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Enteric Fever As An Antecedent To Development Of Miller-Fisher Syndrome And Possible Role Of COVID-19 Vaccination

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Abstract

Summary: Guillain-Barre Syndrome is an immune-mediated demyelinating disorder. Miller-Fisher Syndrome is an uncommon subtype of GBS. It is characterized by findings of ophthalmoplegia, ataxia, and areflexia. Here we present the case of Miller-Fisher Syndrome following an episode of typhoidal diarrhea. The presentation was of rapidly progressing weakness beginning in the lower extremity with diplopia. Examination revealed diminished reflexes. CSF testing revealed albuminocytologic dissociation which was later supported by neurophysiological testing. The patient was treated with intravenous immunoglobulins (IVIG).

We conclude that Miller-Fisher syndrome should be considered in the diagnostic workup of patients presenting with new sensorimotor deficits following diarrheal illnesses and/or COVID-19 mRNA vaccination. Early recognition is essential given the propensity of GBS to cause life-threatening respiratory failure and prompt IVIG administration is associated with a better prognosis.

Keywords: Enteric Fever, Miller-Fisher Syndrome, COVID-19, Vaccination

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1. Introduction

Guillain-Barré Syndrome (GBS) is an acquired immune-mediated demyelinating disorder described by progressive symmetrical ascending paralysis. It includes several types of acute immune-mediated polyneuropathies. This case report has been reported in line with the SCARE Criteria.[1] Collier first explained Miller-Fisher Syndrome as a rare subclass of Guillain-Barré Syndrome.[2] It is primarily axonal neuropathy. In its purest form, Miller-Fisher Syndrome presents with ataxia, ophthalmoplegia, and areflexia.[3] The major difference between MFS and the other, more common subtypes of GBS is that the first nerve groups to demyelinate in GBS are commonly located in the cranium. This results in difficulties with balance and coordination, ocular muscle movement, vision impairment, and neuronal reflexes. Most cases of MFS occur as an antecedent to either a viral or bacterial infection. Although the mechanism of this syndrome is not accurately described, it is speculated that MFS results from a cross-reaction between the antigens of the peripheral nerve with the antigens of bacteria or different types of Viruses.[4] Miller-Fisher Syndrome is diagnosed mainly clinically but anti-GQ1b antibodies have been associated with it and can assist in the differential diagnoses.[5] We will discuss and talk about a patient presenting with a diagnosis of Miller-Fisher Syndrome and the events leading up to the diagnosis. As required and necessary, we got Informed consent from the patient.

2. Case Presentation

A female of 26 years presented to the ER Department of our hospital with a complaint of bilateral lower limb weakness in the last four days. The weakness had a sudden onset, was progressive, ascending, symmetrical, and associated with paraesthesias and intense myalgia of the lower limbs. The patient also reported bilateral eye pain for the past three days. She had no previous history of respiratory or neurological disorders. The patient had received 2 doses of Pfizer BioNtech COVID-19 mRNA intramuscular vaccine a month ago. The patient complained of abdominal pain two months ago and after investigations, the patient was diagnosed with enteric fever. She was admitted to our medical ward and at that time she was one month pregnant. On examination, she was well-oriented and afebrile. Her vitals were stable. She had dysphagia, a diffusely tender abdomen, decreased air entry on the right side of the chest, and a positive Babinski sign on the left foot. Scores of Muscle power test were: left upper limb 3/5, right upper limb 3/5, right lower limb 3/5, and left lower limb 2/5. Her

deep tendon reflexes were also assessed, which were absent. On eye examination, the Patient had slow extra ocular eye movements. Further Eye examination showed diplopia, which was horizontal for both far and near, ptosis was noted in the left upper eyelid, and weakness of bilateral extra-ocular eye muscles was also observed. No abnormalities were detected in serum electrolytes, renal function tests, liver function tests, and CBC (Complete blood count) profile. Ultrasound and X-ray Chest were performed which came out to be unremarkable. CSF findings were as follows: normal White Blood Cell count, Elevated protein level, normal cell count, and serum IgG antibody against GQ1b were present. Electromyography (EMG) was conducted which revealed bilateral axonal sensory neuropathy. Motor nerve conduction abnormalities were observed with low amplitude and decreased velocities in both sensory and motor nerves of the upper and lower limbs and persistence of distal latencies. Compound muscle action potential reduction was also observed. The clinical presentation and investigations suggested the diagnosis of MFS (Miller Fisher Syndrome), which is a subtype of GBS (Gullian Barre syndrome). The patient was treated as follows: Intra Venous Heparin 5000 units subcutaneously, intravenous Omeprazole 40mg Once Daily, and Intramuscular Methyl cobalamin Once daily. The patient also received plasmapheresis. A total of 5 plasma exchanges (each 220 to 260 ml per Kg body weight) Were given to the patient after the diagnosis. Power in all four limbs was monitored continuously and the power returned after 5 weeks of plasmapheresis. The power noted in each limb was as follows: Right upper limb 5/5, Right lower limb 5/5, and 4/5 and 5/5 in left upper and lower limbs respectively. After the resolution of power, the patient was discharged. The patient was called up for a follow-up after 3 weeks of initial discharge. During the very first follow-up, it was noted that the patient's initial presenting symptoms were resolved. An ocular exam at the follow-up also had normal findings confirming that all initial complaints had been resolved.

