Miller Fisher syndrome after Pfizer BioNTech vaccine booster responsive to intravenous Ig treatment

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DESCRIPTION

A woman in her 70s received the Pfizer BioNTech (BNT162b2) COVID-19 vaccine booster. Two weeks later, she developed progressive gait imbalance, diplopia and headache without antecedent constitutional or infectious symptoms. Her medical history was significant for hypertension and breast cancer in remission.

On presentation, the patient was hypertensive, with blood pressure fluctuations between 133/61 mm Hg and 191/79 mm Hg over the 2 days after admission, perhaps reflecting a degree of autonomic dysfunction. The initial examination demonstrated partial global ophthalmoparesis, bilateral ptosis, slowed saccades in restricted range, minimally responsive pupils with a degree of light near dissociation (video 1), bilateral limb ataxia with preserved reflexes, and preserved sensation to light touch, pinprick, vibration, proprioception and temperature in all four limbs. Lumbar puncture showed 0 nucleated cells, glucose of 87 mg/dL and protein of 29 mg/dL. Bacterial and fungal cultures were negative. MRI of the brain with and without contrast showed no abnormalities. Nerve conduction study (NCS) and electromyography showed acute left facial neuropathy, reduced fibular and tibial motor amplitudes, and a mildly prolonged ulnar F wave relative to the F estimate, but no additional abnormalities and no electrophysiological evidence of a neuromuscular junction disorder (table 1). A 5-day course of intravenous Ig 0.4 g/kg resulted in symptom improvement. Serum GQ1b IgG antibodies titres were elevated at 1:12 800 (normal <1:100), supporting the diagnosis of Miller Fisher syndrome (MFS). As for other serum labs, the patient had unremarkable comprehensive metabolic panel, complete blood count with differential, sedimentation rate, C reactive protein, rapid plasma reagin, aquaporin-4-IgG, myelin oligodendrocyte glycoprotein antibody and myasthenia gravis panel.

At the 2-month follow-up visit, the patient had further improvement in symptoms (video 1). She continued to have mild ophthalmoplegia and mild ataxia but was able to ambulate independently and complete her activities of daily living.

MFS is a subtype of Guillain-Barre Syndrome (GBS), a group of immune-mediated acute neuropathies. It is rare, with an incidence of approximately 1 per 1 million. MFS can present after infections or following vaccinations. Postvaccination MFS incidence is unclear in the literature due to its uncommon occurrence. Postvaccination GBS has been reported more frequently, especially in association with the influenza vaccine. The risk of developing GBS is low following vaccination, increasing by one case for every million cases. The prognosis of MFS is generally good, with most patients showing significant improvement or resolution of their symptoms by 6 months. There is some evidence that intravenous Ig therapy may reduce the time to symptom recovery, but plasmapheresis does not appear to affect it. Neither intravenous Ig or plasmapheresis had been shown to affect patient outcomes compared with no immunotherapy.

In patients who developed MFS after COVID-19 vaccines, there is currently no long-term data. In the previously reported cases, patients significantly improved 4–6 weeks after immunotherapy.

The Pfizer BioNTech vaccine contains a nucleoside-modified mRNA that encodes the SARS-CoV-2 spike glycoprotein and was designed to elicit B-cell and T-cell responses against the spike protein. MFS had been reported in patients after COVID-19 infection and following the first and second doses of the Pfizer vaccine. There had also been multiple cases of GBS reported in patients after receiving COVID-19 vaccination.

A causal link cannot be established with the very low number of cases compared with the number of vaccines administered, but the timing is supportive. To the best of our knowledge, there has not been a published report of MFS or GBS after the Pfizer vaccine booster.

The classic triad of MFS is ophthalmoplegia, ataxia and areflexia; however, many patients present with incomplete forms. Berlit and Rakicky reported that global ophthalmoplegia was present in 48.9% of patients, and areflexia in 81.6%. Odaka et al reported hyporeflexia or areflexia in 53% of MFS patients. The reason for the variability in symptom presentation between individuals is unclear, but it may be secondary to the

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| Nerve conduction | Record | Rep | Normal | Normal | Distal | Normal | F-Wave | F-Wave | Temp (°C) |
|------------------|--------|-----|--------|--------|--------|--------|--------|--------|-----------|
| Nerve            | Type   | Site | Stim   | Side   | Amp    | Amp    | CV     | CV     | Lat       | Lat       | Est       |
| Fibular          | Motor  | EDB  | L      | 0.5    | (> 2.0)| 43     | (> 41) | 5      | (< 6.6)   | 30.5      |
| Spinal Accessory | Motor  | Trapezius | * | L | 6.8 | - | - | 2.2 | - | 32.7 |
| Facial           | Motor  | Nasalis | * | L | 1.5 | (> 1.8) | - | 3 | (< 4.1) | 33.9 |
| Tibial           | Motor  | AH   | L | 1.7 | (> 4.0) | 41 | (> 40) | 4.7 | (< 6.1) | 63 | 59.8 | 30.5 |
| Sural            | Sensory | Ankle | L | 4 | (> 0.0) | (> 40) | 3.3 | (< 4.5) | 30.5 |
| Median           | Motor  | APB  | L | 9.3 | (> 4.0) | 49 | (> 48) | 4.4 | (< 4.5) | 29.4 | 31.3 | 32.3 |
| Ulnar            | Motor  | ADM  | * | L | 8.5 | (> 6.0) | 59 | (> 51) | 3 | (< 3.6) | 31 | 25.4 | 33 |
| Median           | Sensory | Dig II | L | 24 | (> 15.0) | 58 | (> 56) | 3.3 | (< 3.6) | 32.6 |
| Ulnar            | Sensory | Dig V | L | 30 | (> 10.0) | 63 | (> 54) | 2.7 | (< 3.1) | 33.3 |

