CASE REPORT

Miller Fisher Syndrome in a Healthy Male with Positive ANA: A Rare Presentation and Successful Outcome with IVIG Therapy

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ABSTRACT

A 29-years-old man presented with a sudden onset of double vision, oscillopsia, headache and vomiting, four days after recovering from an upper respiratory tract infection. Examination revealed bilateral painful ophthalmoplegia, ataxia, areflexia and loss of sensation over the left upper and middle thirds of his face. Neuroimaging was normal, and lumbar puncture showed albuminocytological dissociation. GQ1B and anti-nuclear antibody tests were positive. The patient's symptoms improved after completion of intravenous immunoglobulin, with no residual neurological deficit after three months.
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Keywords: Miller fisher syndrome, Antinuclear antibody, GQ1b antibodies, Intravenous immunoglobulin therapy, Albuminocytological dissociation

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INTRODUCTION

Miller fisher syndrome (MFS) is a rare variant of Guillain–Barré syndrome (GBS), an acute immune-mediated neuropathy characterised by the triad of ophthalmoplegia, ataxia and areflexia. The incidence of MFS worldwide is 1 to 2 in 1,000,000, with a male predominance, it and can occur across all age groups(1). Similar to GBS, MFS is believed to result from an acute autoimmune reaction following an infection. However, unlike GBS, MFS is more frequently preceded by an upper respiratory tract infection (76%) rather than gastrointestinal infection (4%)(2). The inflammatory process in MFS is thought to be triggered by molecular mimicry, where antigens found in peripheral nerves are mistakenly targeted by the immune system due to their similarity to components of microbes or viruses(2). We report a case of MFS diagnosed through clinical, radiological, and immunological findings.

CASE REPORT

A 29-year-old Malay man presented to the emergency department with a two-day history of acute onset double vision, associated with frontal headache, oscillopsia, nausea, and vomiting. He had fever for three days and cough for two weeks, both of which had resolved four days prior to the onset of his current symptoms. Additionally, he reported numbness over his palms and soles that developed two days later. He denied any recent vaccinations, Covid-19 infection, limb weakness, neck stiffness, tinnitus, fatiguability, difficulty in breathing, dysphagia, ileus, or urinary retention. His past medical, surgical, family and allergy histories were unremarkable. He did not smoke, consume alcohol, or illicit drugs and denied history of sexual promiscuity.

On examination, his vital signs were within normal ranges. He was alert, oriented, cooperative and articulate in speech. There was no ptosis or proptosis. His visual acuity in both eyes was 6/6. Both pupils were round, equal, and reactive to light and accommodation with no relative afferent pupillary defect. Neurological examination revealed painful external ophthalmoplegia in both eyes with horizontal gaze nystagmus. He complained of binocular diplopia in all gazes except inferior gaze. Hess chart showed limited elevation of the left eye and limited abduction of both eyes. There was reduced superficial sensation over left upper and middle thirds of the face. Other cranial nerves examinations were normal. He exhibited significant ataxia and dysmetria but no dysdiadochokinesia. While motor power was grade 5 in all limbs and muscle tone was normal, a striking finding was the presence of global areflexia. Slit-lamp examination of both eyes revealed normal anterior segments and fundi with no optic disc swelling or hyperaemia. Spontaneous venous pulsation was absent.

Contrast-enhanced computed tomography (CT) of the brain and orbit was normal. The lumbar puncture

opening pressure was 14cm H_2O and the cerebrospinal fluid (CSF) was clear. CSF analysis showed albuminocytological dissociation and elevated globulin. CSF screenings for viral serology, gram stain and cultures were all negative. Laboratory tests including full blood count, coagulation profile, renal profile, thyroid function test, serum glucose level, lipid profile and urine analysis were normal. Anti-nuclear antibody was positive using chemiluminescence immunoassay but double stranded DNA antibody was negative. C3 was 1.69g/L (0.8-1.60), C4 was 0.42g/L (0.12-0.36), erythrocyte sedimentation rate was raised (28mm/Hr) but C-reactive protein was not elevated. GQ1b antibodies were positive. Visual evoked potential test and nerve conduction study were normal. A contrast-enhanced magnetic resonance imaging (MRI) of the brain, orbit and spine, performed two weeks later, was normal.

During his hospital stay, patching was done to relieve the symptom of diplopia. He received intravenous immunoglobulin (IVIG) 0.4g/kg/day for 5 days from day two to day six of hospitalisation. Two days after completing IVIG treatment, ataxia and headache started to improve. After gradual symptoms improvement, he was discharged on day ten of hospitalisation. Complete resolution of the frontal headache, painful eye movements, and diplopia occurred after a month, while oscillopsia resolved after three months.

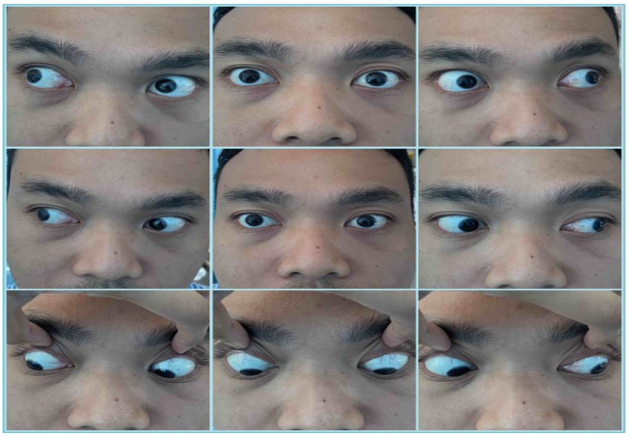

Figure 1: A 9-gaze photo at initial presentation showing right eye exotropia in primary gaze, limitation in elevation, abduction and adduction in both eyes.

