Shadows of a triad: Exploring the gaps in miller fisher syndrome

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SUMMARY

We describe a case of incomplete Miller Fisher Syndrome (MFS) in a 36-year-old previously healthy woman who presented with three days of binocular diplopia accompanied by internal ophthalmoplegia and horizontal nystagmus, preceded by a week of distal paraesthesia without an infectious prodrome. Clinical examination revealed non-reactive mid-sized pupils, mild limitations in ocular motility, bilateral non-fatigable ptosis, distal sensory impairment, and generalized areflexia, in the absence of ataxia. Neuroimaging and nerve conduction studies were unremarkable. Cerebrospinal fluid analysis demonstrated albumin–cytological dissociation, and serum anti-GQ1b IgG antibodies were positive, supporting the diagnosis of an incomplete MFS variant. The patient was treated with intravenous immunoglobulin (0.4 g/kg/day for 5 days), with progressive clinical improvement noted over two weeks. This case highlights the importance of recognising atypical MFS presentations, particularly those dominated by internal ophthalmoplegia without ataxia, and emphasizes the diagnostic utility of anti-GQ1b serology in incomplete variants.

INTRODUCTION

Gullain-Barre Syndrome (GBS) is an autoimmune disorder with the most common clinical presentation of neuromuscular weakness. Acute inflammatory demyelinating polyradiculoneuropathy (AIDP) is the most commonly occurring subtype in North America and Europe accounting for about 90% of all cases. However, in other parts of the world (Asia, Central and South America) axonal variants of GBS i.e. acute motor axonopathy (AMAN) and acute motor sensory axonopathy (AMSAN) are found to represent 30% to 47% of cases.[1]

A rare clinical variant of GBS, known as Miller Fisher Syndrome (MFS) is an acute immune-mediated demyelinating polyneuropathy which features were first identified by James Collier in 1932 and described it as a unique classical triad of symptoms including ophthalmoplegia, ataxia and areflexia. Miller Fisher later characterized it in 1956, classifying it as a unique entity within the GBS spectrum. The predominant features of MFS are ophthalmoplegia and ataxia, with a peripheral neuropathy being only a very mild clinical feature. Biochemically, there is elevated cerebrospinal fluid (CSF) protein and presence of ganglioside GQ1b antibody.[2] This is in contrast with classical GBS, where weakness and sensory disturbance are usually the presenting features.[3] We share our experience in diagnosing and managing a case of incomplete Miller Fisher Syndrome without ataxia, emphasizing the role of anti-GQ1b serology in confirming incomplete variants.

CASE PRESENTATION

A 36-year-old healthy female lady presented with seeing double images at near and far distance for three days duration. She was found to have internal ophthalmoplegia with horizontal nystagmus. Further history revealed that it was preceded by bilateral upper and lower limb numbness for one week. There was no prior history of upper respiratory tract infection or gastrointestinal symptoms. She denied any photophobia or using any eyedrops.

Uncorrected visual acuity was 6/9 bilaterally, no reduced contrast sensitivity and colour vision documented. Ocular examination revealed non-reactive mid-size pupils with horizontal nystagmus. No flutter or opsoclonus seen. There was no light-near dissociation noticed. Ocular motility was mildly limited at dextro-version, dextro-elevation and elevation. Bilateral eye also revealed mild bilateral non-fatigable blepharoptosis. Otherwise, fundus bilaterally was unremarkable. Neurological examination revealed reduced sensation in glove and stocking distribution with areflexia without presence of ataxia. Electrophysiologically there is no evidence of large fibre neuropathy on nerve conduction study. Magnetic Resonance Imaging (MRI) Brain and orbit is normal. She was given intravenous immunoglobulin 0.4g/kg for 5 days and her condition gradually improved after 2 weeks on follow up with residual diplopia at near (Figure 1). Cerebrospinal Fluid (CSF) studies showed albumin-cytological dissociation. Serum anti-GQ1b IgG is positive.

DISCUSSION

A diagnosis of MFS can be made with compatible clinical history taking, cardinal symptoms, normal findings on CT or MRI, and presence of albumin-cytologic dissociation (hyperproteinorrachia without pleocytosis) in the CSF of affected patients. Antibodies against ganglioside GQ1b are

