ORIGINAL RESEARCH PAPER
Volume - 11 | Issue - 11 | November - 2022 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A CASE OF OPHTHALMOPLEGIA,ATAXIA,AREFLEXIA AND BULBAR WEAKNESS :PHARYNGO-CERVICAL-BRACHIAL VARIANT OF GUILLIAN BARRE OR MILLER FISHER SYNDROME ?

General Medicine

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ABSTRACT

Miller Fisher Syndrome (MFS) is a rare variant of Guillain-Barré Syndrome (GBS). It is largely a clinical diagnosis based on the classical features of ataxia, areflexia, and opthalmoplegia. Its clinical evolution is most often favorable. However, other neurological signs and symptoms may also be present. Supportive laboratory studies (positivity of antibodies, CSF albumin-cytological dissociation and nerve conduction studies) are useful especially in uncommon presentations. We report a case of a 52 year-old patient who exhibited dysphonia and difficulty to swallowing previously to the classic triad of ataxia, areflexia, and opthalmoplegia, characteristic of MFS. CSF analysis demonstrates an albumin-cytological dissociation. Anti-GQ 1b antibodies were found to be positive . The patient has spontaneously and completely recovered after 6 weeks following therapy with IVIg.

KEYWORDS

Miller Fisher Syndrome; Guillain Barré Syndrome variant; dysphonia; dysphagia

INTRODUCTION

The concept of Guillain–Barré syndrome (GBS) has changed over the years. In the past, it used to be defined as a single condition, while now it is referred to as a group of acute neuropathies of a one-phase course induced by autoimmune factors.[1] The condition is most likely caused by molecular mimicry between antibodies reacting with antigens of infectious agents such as viruses and bacteria cross-reacting with epitopes present in the peripheral nervous system. This, in turn, results in damage to myelin and/or nerve axons.[2] Clinically, the most common, 'classic', form of GBS accounting for 60–90% of all GBS cases is acute inflammatory demyelinating polyradiculoneuropathy. Other, much less common forms, include acute motor sensory axonal neuropathy – 5–10% and Miller–Fisher syndrome (MFS) – 3–5% of GBS cases.[3]

Miller Fisher's syndrome (MFS) is a rare variant of Guillain Barré Syndrome (GBS) characterized by the acute onset of ataxia, ophthalmoparesis, and areflexia. The appearance of symptoms following an infection of the respiratory or digestive tract is a common ground for all GBS variants. The diagnosis of MFS is essentially clinical and it is mostly supported by serum positivity for anti-ganglioside antibodies.[2] Others supportive laboratory findings include CSF albumin-cytological dissociation and presence of sensitive abnormalities in nerve conduction studies. Currently, there are no consensus diagnostic criteria.[3] In addition to the classical form, the spectrum of MFS includes incomplete and extensive forms, with additional central clinical features such as the Bickerstaff rhombencephalitis phenotype or peripheral symptomatology suggesting overlap with classical GBS or its other variants.[3]Of the GQ1b-positive subtypes of GBS, the pharyngeal-cervical-brachial (PCB) variant is most commonly associated with oropharyngeal weakness. Patients with the PCB variant of GBS typically present with rapidly progressive oropharyngeal and cervicobrachial weakness associated with areflexia in the upper limbs. 'Incomplete' PCB variants have been described in the literature; for instance, 'acute oropharyngeal palsy' represents a subtype of PCB in which upper limb weakness is absent.[4] Therefore, our patient appears to reflect an overlap syndrome of MFS with incomplete PCB, given the involvement of bulbar cranial nerves responsible of difficulty of swallowing and dysphonia in addition to the MFS triad, which is an extremely rare clinical presentation.

CASE REPORT

A previously healthy 52-year-old man presented to our hospital with a sudden onset paraesthesias of both upper and lower limbs along with diplopia after waking up in the morning 3 days ago, followed by drooping of eyelids. He also complained of dysphonia in the form of nasal tone in speech . he could not swallow properly, and fluids regurgitated through his nose when he drank water. he also complained of dizziness and unsteadiness while walking. he did not have limb weakness and bowel or bladder difficulties. he had symptoms, including nasal congestion, sore throat, and fever to 38◦C, suggestive of an upper respiratory tract infection (URTI) 6 days before the neurological symptoms. On admission, he was afebrile and mentally alert.

