

Miller Fisher Syndrome in the Setting of Influenza A Infection

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Abstract

Miller Fisher syndrome (MFS) is a rare, and milder, variant of Guillain-Barre syndrome (GBS) that is characterized by ophthalmoplegia, areflexia, and ataxia, with the additional possibility of limb weakness. There is not a specific demographic or common situation in which MFS is usually seen. This paper details a suspected case of MFS in a 59 year-old male with concurrent influenza infection. He had been experiencing progressive flu-like symptoms a few days prior to the onset of his neurological symptoms, presenting to the hospital with diplopia and paresthesias of his extremities. His physical exam on admission revealed areflexia and gait instability, as well as oculomotor nerve palsies that were causing his diplopia. After running tests to rule out other possible causes of his presentation, along with having a positive influenza A test, he was diagnosed with MFS and started on intravenous immunoglobulin (IVIG). His symptoms resolved by the end of the treatment course. Based on his presentation and resolution of symptoms, this would be one of the few reported cases of MFS following influenza A infection.

Keywords: Miller fisher syndrome • Influenza A infection • Anti-GQ1b antibody • IVIG

Introduction

Miller Fisher syndrome is one of four rare variants of Guillain-Barre syndrome, with the others being acute motor axonal neuropathy, acute motor and sensory axonal neuropathy, and Bickerstaff brainstem encephalitis [1]. Both GBS and MFS are associated with bacterial or viral illness preceding neurological symptoms, with the most common contender for GBS being gastrointestinal illness caused by *Campylobacter jejuni*, and the causative infective agent often unknown in MFS [1,2]. The main difference between MFS and GBS is the severity and constellation of symptoms. GBS is characterized by ascending flaccid paralysis of the extremities, as well as sensory and autonomic dysfunction [3]. MFS tends to be milder and have a descending pattern of neurologic involvement, the most common symptoms being ophthalmoplegia, ataxia, and areflexia [1,4]. Antibodies against GQ1b ganglioside are found in 80-95% of patients with MFS; GQ1b ganglioside is part of oculomotor nerve (CN III) myelin [1,5]. Anti-GQ1b antibodies are thought to directly affect the neuromuscular junctions between cranial nerves and ocular muscles, therefore damage to CN III, IV, and VI is autoimmune in nature and explains the primary finding of ophthalmoplegia [1,2]. Mainstay of treatment for MFS is a course of IVIG. It is a product composed of antibodies prepared from donated blood, meaning the antibodies collected are diversified [6]. IVIG is often given to aid in acute episodes of autoimmune conditions, theoretically modulating the activation and effector functions of B and T lymphocytes, thereby neutralizing pathogenic autoantibodies; however, the exact mechanism is unknown due to its complexity. Nonetheless, this treatment confers an excellent prognosis.

Case Presentation

The patient in this case was evaluated on April 4, 2022. He is a 59 year-

old male who presented to the hospital with a cough, diplopia, and worsening numbness and tingling of his hands and feet. Prior to admission he had been experiencing five days of malaise, with nausea, diarrhea, and bilateral leg aches in addition to his cough. His diplopia developed along with his cough two days before admission, with gait unsteadiness soon following. His past medical history was significant for left-sided facial shingles and subsequent Bell's palsy one year prior to presentation, with residual left-sided facial numbness and weakness.

On initial examination, he appeared ill and had a persistent nonproductive cough. He had midline-restricted leftward gaze bilaterally and restricted right inferolateral gaze of his right eye. He had binocular diplopia that resolved with monocular vision. Of note, he did not have decreased visual acuity of monocular vision or pain with eye movements. The rest of cranial nerves (CN) that did not innervate extraocular muscles were intact besides CN V and VII, consistent with his history of facial shingles and Bell's palsy. He described a subjective numbness in his hands and feet bilaterally despite normal sensation on physical exam. Muscle strength was 5/5 globally, while reflexes were absent. He denied neck pain, neck stiffness, dizziness, vertigo, bowel incontinence or bladder incontinence. His Romberg test was positive, his gait was unsteady. The remainder of his neurological exam was normal.

