CASE REPORT

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Ocular Manifestations of Miller Fisher Syndrome: a Case Report

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ABSTRACT

Background: Miller Fisher syndrome (MFS) is a variant of Guillain-Barré syndrome and is characterised by a clinical triad of ophthalmoplegia, ataxia and areflexia. **Objectives:** This report presents an atypical case of MFS characterized by ocular and gastrointestinal involvement, and anti-ganglioside antibody-positivity. **Methods:** A 17-year old boy was referred to our ophthalmology emergency room with signs and symptoms of diplopia and upper lid ptosis of the right eye. He underwent a complete ophthalmologic examination with special reference to strabologic status, as well as a neuropediatric examination with serum antiganglioside antibody panel. **Results:** Strabologic examination showed horisontal diplopia (near and far), ptosis of the upper eyelid on the right and bilateral ophthalmoplegia (limited elevation). Orthoptic examination revealed esotropia of 8 prism dioptres (PD) at near and 18 PD at far distance. A pediatric neurologist found normal limb power, deep tendon reflexes and flexor plantar responses, but attenuated right patellar reflex. Serum anti-GQ1b IgG (+++), anti-GQ1b IgM (++) and anti-GD1a IgM(++) were positive. Positivity of anti-GQ1b IgG antibody confirmed the existence of incomplete MFS. We treated the patient with systemic intravenous immunoglobulins for five days, and after five months of follow-up, all symptoms resolved. **Conclusion:** MFS can present itself as a wide range of clinical features and its timely recognition is important. Despite the alarming nature of the disease, patients with MFS tend to have a good recovery of presented symptoms, and without any significant residual deficit.

Key words: Miller Fisher syndrome, ophthalmoplegia, antiganglioside antibody, diplopia, ptosis.

1. BACKGROUND

Miller Fischer syndrome (MFS) is a clinical variant of Guillain-Barré syndrome (GBS), typically characterized by a triad of ophthalmoplegia, ataxia and areflexia, although it may present itself with only 2 or even 1 of these clinical findings (1). Incomplete forms of MFS include acute ophthalmoparesis without ataxia (AO) and acute ataxic neuropathy without ophtalmoparesis (AAN).

This acute polyneuropathy is often preceded by a respiratory or gastrointestinal tract illness (2). Chiba et al found anti-GQ1b IgG in all five subjects with acute postinfectious ophthalmoparesis, "atypical MFS" in their designation (3).

Anti-GQ1b is an antiganglioside antibody that is self-reactive to the GQ1b ganglioside component of a nerve and is present in about 85-90% of all patients with MFS (4).

2. OBJECTIVE

We present a case of incomplete Miller Fischer syndrome, characterized by ocular and gastrointestinal (GI) involvement, and anti-ganglioside antibody positivity.

3. CASE REPORT

A 17-year old boy was referred to our ophthalmology emergency room with a history of double vision and headache. Two weeks prior to this, patient had gastroenteritis with diarrhea and fever up to 38.2°C, lasting for four days. All members of his family have had similar disturbances. His medical and family history was unremarkable.

Ophthalmic examination revealed best corrected distance visual acuity of 20/20 in both eyes. Strabologic examination showed horisontal diplopia (near and far), and ptosis of the upper eyelid on the right eye (palpebral fissure of 8 mm on the right side and 12 mm on the left side and marginal reflex distance one of 2 mm on the right eye and 4 mm on the left eye), (Figure 1A).

Figure 1. Ptosis of upper right lid (A) and bilateral limitation of elevation (B).

Figure 2. Completely resolved ptosis of upper right lid (A) and normal elevation of eye motility (B).

He had bilateral ophthalmoplegia with limited elevation (Figure 1.B), and doll's head maneuver did not lead to improvement of the eye movements . Orthoptic examination revealed esotropia of 8 prism dioptres (PD) at near and 18 PD at far distance. Stereoacuity Lang test was normal. Patient denied worsening of double vision with any particular eye movement and it disappeared with closing of either eye. Ptosis displayed no diurnal variation. Pupils were round, equal in size, and reactive to light and mydriatic eye drops, and relative afferent pupillary defect was negative. No nystagmus was found. Humphrey Kinetic Visual Field test and fundus examination were normal.

Patient was reffered to pediatric neurologist for further evaluation. They found no signs of aphasia or dsyarthria and normal language interpretation. Patient had normal limb power, deep tendon reflexes and flexor plantar responses, but atenuated right patellar reflex. Meningeal irritation signs were negative. Other physical findings was normal.

His laboratory findings were normal (complete blood count, erytrocyte sedimentation rate, C-Reactive Protein, electrolytes, urine analysis, renal, hepatic, and thyroid function tests). Cranial and orbital magnetic resonance imaging (MRI) with contrast was normal. Cerebrospinal fluid examination showed white cell count <1/mm^3 (normal: <5/ mm^3), protein 0,4 g/L (normal: 0.15-0.45 g/L), and glucose contents of 2,8 mmol/L (simultaneous blood glucose level of 4,6 mmol/L). Serology for *Rubella*, *Borrelia*, *Morbili*, *Varicella/Zoster virus* (VZV), *Herpes simplex virus* (HSV) type 1, and HSV type 2 were negative. Tensilon test was normal. Stool culture was negative for enteritic pathogens, including *Camylobacter jejuni*.