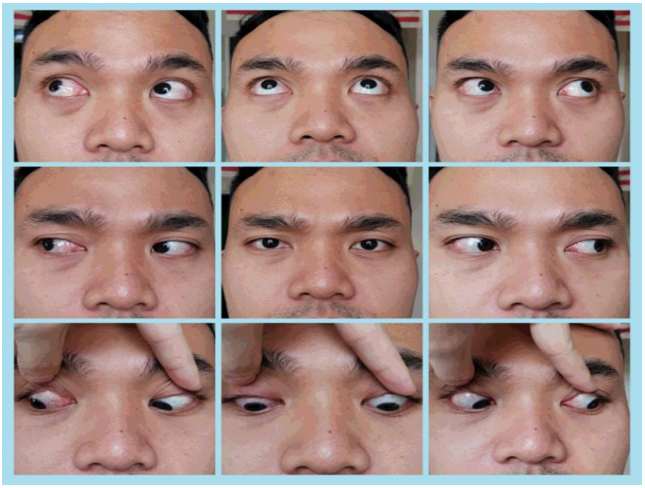

Figure 2: A 9-gaze photo one month later with complete resolution of bilateral ophthalmoplegia.

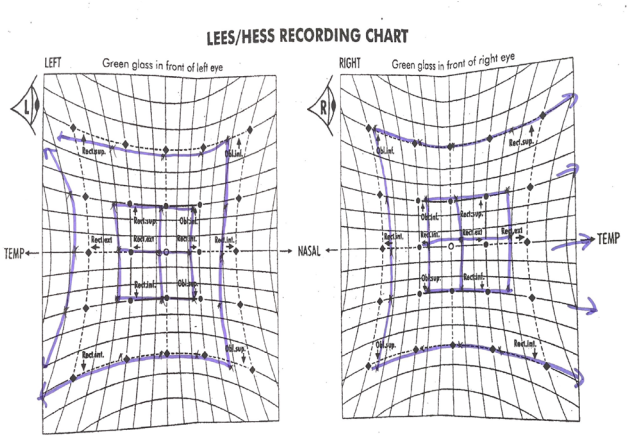

Figure 3: Hess chart showing limited elevation of the left eye and limited abduction of both eyes.

DISCUSSION

The GQ1b antibody is closely linked with Miller Fisher Syndrome (MFS). It is present in 85-90% of MFS patients and absent in unaffected individuals, indicating its high level of specificity for this condition(1). Its concentration is higher in the earlier stages of the disease and decreases over time. GQ1b antibody binds to gangliosides found in abundance in oculomotor, trochlear, abducens, dorsal ganglia and muscle spindles, resulting in ophthalmoplegia and ataxia(1). In addition, it can also

bind to GQ1b at the brainstem, affecting the level of consciousness. While GQ1b antibody is very crucial marker supporting the diagnosis of MFS, it is important to recognise that this antibody can also be found in GBS associated with ophthalmoplegia, the pharyngeal-cervical-brachial variant of GBS, and Bickerstaff brainstem encephalitis(1).

Our patient was diagnosed with MFS based on a combination of clinical, radiological and immunological findings. In addition to the clinical triad of ophthalmoplegia, ataxia and areflexia, our patient also exhibited loss of light touch sensation over the distribution of cranial nerve V1 and V2. Loss of sensation is an infrequent presentation but is found in 20% of MFS patients(2).

A notable discovery in our patient was the presence of antinuclear antibody (ANA), which is particularly rare in male patients. In the literature, positive ANA results have been documented in a small number of MFS cases, typically in patients with underlying systemic lupus erythematosus (SLE) who developed MFS(3, 4). Although a rheumatologist was consulted, a diagnosis of connective tissue diseases could not be established as our patient did not display clinical features consistent with such conditions. While a positive ANA is often associated with autoimmune diseases, it can also be present in non-autoimmune conditions, including infections, malignancies, drug use, and even in healthy individuals(5). It remains uncertain whether our patient's positive ANA finding is linked to cross-reactivity associated with myelin damage, as observed in cases of MFS.

IVIG and plasmapheresis are the mainstay of treatment for MFS. As a rare and self-limiting disease, treatment recommendations are based on retrospective analyses. IVIG has been found to slightly shorten recovery time by reducing the binding of GQ1b antibodies, but does not affect the final outcome(1). On the other hand, plasmapheresis has not shown a significant difference in recovery time compared to untreated patients, likely due to the natural course of the disease, in which patients typically experience good spontaneous recovery(1). Our patient completed IVIG therapy and achieved complete resolution of symptoms within three months.

CONCLUSION

MFS can be diagnosed based on clinical presentation, supported by the presence of positive GQ1b antibodies. MFS associated with positive ANA in an otherwise healthy male is a rare presentation. Despite the presence of multiple autoantibodies, we report a case of MFS with favourable outcome following IVIG therapy.

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