Persistent Diplopia in Miller Fisher Syndrome: A Case Report

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ABSTRACT

Miller Fisher syndrome is a rare variant of Guillain-Barre syndrome characterised by ataxia, ophthalmoparesis and areflexia. This case report describes a 57-year-old Caucasian woman who presented with acute diplopia, progressive areflexia and ataxic gait. Past ocular history reported an intermittent childhood esotropia. Clinical examination found a left esotropia, limited abduction on both right and left gaze, small amplitude nystagmus and mild left ptosis.

After a two-year follow-up, her areflexia and ataxia were completely resolved. However, diplopia and strabismus were still present. As generally those with Miller Fisher syndrome show complete resolution of their symptoms, it was hypothesised that the persistent diplopia was likely to be related to a childhood intermittent strabismus which precluded total remission. A period of temporary fusion disruption may have led to decompensation of a pre-existing heterophoria, precipitating an acute acquired concomitant esotropia.

Keywords: childhood intermittent esotropia, Miller Fisher syndrome, ophthalmoparesis, presistent diplopia

INTRODUCTION

Miller Fisher syndrome (MFS) is an acute inflammatory polyneuroradiculopathy[1] that is a diffuse damage with multiple nerve root involvement, characterised by sudden onset ophthalmoplegia, ataxia and areflexia.[1-3] The classical clinical triad was first described in 1932 by James Collier and subsequently reported in 1956 by Charles Miller Fisher as 'an unusual variant of acute idiopathic polyneuritis'.[3-4] With an annual incidence of 1/1,000,000,[2] MFS represents a rare variant of Guillain-Barre syndrome (GBS). It is observed in only about 1 to 5% of GBS cases in western countries,[3] with higher rates reported in Asian populations (19% and 25% in Taiwan and Japan, respectively).[1-3] The mean age of onset is reported to be 34 to 43.6 years,[1-3] with the male:female ratio of 2:1.[1-3]

A variety of infections can precede the onset of signs and symptoms,[5] with ophthalmoplegia and diplopia as the first manifestations, associated with ataxia and areflexia.[1-3] The main difference between MFS and GBS is that the cranial nerves are affected first.[3] The presence of the anti-GQ1b IgG antibody in serum is an excellent diagnostic marker for MFS.[1-3,5] Most patients show a benign monophasic evolution with a complete remission without residual deficits.[1-3]

This report describes a patient with persistent diplopia as the only residual symptom of MFS two years after the onset. This occurrence has rarely been reported in the literature, as resolution is usually complete after weeks or months, with a reported mean recovery time of 10 weeks.[1-3]

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CASE REPORT

March 2014:

A 57-year-old Caucasian woman presented to the Emergency Department of Careggi Hospital suffering from worsening diplopia for four days, along with a one-day history of progressive ataxic gait. Previous medical history included hypertension, well controlled with angiotensin-converting enzyme (ACE) inhibitors. She reported a gastrointestinal upset with high fever 10 days before the onset of diplopia. Patient recollection of past ocular history suggested an intermittent convergent strabismus and hypermetropic spectacle wear in childhood. She denied any previous episodes of diplopia or ptosis.

On examination, uncorrected visual acuity, measured with Snellen chart, was 6/9 in the right eye (RE) and 6/15 in the left eye (LE). Best corrected acuity was RE 6/6 with +1.00 DS and LE 6/7.5 with +1.75 DS. Near visual acuity, tested

with the Jager Chart, was J1 with a near addition of +2.75 DS in each eye. Pupils were round and equal, with bilateral, mild and sluggish pupillary reflexes. She showed a mild left eyelid ptosis.

Corneal reflections showed a primary position left esotropia (ET) larger for distance than near. Diplopia was horizontal, with an intermittent oscillopsia sensation in lateral gaze. Prism cover test (PCT) revealed 30^{Δ} ET at distance and 14^{Δ} ET' at near. Ocular movements revealed limited abduction on right and left gaze, with the left lateral rectus (LR) more severely affected. Small amplitude nystagmus was observed, respectively right-beating in right gaze and left-beating in left gaze. The Hess chart showed underaction of both lateral recti, left more than right, with the development of muscular sequelae, and slight underaction of both superior recti (Figure 1).