Neurological examination revealed bilateral blepharoptosis and restriction of ocular motility in all directions with fixed eyeballs bilaterally and severe dysphagia to both liquids and solids. There was bilateral paralysis of the soft palate and loss of pharyngeal reflex. His pupils were symmetric and of a normal size, reacting briskly to light. Corneal reflexes were intact bilaterally, and examination of the facial nerves was normal. There was no weakness of neck or limb muscles. All the deep tendon reflexes were absent, and the plantar responses were flexor. Sensory examination revealed absent vibration sense in bilateral knee and ankle joints with intact joint position sense and proprioception, and Romberg test was positive. There were no cerebellar signs or evidence indicative of autonomic or sphincter dysfunction.

Laboratory studies, including complete blood count, routine biochemical tests,ESR, hemoglobin A1c, thyroid function, tumor markers, were unremarkable. .

A non-contrast brain magnetic resonance imaging (MRI) scan on day 18 and an MRI scan with gadolinium on day 25 showed no abnormalities. A modified tensilon test(using Neostigmine) didn't show any improvement in signs and symptoms. Cerebrospinal fluid (CSF) analysis done on 14th day of admission demonstrated normal glucose level, cell count of 1 /µL,marked elevation of protein concentration of 96 mg/dL (normal range; 10-40 mg/dL), and negative cytological findings.

Serological analysis showed negative results for potential viral infection (antibodies to herpes simplex virus 1 and 2, Varicella-zoster, cytomegalovirus, and Epstein-Barr). Serum analyses for anti-nuclear antibodies, anti-neutrophil cytoplasmic antibodies, anti-acetylcholine receptor antibody, and anti-muscle-specific kinase antibody were negative. The angiotensin-converting enzyme level was normal. A screening test for antiganglioside antibodies showed immunoglobulin G (IgG) anti-GQ1b antibodies positive.

Nerve conduction study (NCS) and repetitive nerve stimulation performed on day 3 of the illness were normal. Serial NCS on day 11 demonstrated decreased persistence of F-wave of left ulnar and bilateral median nerves, as well as reduced amplitude of sensory nerve action potential (SNAP) in the limbs. The results of motor conduction study were otherwise normal.

The patient received intravenous immunoglobulin (IVIg) treatment for 5 days (0.4 g/kg/day) on day 5 of the illness. A nasogastric tube was also inserted because of severe dysphagia. he responded well to IVIg. His bulbar palsy, diplopia, and ataxia started to improve 4 days later and almost completely recovered at discharge on day 16 of the illness.

DISCUSSION

The nomenclature of Guillain-Barre syndrome and all its variants is confusing. Traditionally, two separate cranial nerve variants of Guillain-Barre syndrome are reported: Miller Fisher syndrome and polyneuritis cranialis. Miller Fisher syndrome is characterized by a triad of ophthalmoplegia, ataxia, and areflexia, and in addition, a variable degree of limb muscle involvement and bulbar signs may occur. Patients with polyneuritis cranialis manifest a rapid, simultaneous onset of symmetric lower cranial nerve dysfunction, without other signs. An alternative terminology for categorizing the cranial nerve variants of Guillain-Barre syndrome makes a distinction between ''ophthalmoplegic'(ophthalmoplegic-GuillainBarre syndrome) and "lower cranial nerve" (lower cranial nerve-Guillain-Barre syndrome) forms.[5] The "lower cranial nerve" form shares many similarities with the pharyngeal-cervical-brachial weakness variant of Guillain-Barre syndrome, as described by Ropper.[7] If the patient exhibits disturbances of consciousness in addition to pharyngeal-cervical-brachial weakness, a diagnosis of Bickerstaff's brainstem encephalitis is rendered. Larger studies demonstrate clinical overlap. The antecedent infections are the same, and antiganglioside antibodies are evident in all Guillain-Barre syndrome variants, leading to the conclusion that it is a continuous spectrum.[5]

