ulnar nerves, and moderately slowed motor nerve conduction velocities. Nerve conduction studies were done only at 18 months after clinical presentation in the third patient, and both motor and sensory conduction studies were normal. EMG studies in this patient however were abnormal, with reduced motor unit recruitment and many large polyphasic motor unit potentials in the left tibialis anterior, left vastus medialis, and left deltoid muscles. Brain CT scan was normal in the one patient in whom this test was performed.

3) Multiple Cranial Nerve Palsies with or without Ataxia or Areflexia

This group consisted of five patients (Table 3A). A preceding viral illness was present in one patient. Symptoms were variable, with most patients having at least four cranial nerves involved. The third cranial nerve (CN) was affected in four of five cases, and involvement varied from decreased adduction to complete paralysis of all muscles supplied by this nerve. The seventh CN was affected in four cases, and the severity of involvement varied from mild to almost complete paralysis of all facial muscles. Bilateral involvement was present in three cases.

The fourth CN and sixth CN were each involved in three patients. The twelfth CN was affected in three cases, with bilateral involvement in two of these. The eighth CN was affected in two patients, with both showing only unilateral involvement. Both patients showed hearing loss without dizziness. The fifth CN was affected in two patients and this involvement was unilateral in both cases. The eleventh CN was affected in only one patient, with severe bilateral involvement. Muscle strength in the limbs was normal in all patients. Sensory examination revealed decreased light touch in one patient and decreased vibration sensation in another. Two patients were ataxic and two were hyporeflexic. No patients showed evidence for upper motor neuron signs or drowsiness.

Table 2B: Laboratory Investigations

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>CSF Protein (GMS/L)</th>
<th>CSF WBCs (Cells/mm³)</th>
<th>CT</th>
<th>EEG</th>
<th>Nerve Conduction Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>1.20</td>
<td>1</td>
<td>—</td>
<td>—</td>
<td>Abnormal</td>
</tr>
<tr>
<td>2.</td>
<td>5.20</td>
<td>0</td>
<td>Normal</td>
<td>—</td>
<td>Abnormal</td>
</tr>
<tr>
<td>3.</td>
<td>1.52</td>
<td>0</td>
<td>—</td>
<td>—</td>
<td>Abnormal</td>
</tr>
</tbody>
</table>

(--) Not done

Table 3A: Multiple Cranial Nerve Palsies: Clinical Features

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Preceding Viral Illness</th>
<th>Cranial Nerves Involved</th>
<th>Ataxia</th>
<th>Deep Tendon Reflexes</th>
<th>Strength (Limbs)</th>
<th>Sensory Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>—</td>
<td>3,4,6,7</td>
<td>+</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>2.</td>
<td>—</td>
<td>3,4,6,10,11</td>
<td>—</td>
<td>Normal</td>
<td>Normal</td>
<td>+</td>
</tr>
<tr>
<td>3.</td>
<td>—</td>
<td>3,5,7,8,12</td>
<td>Decreased</td>
<td>Normal</td>
<td>Normal</td>
<td>+</td>
</tr>
<tr>
<td>4.</td>
<td>+</td>
<td>3,4,5,6,7,12</td>
<td>+</td>
<td>Decreased</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>5.</td>
<td>—</td>
<td>5,7,8,12</td>
<td>—</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
</tbody>
</table>

(--) Not present

The CSF was examined in four patients, and all showed increased CSF protein (Table 3B). CSF white blood cell count elevations were minimal except in one patient with a traumatic lumbar puncture. Brain CT scans were done in four patients and were normal. Nerve conduction studies were done in three patients and were normal except for absent H reflexes in one patient.

Time from initial symptom to maximum disability varied from two to seven days, and the duration of hospital stay was one to five weeks. At the time of discharge, all patients were showing significant improvement. A follow-up was obtained in four patients. Three patients had returned to normal within three month’s of discharge from hospital. One patient developed multiple myeloma one year after discharge, and showed mild bilateral facial weakness and mild unilateral tongue weakness three years after discharge.

**DISCUSSION**

Although Miller Fisher syndrome is characterized by the triad of Ataxia, Areflexia, and Ophthalmoplegia, cases reported in the literature frequently show involvement of other cranial nerves in addition to 3, 4, 6.12,13 and occasionally also show mild weakness and sensory changes in the limbs.2,11,16 In these patients with more extensive neurological involvement, the diagnosis of MFS is made because these associated symptoms are over-shadowed by the AAO.

Ophthalmoplegia has been considered essential for the diagnosis of MFS, but, as in our patients, has varied from bilateral ptosis only17 to complete external and internal ophthalmoplegia.13,18-20,30 Some reported clinical findings might suggest brainstem lesions. These include the preservation of Bell’s phenomenon despite paralysis of upward gaze,2,11,15,19,21,22 mild ptosis in the presence of severe ophthalmoplegia12,15,19,22 and horizontal dissociated nystagmus.15,19,23,24,25 As similar disorders of eye movement have however been reported in conditions that do not affect the brainstem directly, including myasthenia gravis, botulism, intracranial aneurysm and pituitary tumor; Ropper has stated that all the eye movement disorders seen in MFS can be explained by cranial nerve dysfunction.26 Furthermore, it is difficult to conceive that inflammation could involve multiple cranial nerves in the brainstem and totally spare adjacent structures,27 so that no changes occur in level of consciousness.