Neurological examination reported ataxia and areflexia. Initially, blood tests and computed tomography (CT) scan were normal but, suspecting Miller Fisher Syndrome, neurologists requested medical resonance imaging (MRI) with gadolinium contrast. This demonstrated enhancement of the cisternal segment of both oculomotor and abducens cranial nerves, without any cerebral tissue involvement. Specific anti-GQ1b IgG dosage demonstrated high serum values. Lumbar puncture showed an increased protein level in the cerebrospinal fluid (CSF). She immediately received intravenous immunoglobulin (IVIg) in a regimen of 0.4 g/kg bodyweight daily for five consecutive days, reporting a mild improvement on walking and marching, but no improvement of her diplopia. Prior to discharge she was advised on a penalisation therapy using an opaque foil over the left eye to avoid diplopia.

May 2014:

Two months later ataxia and areflexia were gradually improved, pupillary reflexes showed a quick reaction to light, but eye movement anomalies were basically stable with unchanged diplopia. The orthoptic clinical picture was similar to the first visit, except for the resolution of ptosis. The large-angle esotropia meant that prism therapy was not yet appropriate, so occlusion was continued with the opaque foil, planning a six-month follow-up if all remained stable.

September 2014:

The patient reported a subjective improvement of diplopia, especially at near where she could read with single vision without discomfort. However, she reported persistent diplopia at distance. Considerable recovery was observed in elevation of both eyes, but horizontal movements were still abnormal, with insufficient abduction right and left. PCT revealed LET for distance (14^{Δ}) and an esophoria with a good fusion recovery at near fixation (8^{Δ}). The Hess chart highlighted a concomitant strabismus, with an improved underaction of both LR. There was no residual elevation defect (Figure 2).

Given the smaller strabismus angle, a prism correction to restore binocularity and align the visual axes was planned. A 14^{Δ} base-out (BO) prism was the minimum correction required to re-establish binocular single vision (BSV). This was first prescribed as a 14^{Δ} BO temporary Fresnel prism, but the patient did not like either the aesthetic effect or the quality of vision, so she chose glass prisms. This was prescribed with her distance refractive correction: RE +1.00 DS 7^{Δ} BO, LE +1.75 DS 7^{Δ} BO, while she did not need prisms at near as she had BSV.

September 2016:

The latest evaluation demonstrated unchanged ocular movements and orthotropia with her prismatic correction. A recent brain MRI with contrast showed decreased nerve intensity enhancement. As her MFS appeared completely resolved, she received strabismus surgery involving bilateral medial rectus recession and lateral rectus resection, under topical anaesthesia with adjustable sutures. A positive post-surgical outcome was obtained, she was straight for both

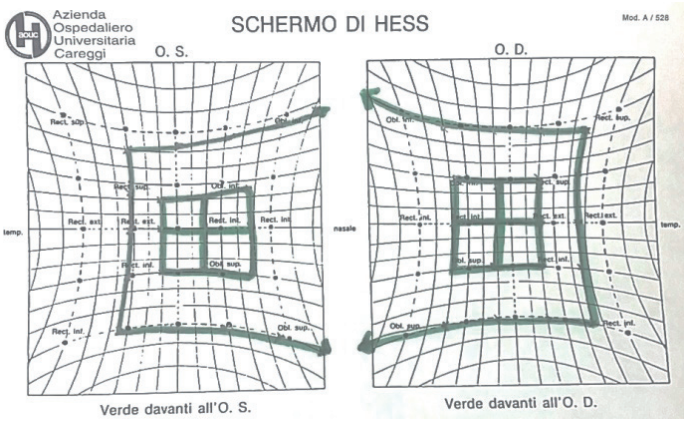

Figure 1. Hess chart demonstrated bilateral lateral recti underactions, left greater than right, and mild bilateral superior recti underactions, left greater than right.

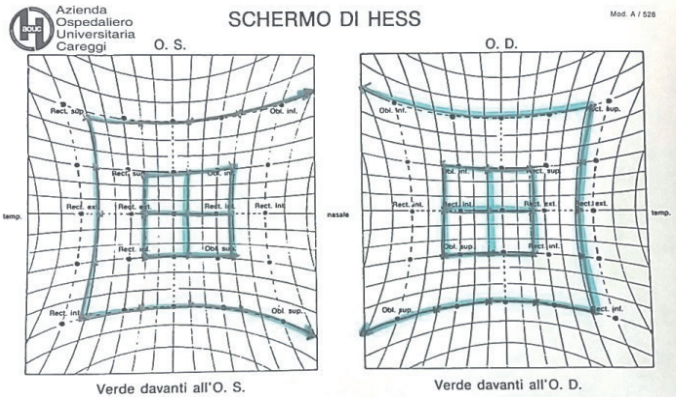

Figure 2. Hess chart demonstrated improvement of lateral recti underactions and resolution of the superior recti underactions.

distance and near, without diplopia. Informed consent was obtained from the patient for publication of this case report.