Serum antiganglioside antibody panel was ordered and serum anti-GQ1b IgG (+++), anti-GQ1b IgM (++) and anti-GD1a IgM(++) were found positive. Other antigangliosides antibodies (anti-GM1, anti-GM2, anti-GD1aIgG, anti-Gd1b, anti-MAG) were found negative.

Patient was diagnosed as incomplete MFS and was treated with intravenous immunoglobulins (IVIG) in a dosage of 2 g/kg for a period of five days. Four weeks after the treatment, diplopia, ptosis and eye motility were improved. Right patellar reflex has completely resolved. At the fifth month of follow-up, patient's strabologic findings, symptoms of diplopia and signs of ptosis have completely resolved, and eye motility was full (Figure 2).

4. DISCUSSION

Miller Fisher syndrom was originally described in 1956 as a triad of total external ophthalmoplegia, ataxia, and loss of tendon reflexes (5). It rarely occurs during childhood and its incidence is unknown, however, its annual incidence is estimated to be less than one in a million (6).

Among the triad, the most common symptom is ophthalmoplegia, usually bilateral. In our patient, elevation deficit was most prominent symptom with esotropia (near and far) and consequential diplopia. According to Ryu et al (7) the lateral rectus muscle was most frequently involved (100%), followed by the superior (60%), inferior (52%), and medial (48%) rectus muscle. Most frequent form of ocular deviation was esotropia (64%).

It is often preceded by prodromal symptoms, which are usually mild. In contrast to GBS, respiratory symptoms precede neurological symptoms in about 76% of MFS cases, and GI involvement is reported in only 4% of MFS patients (4). *Campylobacter jejuni* is most commonly identified as a causing agent of the antecedent infection in patients with acute MFS, those with GBS and related disorders, followed by *Haemophilus influenzae* (1). Although our patient had prodromal symptoms, gastroenteritis, its causative agent was not confirmed by further analysis. Stool culture was negative for enteritic pathogens, including *Camylobacter jejuni*. Yuki (3) recorded a GI infection in only five out of twenty one subjects, but *Campylobacter jejuni* was isolated just from one subject. However, in most of them, no clear infectious association has been detected (1).

The ganglioside, GQ1b, can be found in abundance in the paranodal region of the extramedullary portion of the oculomotor, abducens and trochlear nerves, and these areas are mostly affected by the self-reactive an-

ti-GQ1b antibody (4). It contains polysaccharides identical to the lipopolysaccharides (LPS) contained in the outer membranes of certain bacteria and may thus be the target of an immune response initiated against epitopes shared by these nerve fibers and various infectious agents (1, 3). So, MFS can occur after an infection with a „molecular mimicry", believed to be the main underlying pathogenic mechanism (8).

Anti-GQ1b antibody has been found in GBS with ophthalmoplegia, MFS, Bickerstaff brainstem encephalitis, and acute ophthalmoplegia without ataxia, and these diseases were designated as anti-GQ1b antibody syndrome (9). Differential diagnosis can be challenging for they all pertain to the spectrum of conditions of the common origin. Some studies have shown that anti-GQ1b antibody was significantly correlated only with ophthalmoparesis (6).

MFS is usually a clinically-based diagnosis but its differential diagnoses include brainstem lesions (vascular, tumor, demyelinating, inflamatory lesions, etc.), botulism, myasthenia gravis, Wernicke's encephalopathy, thyroid eye disease, and anti-GQ1b antibody syndrome.

Patients with MFS have a favorable prognosis and a mostly spontaneous complete recovery with in a few months of disease onset. Despite that, many studies have shown a benefit of intravenous immunoglobulins (IVIG) and plasma exchange (PLEX), although there is little or no difference between these two treatments in terms of length of intubation, disability, and mortality (2). In this case, our preferred therapy of choice was IVIG, with an aim to shorten the duration of visual problems that decreased patient's quality of life.

5. CONCLUSION

This case represents a wide range of clinical features of an atypical MFS with the absence of ataxia and areflexia. Although MFS is usually a clinically-based diagnosis, antiganglioside antibodies were found to be helpful in establishing the diagnosis. Recognizing MFS is important for its alarming nature, although the prognosis is usually favorable, with good recovery of presented symptoms and without significant residual deficit.

- **Patient Conset Form**: An informed written consent was taken from the family caregivers, following the tenets of the Declaration of Helsinki.
- **Author's contribution**: All authors were involved in the preparation this case report. Final proofreading was made by the first author.
- **Conflicts of interest**: The authors declare that they have no conflicts of interest regarding the publication of this case report.
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