Miller Fisher Syndrome-Bickerstaff brainstem encephalitis overlap-A case report

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Abstract:
Miller Fisher syndrome is a rare, acquired nerve disease that is considered to be a variant of Guillain-Barré syndrome. It is characterized by abnormal muscle coordination, paralysis of the eye muscles, and absence of the tendon reflexes. Like Guillain-Barré syndrome, symptoms may be preceded by a viral illness. Additional symptoms include generalized muscle weakness and respiratory failure. The majority of individuals with Miller Fisher syndrome have a unique IgG anti-GQ1b antibody that characterizes the disorder. In this report we describe a unusual presentation of Miller Fisher syndrome, having wasting of small muscles of both hands and plantars extensors.

Key words: guillain-barré syndrome, miller fisher syndrome, bickerstaff brainstem encephalitis

Introduction:
Miller Fisher Syndrome (MFS) is an uncommon variants of Guillaine-Barre syndrome (GBS), which typically presents as a triad of ophthalmoplegia, ataxia and areflexia. It was first described by Charles Miller Fisher in 1956 [1]. GuillainBarre Syndrome, Miller Fisher Syndrome and Bickerstaff’s brainstem encephalitis are considered as a spectrum of inflammatory polyneuropathy having many similarities [2]. The global incidence of GBS is 1-2 per 100,000 [3]. MFS accounts for up to 5% of GBS in Western countries, and 19-25% in Asian countries [4]. The diagnosis of MFS depends on the clinical characteristics of the syndrome. A rare and unusual case of Miller Fisher syndrome having ataxia, areflexia, ophthalmoplegia with limb weakness and small muscles of both hands wasting with plantars extensor (bilateral) is reported here for its rarity.

Case Report
An 18year old, previously healthy girl child presented to our emergency department with ataxia, slurring of speech & generalized weakness of four limbs since 22 days. Twenty days back she started with sudden onset of unsteadiness of gait in the early morning. Her imbalance was more as compared to weakness. She had no history of unconsciousness, abnormal behavior, convulsion, headache, vomiting, hearing difficulty, vertigo, tinnitus, dysphagia.

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Bladder & bowel function were normal. There was no history of fever, loose motion, upper respiratory tract infection or history of recent vaccination or surgery in last 3-4 weeks. She was 3rd order by birth born out of 2nd degree consanguineous marriage, developmentally normal, immunized child without any history of similar attack in past. On the day of admission, on examination patient was conscious, co-operative. Pallor, icterus, cyanosis, clubbing, lymphadenopathy were absent. Her length was 134cm, and weight was 50kg. Her blood pressure was 110/68 mm Hg, pulse was regular rate 76/min, respiratory rate 18/min, temperature 98.6°F. On neurological examination her mental function was normal but speech was weak. She was oriented to time, place person. Cranial and spine examination were normal. Cranial nerve examination revealed, restriction in right eye movement in lateral direction suggesting of right VI nerve palsy. oculomotor nerve palsy was present. Right VII nerve palsy was present. Nystagmus was absent. Optic nerve including fundus was normal. Other cranial nerves were normal. On motor system examination, tone of muscles of all four limbs was reduced. Power of lower limbs was 4/5 in both sides. Power of upper limbs was 3/5 bilaterally. There was marked wasting of small muscles of both hands there was no involuntarv movements. Deep tendon jerks were absent in four limbs. Plantar was extensor bilaterally, abdominal reflexes were preserved. On sensory examination, all sensory modality were present. Finger nose test was mild impaired. Rhomberg test was negative. Rests of the systemic examinations were normal. Clinical diagnosis of GBS variant Miller Fisher Syndrome was thought. The complete blood count, electrolyes, urea, creatinine, random blood sugar was within normal limit. MRI brain & EEG was normal. Nerve Conduction Velocity (NCV) showed CMAPs of median and ulnar nerves are reduced in amplitude also corresponding SNAPs are normal, thus giving impression of Motor axonal neuropathy. CSF study showed atypical pleocytosis with 8 cells, lymphocytes predominant, protein 80 mg/dl. She was treated conservatively with iv methyl prednisolone for 5 days. She showed a favourable response, her diplopia improved completely in less than two weeks, she started walking without support in 3 weeks, her cranial nerve deficits of third and sixth also improved in 22 days time. The patient was discharged and advised to be in follow-up.

Discussion
Miller Fisher syndrome is an acute demyelinating rare disorder that is considered a cranial nerve variant of Guillain-Barré syndrome. Miller Fisher syndrome, Guillain-Barré syndrome, and Bickerstaff brainstem encephalitis may be forms of a continuous spectrum [5]. Bickerstaff brainstem encephalitis differs from Miller Fisher syndrome in that the former also includes disturbance of consciousness and/or hyperreflexia. Combined features of Bickerstaff brainstem encephalitis and Miller Fisher syndrome are uncommon. Here we are reporting a case of Miller Fisher variant with Bickerstaff brainstem encephalitis overlap in which ataxia, areflexia, oculomotor disturbance, plantars extensor and limb weakness with small muscles of hand wasting occurred within few days and partial
rapid recovery beginning in 2 weeks after admission. The patient is in follow up.