The ophthalmoplegia that occasionally occurs with typical GBS is clinically indistinguishable from that reported with MFS.28

Table 3B: Laboratory Investigations

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>CSF Protein (GMS/L)</th>
<th>CSF WBCs (Cells/mm³)</th>
<th>CT</th>
<th>EEG</th>
<th>Nerve Conduction Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>.56</td>
<td>5</td>
<td>—</td>
<td>—</td>
<td>Absent H-Reflex</td>
</tr>
<tr>
<td>2.</td>
<td>.64</td>
<td>1</td>
<td>Normal</td>
<td>—</td>
<td>Normal</td>
</tr>
<tr>
<td>3.</td>
<td>.76</td>
<td>0</td>
<td>Normal</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>4.</td>
<td>1.50</td>
<td>26*</td>
<td>Normal</td>
<td>—</td>
<td>Normal</td>
</tr>
<tr>
<td>5.</td>
<td>—</td>
<td>Normal</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

(--) Not done

* CSF Bloodstained (Traumatic Tap)
and some patients present with AAO only to develop profound peripheral weakness later. A recent autopsy report of a patient with GBS and ophthalmoplegia showed no evidence of brainstem inflammation or demyelination, but did show widespread demyelination of cranial nerves. The prominent ataxia seen in MFS has been considered by some to be due to lesions in cerebellar outflow pathways in the brainstem. In his original report Miller Fisher considered a “unique and widespread attack on the sensory neurons underlying postural adjustment”, to be responsible for the ataxia, and recent physiological studies have shown evidence for a selective Ia afferent nerve fiber dysfunction in MFS. A disparity between proprioceptive information from muscle spindles and kinesthetic information from joint receptors has also been suggested as a cause for the underlying ataxia. Although involvement of sensory tracts in the spinal cord has been reported in autopsy series of GBS including “ataxic” GBS, these changes may all be due to severe involvement of spinal nerve roots. In our experience, the ataxia in MFS improves quickly, with almost complete recovery in 5 of our 7 cases at the time of discharge from hospital within 15 days of admission.

Five of our patients with MFS had abnormal nerve conduction studies. Similar findings have been reported previously and support the hypothesis that the pathogenesis of MFS is similar to that of GBS.

Normal nerve conduction has also been reported in MFS, but this does not rule out peripheral nerve involvement as the underlying mechanism as 9 to 41% of patients with typical GBS also show normal nerve conduction studies.

In addition to MFS, other variants of GBS likely share a similar pathogenesis. Reports of multiple cranial nerve dysfunction as a variant of GBS have been infrequent. Our 5 patients with multiple cranial nerve dysfunction, showed many features in common with GBS. All patients remained alert, 4 of 5 had A-C dissociation in the CSF, and all showed a good recovery where follow-up was available. Cranial nerves 3, 4 & 6 were the most frequently involved nerves, similar to MFS, but only 2 out of 5 cases showed ataxia. In contrast to MFS, 3 out of 5 patients showed normal stretch reflexes. All of our 5 patients had 4 or more cranial nerves involved, and with the exception of one patient, involvement was always bilateral.

Our 3 patients with facial diplegia, ataxia and areflexia may represent a further variant of GBS. Two patients showed slowed nerve conduction velocities, and a third patient, studied eighteen months after admission, showed neurogenic changes on EMG studies. All showed a marked increase in CSF protein levels. A brain CT scan done in one patient showed no evidence of CNS involvement. Although ophthalmoplegia was not present, the ataxia and areflexia in the absence of marked sensory abnormalities and weakness might suggest a relationship to MFS. Of interest, in patients with MFS with involvement of additional cranial nerves, the 7th cranial nerve is the one most frequently involved. The favourable outcome in all 3 patients is in keeping with peripheral neuropathy, as the underlying mechanism.
without drowsiness or upper motor neuron signs. In our experi-
ence CT scans are usually normal in such patients, and CSF
shows A-C dissociation. These patients have an excellent
prognosis, with no deaths attributable to this syndrome to our
knowledge.

Patients with involvement of other cranial nerves but without
drowsiness or upper motor neuron signs also have a good
prognosis, and show clinical, laboratory, and radiological find-
ings similar to GBS. These patients may or may not show
ophthalmoplegia, ataxia or areflexia. We speculate that the
pathological changes in these patients may also be restricted to
the peripheral nerves, the cell bodies of neurons with axons in
peripheral nerves, and the central processes of peripheral sen-
sory neurons. These patients are in many ways similar to MFS,
and whether or not they should be included in this nosological
entity is a matter of debate. In the past many authors have
included such patients within the spectrum of MFS. 5,10 Juncos
and Beal, 41 however, reported 14 patients with idiopathic multi-
ple cranial nerve palsies and concluded that only one of their
patients might have had an "oligosymptomatic" form of GBS.