**Blinks**

| Nerve   | Recording | Stim | R1 | R2 | R2 |
|---------|-----------|------|----|----|----|
| Blink supra Orb | Orbicularis oculi | Supra Orb | L | 11.4 | 32.5 | 35.5 |
| Blink supra Orb | Orbicularis oculi | Supra Orb | R | 11.4 | 31.1 | 34.7 |

**Needle EMG**

| Muscle | Ins | Spont | MUP | Recruitment | Duration | Amplitude | Phases |
|--------|-----|-------|-----|------------|----------|-----------|--------|
| NL     | 0   | 0     | NL  |            |          |           |        |
| NL     | 0   | 0     | NL  |            |          |           |        |
| NL     | 0   | 0     | NL  |            |          |           |        |
| NL     | 0   | 0     | NL  |            |          |           |        |
| NL     | 0   | 0     | NL  |            |          |           |        |
| NL     | 0   | 0     | NL  |            |          |           |        |
| NL     | 0   | 0     | NL  |            |          |           |        |
| NL     | 0   | 0     | NL  |            |          |           |        |
| NL     | 0   | 0     | NL  |            |          |           |        |
| NL     | 0   | 0     | NL  |            |          |           |        |
| NL     | 0   | 0     | NL  |            |          |           |        |
| NL     | 0   | 0     | NL  |            |          |           |        |
| NL     | 0   | 0     | NL  |            |          |           |        |
| NL     | 0   | 0     | NL  |            |          |           |        |

*, repetitive nerve stimulation applied; AD, abductor hallucus; ADM, abductor digiti minimi; APB, abductor pollicis brevis; CV, conduction velocity; EDB, extensor digitorum brevis; EMG, electromyography; NL, normal limits.
variation in GQ1b expression sites in the central and peripheral nervous systems. In our case, the patient had ophthalmoplegia and bilateral ataxia with preserved reflexes. There has been much debate regarding whether ataxia in MFS is central or peripheral, or both. In addition to the heavy expression of GQ1b in the ocular motor nerves, GQ1b has also been found in the cerebellum, muscle spindles and large-diameter dorsal root ganglion neurons. Berlit and Rakicky reported that in MFS patients that presented with ataxia, 90.1% presented with cerebellar ataxia and only 0.9% presented with sensory ataxia. In patients that presented with ataxia, 90.1% presented with cerebellar ataxia and only 0.9% presented with sensory ataxia.15 In MFS patients with evidence of sensory neuropathy on NCS, the sensory NCS can often be incongruent with the level of ataxia and areflexia/hyponreflexia found. Motor and sensory NCS can oftentimes be normal in symptomatic MFS patients and are not reliable for diagnosis or exclusion.6–9

In conclusion, we describe a case of MFS after the Pfizer COVID-19 vaccine booster. In patients with symptoms involving ophthalmoplegia, ataxia and/or areflexia after receiving the COVID-19 vaccine, MFS should be included in the differential diagnosis. GQ1b antibodies can help confirm diagnosis, and immunotherapy may reduce time to symptom recovery and should be considered. MFS is very rare and should not dissuade people from receiving the vaccine, especially given its favourable risk–benefit ratio.

Contributors BC, SL and EE treated the patient in the report for her condition both in the inpatient and outpatient settings. SL had the initial idea for the article. BC, SL and EE had access to all patient data, met and reviewed the patient’s case, and planned to publish an article regarding the novel findings discussed in the report. BC was determined to be the primary author given the most time spent caring for the patient clinically. BC was responsible for discussing with the patient regarding the article and obtaining consent from the patient in written form. BC was responsible for drafting the article, and SL and EE were responsible for revising it critically for important intellectual content. EE was responsible for recording the patient videos before and after treatment. BC, SL and EE agreed on a finalised version of the case report to be submitted for publication once all agreed revisions were made on previous drafts. BC accepts full responsibility for the finished article and controlled the decision to publish. BC, SL and EE agreed to be accountable for the article and to ensure that all questions regarding the accuracy or integrity of the article are investigated and resolved.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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