Although it remains controversial as to whether the central or peripheral nervous system is primarily involved in Miller Fisher syndrome, most authors are proponents of the peripheral hypothesis. In contrast, Al-Din et al revealed that Miller Fisher syndrome is a variant of brainstem encephalitis [6], Berlit et al viewed 223 cases of MFS. The first symptom was diplopia (38.6%) or ataxia (20.6%). Areflexia was present in 81.6% of cases. The cranial nerves other than III were involved in 127 cases (56.9%): cranial nerve VII (45.7%), IX and X (39.9%) and XII (13%) were involved. In 53 cases tetraparesis occurred. Elevated CSF protein was present in 134 cases (64.4%). CSF finding were normal in 56 patients and 18 patients had mild pleocytosis. The prognosis of MFS was good. Recovery occurred after a mean time period of 10.1 weeks. Residual symptoms were present in 74 cases (33.2%), recurrence of MFS was reported in 7 patients, and 8 patients died [7]. Variant forms of MFS--Different variants of MFS are present with a common tie of the GQ1b antibody. Some cases have only one or two symptoms out of the triad. There are also lower cranial nerve variants of GBS and atypical MFS. It was reported that the oculomotor nerves were involved early in 7 cases of the ophthalmoplegic variants of GBS, and the cranial nerves IX, X and XI were involved early in 9 cases of a lower cranial nerve variant of GBS [8]. Our patient was diagnosed with Miller Fisher syndrome, as she had ataxia, areflexia and ophthalmoplegia. We included Bickerstaff brainstem encephalitis, because she developed impaired consciousness and plantars were extensor along with the above features. Although albumin-cytological dissociation in CSF is often present, protein concentration was increased in only 25% of Miller Fisher syndrome patients during the first week, while it was increased in 71% during the second and 84% during the third week [9]. This is consistent with our case as she presented in third week. Nerve conduction studies in Miller Fisher syndrome are usually normal or only slightly abnormal [10]. Ito et al.[11] suggested that the most frequent abnormality in nerve conduction and H-reflex studies was the absence of soleus H reflexes, in 75% of four Bickerstaff brain stem encephalitis and 74% of 28 Miller Fisher syndrome patients, whereas routine motor and sensory nerve conduction study results were normal for both groups. Our patient had unilateral facial nerve palsy, which is atypical features of Miller Fisher syndrome. There were no signs of corticobulbar dysfunction in our patient. Usually MFS is associated with axonopathy affecting predominantly the large diameter sensory fibers with only mild motor conduction abnormalities. F-wave latencies are usually normal in MFS. These findings were inconsistent to our case which revealed opposite findings on NCV. Anti-GQ1b antibody is one of the key factors in the pathogenesis of MFS, especially for ophthalmoplegia, and it is a useful marker in diagnosis of MFS but it was not done in our case because of unavailability of the test. For wasting of small muscles of hand a plausible explanation may be involvement of a peripheral nerve or reduced amplitude of CMAPs of both median and ulnar nerve. In MFS Serial neurophysiologic studies have shown involvement of peripheral nerve, with prolonged peripheral conduction in the blink reflex arc [12]. In addition there was no ulnar nerve thickening and hypopigmented patches or dysthesias. We ruled out cervical spine pathology as MRI cervical spine was normal and MND and its variants are extremely rare in this age group, besides MND has no association with cranial nerve deficit. Clinically our case is a Miller Fisher variant with Bickerstaff brainstem encephalitis having ophthalmoplearesis, unilateral facial nerve palsy and lower limbs motor weakness, plantars extensor and wasting of small muscles of hand.

**Conclusion**

Miller Fisher syndrome may present with a wide range of clinical features. Our patient started with diplopia, ataxia, areflexia and later limb weakness progressed to involve small muscles of hand along with oculomotor, lateral rectus and facial palsy. In contrast to GBS she was recovering fast in that diplopia subsided in 2 weeks and she walked without support in 3 weeks. We should suspect Miller Fisher syndrome Bickerstaff brainstem encephalitis when patient presents with impaired consciousness and areflexia quadriparesis with plantars extensor.

The debate over the years about whether Miller Fisher syndrome was an immune mediated polyneuritis or a brain stem viral infection, is still unclear. Anti-GQ1b antibodies are considered to be the key factor in mediating the ophthalmoplegia. Defects in neuromuscular transmission may be only one mechanism by which these antibodies mediate disease.
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