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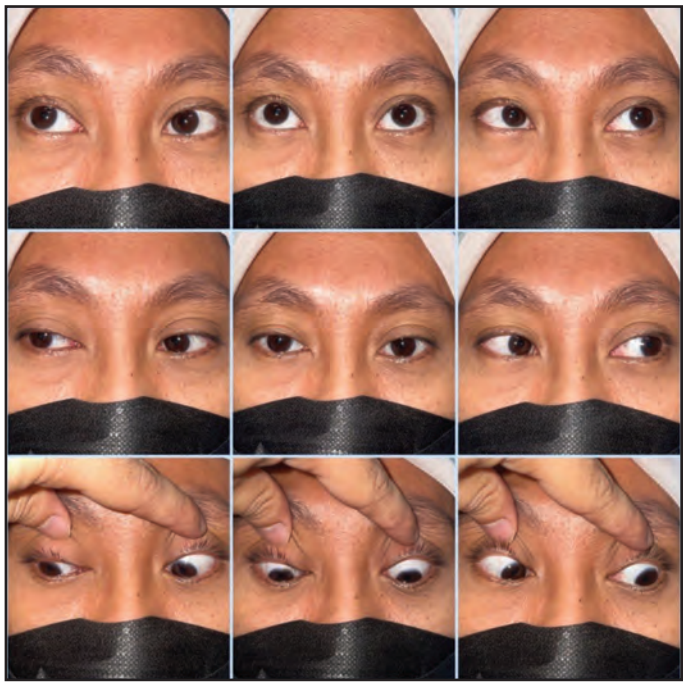

Fig. 1: showed mild ocular motility limitation at dextro-version, dextro-elevation and elevation

detected in the acute-phase sera in more than 90% of MFS cases which is useful for confirmation of MFS in this case.[4]

Diagnosis is usually based on clinical history, and the infectious antecedent appears to be present in the majority of patients: previous infection of the upper respiratory apparatus is most frequent (56–76% of patients). Gastrointestinal infection (4%), typical of classical GBS, and isolated fever (2%) are rarer.[5] However, our patient didn't have any preceding symptoms of illness. Although initial symptoms include progressive symmetrical paraesthesias in the upper and lower limbs, patients can also complain of diplopia without blurring of vision as the first symptom which bring her to our attention. Other symptoms include distal weakness, and absent deep tendon reflexes. This highlights that although the defining features of ataxia, ophthalmoplegia, and areflexia are generally required for the diagnosed as MFS, other symptoms and signs may be present without one of the classical triad and confound a clinician's diagnostic decision making.

The most common differentials for MFS include myasthenia gravis. However, absence of fatiguability and bulbar symptoms makes myasthenia gravis less likely in this case. GQ1b ganglioside complex is most often associated with MFS, positive in over 90% of patients with MFS and is not present in unaffected individuals.[6] It is now known that elevated anti-GQ1b antibody production can be seen within a spectrum of conditions, including acute ophthalmoparesis, Bickerstaff's brainstem encephalitis, and Guillain–Barre syndrome, in addition to MFS.[7] Its high occurrence in patients with MFS is very useful for the diagnosis especially in incomplete type of MFS.

To our knowledge, only two previous cases of MFS presenting with internal ophthalmoplegia as first presentation has been documented. The first case was a woman with typical MFS whose initial manifestation was blurred vision because of bilateral tonic pupils. Investigations, including brain imaging, cerebrospinal fluid examination and nerve conduction studies were normal except for elevated serum levels of immunoglobulin G anti-GQ1b antibody. During the disease, she subsequently developed bilateral sixth and seventh nerve palsies, gait ataxia, and areflexia.8 However, in our patient, there is no ataxia.

The second case was an elderly lady who presented with internal ophthalmoplegia as most notable feature, consisting of mid-sized non-reactive pupils, as well as fronto-orbital headache. The patient had a history of upper respiratory tract infection a week before symptoms and subsequently developed classical triad of ophthalmoparesis, ataxia and areflexia. Among ophthalmoplegias, internal ophthalmoplegia is much less common than external ophthalmoplegia. There are very few references in the literature regarding isolated internal ophthalmoplegia without external involvement. Pupillary disorders in MFS can be seen in up to 50% of cases, tend to progress independently of the presence of external ophthalmoplegia, and usually resolve in a significantly shorter period than external ophthalmoplegia. These findings suggest that the involvement of pupil-motor fibers is independent of lesions in the other subdivisions of the oculomotor nerve.[9]

Pupillary abnormalities like mydriasis and light-near dissociation, though rare, correlate strongly with anti-GQ1b antibodies. These antibodies target gangliosides enriched in ocular motor nerves and autonomic pathways, with cross-reactivity to GT1a potentially disrupting sympathetic

innervation of the iris.[10] Such mechanisms may underlie atypical autonomic features, including bilateral mydriasis, in MFS. This explains the presence of pupillary involvement in our case.

CONCLUSIONS

This case highlights pupillary involvement in a case of mild upper and lower limb weakness or numbness and areflexia should lead the clinician to the suspicion of Miller Fisher syndrome. Early recognition with timely treatment can lead to early recovery with good prognosis without residual deficit.

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