3. Discussion

A subclass of Gullian-Barre Syndrome has been identified as MFS (Miller-Fisher Syndrome). It most commonly presents with the triad, which includes: ophthalmoplegia, ataxia, and absence of reflexes.[6] Miller-Fisher Syndrome has been associated with antecedent infections with Haemophilus Influenza, Campylobacter Jejuni& CMV.[7] Good Clinical history can aid in making the diagnosis of Miller Fisher Syndrome correlating with normal MRI, and CT findings. CSF analysis shows albumin-cytologic dissociation (Increased proteins with a normal cell count). Antibodies against GQ1b which block acetylcholine release can be used for disease activity and as a diagnostic marker. However, it is important to note that these antibodies are not unique to MFS. Many patients with MFS and GBS report diarrheal illnesses before the onset of neurological symptoms similar to those seen in our patients. Chida et al reported that recurrent cases of MFS were either associated with diarrheal illnesses or upper respiratory tract infections.[8] While Campylobacter is the most frequently associated pathogen with MFS and GBS, our patient's history is significant for typhoidal illness.[9] Other than respiratory and diarrheal illnesses, other triggers for MFS include immunizations. Post-immunization GBS is reported more frequently than MFS although we were able to find reports of MFS after Covid-19 and influenza vaccines.[10,11] Siddiqi et al reported a case of a patient presenting with the clinical triad of MFS after the Sinovac-Coronavac vaccine without any other recognizable causes.[12] Michaelson et al reported a similar case of MFS after 2 doses of the Pfizer-BioNTech COVID-19 vaccine.[13] Our patient also reported getting the Pfizer-BioNtech SARS-Cov-2 mRNA vaccine one month ago. The pathophysiology of MFS after COVID-19 is unclear; however, it is suggested that an immune response to the constituents of the virus can lead to the development of MFS.[14] We did find anti-GQ1b antibodies in our patient, although these antibodies have variable specificity. We cannot be sure whether the acute presentation of Miller Fisher Syndrome was related to the antecedent gastrointestinal illness or response to the COVID-19 vaccine. It is interesting to note that there could be two possible triggers leading to the development of MFS in our patients. A review of the literature suggests that most cases of MFS show significant improvement with the administration of IV immunoglobulins with the majority of patients showing almost complete functional recovery.[15] Cases of MSF during pregnancy have been observed similarly to our patient. These cases were also treated with and responded to immunoglobulins.[16] MSF is an immune-mediated self-limiting condition that rarely progresses to serious complications. A near-

complete recovery can be expected in 6 months. Our case shows various similarities to other cases and displays the typical triad of MFS along with the specific CSF results and distinctive results representing a common pathogenic mechanism and disease course.

4. Conclusion

MSF is a rare disorder often misdiagnosed by clinicians. It is to be highlighted that in this exciting case, Miller-Fisher Syndrome has presented itself as bilateral upper and lower limb paralysis. This case also brings light to the importance and value of history-taking since that is the only way to narrow down and make the diagnoses of MSF.

CONFLICTS OF INTEREST- None

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Contributions:

F.F, M.E.R, A.A.I, H.N - Conception of study
T.B.S, M.I, M.E.R, A.A.I - Experimentation/Study Conduction
T.B.S, M.I, F.F, H.N - Analysis/Interpretation/Discussion
T.B.S, M.I, M.E.R, A.A.I - Manuscript Writing
M.I, F.F, M.E.R, A.A.I, H.N - Critical Review
T.B.S, M.I, F.F, M.E.R, H.N - Facilitation and Material analysis

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