Because many of their patients presented with facial pain and
responded to corticosteroid treatment, these authors concluded
that their patients had a condition related to Tolosa-Hunt
syndrome. It is of interest that, similar to our patients with
multiple cranial nerve palsies, the oculomotor nerves were the
cranial nerves most commonly involved, followed by cranial
nerves 5 and 7.

Patients with drowsiness or upper motor neuron signs on
admission in addition to AAO and ataxia frequently show EEG
and CT scan abnormalities. These patients likely represent
examples of brainstem encephalitis. The prognosis in such
patients may not be as favorable as in MFS. From our experi-
ence and a review of the literature we conclude that MFS and
brainstem encephalitis, both of which may cause ophthalmoplegia
and ataxia, are two distinct syndromes. Failure to recognize
this had led to confusion and controversy regarding the under-
lying pathological mechanisms.

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REFERENCES

epidemique de cas de polyradiculonevrite avec dissociation
albuminocytologique du liquide cephilo-rachidien (type Guillain
Barre) chez l’enfant et l’adulte, J Belg Neurol Pschiat 1938; 38:
151-211.

2. Fisher CM. An unusual variant of acute idiopathic polyneuritis
(Syndrome of ophthalmoplegia, ataxia, and areflexia). New


5. Ropper AH, Shahani BT. in Peripheral Nerve Disorders. Asbury
AK, Gilliat RW, eds. Neurology 4, Butterworths International

6. Trautmann JC, Barnett RC, in Peripheral Neuropathy. Dyck PJ,
Thomas PK, Lambert EH, Bunge R, eds. WB Saunders Com-

7. Asbury AK. Diagnostic considerations in Guillain Barre Syndrome.

8. Guillain G. Les polyradiculonevrites avec dissociation albumino-
cytologique et a evolution favorable. (syndrome de Guillain et

9. Munsat T, Barnes J. Relations of multiple cranial nerve dysfunc-
tion to the Guillain Barre syndrome. J Neurol Neurosurg Psychi-
atri 1965; 28: 115-120.

of an Unusual case, with a comment on Bell’s Palsy. The New

11. Elizan TS, Spire JP, Andman RS, Baughman FA, Lloyd Smith
DL. Syndrome of acute idiopathic ophthalmoplegia with ataxia

Fisher syndrome: Clinical and physiologic evidence of periph-

13. Weiss JA, White JC. Correlation of 1A afferent conduction with

14. Al-Din ASN, Anderson M, Bickerstaff ER, Harvey I. Brainstem
encephalitis and the syndrome of Miller Fisher. A clinical study.
Brain 1982; 105: 481-495.

15. Barontini F, Sita D. The nosological position of Fisher’s syndrome
(ophthalmoplegia ataxia and areflexia). J of Neurol 1983; 229:
33-44.

16. Meienberg O, Ryffel E. Supranuclear eye movement disorders in
Fisher’s syndrome of ophthalmoplegia, ataxia, and areflexia.
Report of a case and literature review. Arch of Neurol 1983; 40:
402-405.

17. Guiloff RL. Peripheral nerve conduction in Miller Fisher Syndrome.

18. Schapira AHV, Thomas PK. A case of recurrent idiopathic
ophthalmoplegic neuropathy (Miller Fisher Syndrome). J Neurol


20. Allen MW, MacQueen JC. Ophthalmoplegia ataxia and the syn-
drome of Landy Guillain Barre. Tran Am N Assoc 1964:89:
98-103.

21. Jampel R, Haidt SJ. Bell’s phenomenon and acute idiopathic

22. Ricker K, Hertel G. Electrophysiological findings in the syndrome
of acute ocular muscle palsy and ataxia. (Fisher Syndrome). J of
Neurology 1976; 214: 33-34.

23. Becker WJ, Watters GU, Humphreys P. Fisher syndrome in

24. Swick HM. Pseudointernuclear ophthalmoplegia in acute idiopathic
polyneuritis. (Fisher syndrome). Am J Ophthalmol 1977; 83:
355-357.

25. Weintraub MI. External ophthalmoplegia complicating acute infec-

26. Ropper AL. The CNS in Guillain Barre syndrome Arch of Neurol

27. Meienberg O. Lesion site in Fisher’s syndrome. Arch of Neurol
1984; 41: 250-251.


29. Blau I, Casson J, Lieberman A, Weiss E. The not so benign Miller

30. Dehaene I, Martin JJ, Geens K, Cros P. Guillain-Barre Syndrome
and ophthalmoplegia: Clinico pathological study of central and
peripheral nervous system including the oculomotor nerve. Neurol

31. Phillips MS, Steventon S, Anderson JR. Neuropathological findings
in Miller Fisher syndrome. J Neurol Neurosurg Psych 1984; 41:
292-495.

32. Ropper AH, Shahani BG. Proposed mechanism of ataxia in Miller

173-215.

34. Richter RB. The ataxic form of polyradiculitis. (Landry Guillain-

35. Jamal GA, MacLeod NW. Electrophysiological studies in Miller