DISCUSSION

Miller Fisher syndrome is a variant of Guillain Barre syndrome characterised by cranial nerve involvement and the triad of ataxia, areflexia and ophthalmoplegia.[1-3] Berlit and Rakicky reported that diplopia was the first symptom in 38.6% of cases and ataxia in 20.6%. Areflexia affected a high percentage of patients (81.6%) but not necessarily as the onset presentation.[3] The most common ocular finding is bilateral external ophthalmoplegia,[1-3] which can present as unilateral, incomplete, isolated form.[1-2,6-8]

More recent case publications reported internal ophthalmoplegia, with[9] or without[10] external involvement or other neurological defects. Mydriasis has been reported as present in 35 to 50% of cases.[11] Various other ophthalmic conditions have been reported: ptosis, lid retraction, internuclear ophthalmoplegia, divergence paralysis, nystagmus, convergence anomalies, acute angle closure and demyelinating optic neuropathy.[1,6,9,11] Berlit and Rakicky, followed by other authors, reported that the clinical signs are preceded by infections in 71.8% of cases, which generally occur 8 to 10 days before.[1-3,5] Our patient reported a gastrointestinal upset with high fever 10 days before the onset of symptoms. Her first symptom was diplopia and her ophthalmoplegia could be defined as 'bilateral but asymmetric', affecting the left eye more than the right; 'external but incomplete', involving abducens and oculomotor cranial nerves, but excluding its inferior branch; and 'partial internal', showing equal pupils, but sluggish response to light.

MFS diagnosis is based on patient history and clinical features, supported by the diagnostic marker of high levels of serum anti-GQ1b IgG antibody.[1-3,5,12] It is suggested that the ophthalmoplegia is so frequent because the GQ1b ganglioside is highly enriched in the ocular cranial nerves and the ciliary ganglia.[9] Other diagnostic findings are the presence of albuminocytological dissociation in the CSF,[1,3-4,12] normal findings on CT and enhancement of ocular and/or facial cranial nerves, without brainstem abnormalities on MRI.[13-14] The differential diagnosis, in addition to GBS, includes Bickerstaff's brainstem encephalitis, brainstem stroke, Wernicke's encephalopathy, polyneuropathies, neurosyphilis, botulism and anticonvulsant intoxication.[6] The rapid onset of ophthalmoplegia can help to distinguish MFS from chronic diseases such as mitochondrial myopathies, oculopharyngeal or myotonic dystrophy, thyroid ophthalmopathy and myasthenia gravis.[6,15] In our case, clinical pictures, positive serological tests and characteristic MRI findings lead quickly to the diagnosis.

MFS generally has an excellent prognosis; first improvements begin within two to four weeks after the onset of neurological symptoms and may be almost complete within six months.[1,3,11,13,16] The treatment of choice for MFS is IVIg; a combination of Ig with methylprednisolone or plasmapheresis are also indicated.[1-3,17] Our patient immediately received IVIg, reporting a complete resolution of her systemic condition within two months. However, ocular motility demonstrated only a mild, partial improvement.

Concurrent to the neurological management we conducted an orthoptic two-year follow-up, which demonstrated a persistent diplopia, an outcome rarely reported in the literature. It is hypothesised that along with the MFS ophthalmoplegia, the ocular comorbidity of her childhood intermittent heterotropia has exacerbated the binocular imbalance. When heterophoria fails, it gives rise to strabismus and either diplopia or suppression. After the onset of ophthalmoplegia, her fusional reserves likely became inadequate. Fusional vergence did not support binocular vision even after total neurological recovery, causing a permanent decompensation of a pre-existing esophoria.

Once orthoptic stability was achieved after six months, a prismatic correction was prescribed, improving her health-related quality of life. After two years of persistent impairment, strabismus surgery was suggested. The postoperative realignment of visual axis and the disappearance of diplopia have produced a positive and satisfactory outcome

CONCLUSION

This interesting case of persistent diplopia two years after resolution of the other signs and symptoms of Miller Fisher syndrome emphasises the importance of considering past ocular history and comorbidity when assessing ocular motility and binocular status. It appears that the unstable binocularity was likely due to childhood strabismus exacerbated by the neurological complications of Miller Fisher syndrome. Once the neurological condition had resolved, the patient was treated for the acquired concomitant esotropia with excellent results and satisfaction.

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