His complete blood count and comprehensive metabolic panel were normal. His lumbar puncture was unrevealing with increased glucose (87 mg/dL), normal protein (29 mg/dL), and increased lymphocytes (96%). His computed tomography (CT) scan of the brain, CT angiogram of the head, and magnetic resonance imaging of the brain were all unremarkable. He was tested for Lyme disease, syphilis, multiple sclerosis, and West Nile virus, which were all negative. A respiratory viral panel was sent and was positive for influenza A. With this constellation of symptoms and a positive influenza test, MFS was placed higher on the list of differential diagnoses—which included inflammatory conditions, paraneoplastic syndrome, and myasthenia gravis—and anti-GQ1b antibody levels were sent. He completed a course of IVIG 30g per day for 5 days and was discharged on his eighth day of admission, with mildly improved reflexes at 1+/4; his diplopia, extraocular muscle palsy, gait disturbance, and extremity numbness/tingling had resolved. The anti-GQ1b antibody levels were canceled after he was discharged as they never resulted, but based on his clinical picture and his symptom resolution after receiving IVIG, it is highly likely that this was a case of MFS due to influenza A infection.

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Date of submission: 30 August, 2022; Manuscript No. jocr-22-73329; **Editor Assigned:** 31 August, 2022; PreQC No. P-73329; **Reviewed:** 12 September, 2022; QC No. Q-73329; **Revised:** 17 September, 2022, Manuscript No. R-73329; **Published:** 23 September, 2022, DOI: 10.37421/2165-7920.22.12.1525

Result and Discussion

The differential diagnoses and work up for this patient were broad, but

the deciding factor that ultimately pointed to Miller Fisher syndrome was the classic triad of symptoms after a positive influenza test. Even if the anti-GQ1b antibody levels had returned and were negative, the diagnosis would stay the same due to the high pre-test probability that favored MFS over other possible diagnoses.

A case report from 2012 expressed that their case was possibly the first reported of MFS associated with upper respiratory tract infection, the infection being influenza A. In recent years we have seen a few case reports linking Covid-19, which is both an upper and lower respiratory tract infection, to MFS [2,3]. This report we are presenting is likely one of the few cases of MFS following influenza A infection.

Pertaining to treatment, IVIG is first-line. Previous case reports of MFS had eventual curative results with a five day course of IVIG, with dosing based on patient weight. Our patient was able to achieve near-complete remission of his symptoms, only having slightly diminished reflexes remaining by discharge [2,5]. Patients who do not receive IVIG eventually do recover, though taking significantly longer than if they had received the infusion: the median time for symptom disappearance being 1 month for ataxia and 3 months for ophthalmoplegia [5]. Whether or not patients receive IVIG, Miller Fisher syndrome has an excellent prognosis for recovery without lingering residual effects.

Conclusion

To the best of our knowledge the present report is the first to describe *Cryptococcus laurentii* sepsis presenting as *Purpura fulminans* in a child from India. This case report has been prepared to bring out the fact that this organism must also be searched for/considered in patients with sepsis – especially those who are in an immunocompromised state. Further, improved culture and identification techniques can contribute to the timely and correct

diagnosis of such unusual fungal infections further leading to increased recovery of these patients. The reporting of such patients may help to broaden the current spectrum of clinical manifestations of this disease.

Acknowledgements

The patient discussed in the case above signed a written consent for de-identified information relating to his health condition to appear in a journal article, or to be used for the purpose of a thesis or presentation.

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How to cite this article: Afflu, Sharon, Gage Bollinger, Steven R. Wolfe and Benjamin Smolar. "Miller Fisher Syndrome in the Setting of Influenza A Infection." *Clin Case Rep* 12 (2022): 1525.