Our patient presented with the MFS classic symptom triad of ophthalmoplegia, ataxia and areflexia. Concomitant symptoms included paraesthesias in both upper and lower limbs, typical of this syndrome (reported by 40% of MFS patients).[4]accompanied by the absence of limb paresis or any abnormalities in an electronystagmography test. Clinically significant and relatively uncommon MFS symptoms we observed in our patient were hypernasality of speech and dysphagia caused by soft palate paresis. The presenting symptoms did not indicate Bickersaff's brain stem encephalitis (BBE), which is considered a subtype of MFS.[6] Both disorders are heralded by infection and the possible presence of anti-GQ1b antibodies. Patients also develop ophthalmoplegia and ataxia.[6] Unlike MFS, BBE is characterised by quantitative disorders of consciousness such as pathological drowsiness, pyramidal and sensory signs.Myasthenia was ruled out since no typical symptoms were observed and there was no improvement in symptoms with neostigmine challange, with the presence of ophthalmoplegia and ataxia, the nerve stimulation test yielded negative results. In 1986, Ropper.[7] described the pharyngeal-cervical-brachial (PCB) variant of GBS, which is characterised by dysphagia, and weakness of muscles of the neck, arm and shoulder girdle in the dominant limb. Koga et al.[10] proved that 20% of MFS patients can present with paresis of the nasopharynx muscles accompanied by paresis of the muscles of the neck and arm in the dominant upper extremity. It can therefore be assumed that MFS/GBS, BBE/GBS, and PCB/GBS constitute the continuum (spectrum) of the symptoms.In the described case only the soft palate was affected with paresis. Miller–Fisher syndrome diagnosis is established on the basis of typical neurological signs and complemented by albuminocytologic dissociation in the CSF and presence of anti-GQ1b antibodies in the blood serum.

Immunohistochemical tests carried out in MFS patients show an elevated concentration of GQ1b in the subependymal brainstem region encompassing the cerebral aqueduct and the fourth ventricle. The area is the site of centres responsible for vertical and horizontal eye movements. GQ1b antibodies were proved to be directed against nervous tissue of this area, which consequently explains the occurrence of external ophthalmoplegia.[8]The fact that anti-GQ1b antibodies show a tendency for cross-reactivity with GT1a gangliosides, characteristic for PCB patients (here bulbar palsy is the main symptom), may lead to the assumption of the hypothesis that the cross-reactivity can be blamed for the damage to cranial nerves IX and X, observed in MFS patients.[9] It is believed that the presence of the antibodies established through staining of the molecular layer of the cerebellar cortex is connected with the manifestation of ataxia symptoms. In seropositive MFS the highest concentrations of anti-GQ1b antibodies are found in its initial phase. They normally disappear within the next 3–4 weeks, which is the result of clinical recovery. Koga et al.[10]proved the presence of IgG – antibodies to GM1b, Gd1c, Ga1NAc-GM1b and ganglioside complexes as a serological marker for GQ1bseronegative patients. The pathogenesis of these antibodies requires further investigation.[9] The clinical course of both seropositive and seronegative MFS is similar. We found in our patient antibodies to antigens GQ1b. The described case is believed to be an instance of MFS affecting cranial nerves, which results in the paralysis of the soft palate.

CONCLUSION

Our observation aims to draw attention to an overlap syndrome of MFS with incomplete PCB, due to symptoms of oropharyngeal palsy in addition to the MFS triad of ataxia, areflexia and ophthalmoplegia and to reflect the misleading possibility in front of such a rich clinical case. Overall, clinical, immunological and neurophysiological studies provide evidence that PCB makes a continuous spectrum with MFS.

Antiganglioside antibody testing has limited value as negative test result does not rule out GBS. Yet, they may be useful in patient with atypical presentation but their results may be delayed and, therefore, should not be relied on for diagnosis.

Patients with MFS usually show good recovery even without specific immunotherapy. However, in case of an overlapping syndrome with PCB immunoglobulin therapy or plasmapheresis is highly recommended in order to abort the axonal damage and improve the patient's clinical prognosis.

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