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CASE REPORT

Understanding the diagnostic challenges of Miller Fisher syndrome in children: a case report from an ophthalmological perspective

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Abstract

We report a case of a 6-year-old boy with autism spectrum disorder presenting with new-onset squint and 'ptosis' following a recent infection. Clinical examination revealed ataxia and areflexia alongside a dilated pupil poorly reactive to light. Subsequently, his eye movements deteriorated to near-complete ophthalmoplegia at 1-week review. Further investigations inclusive of a magnetic resonance imaging (MRI) brain scan, a computed tomography (CT) venogram and a lumbar puncture were conducted to consider and rule out differential diagnoses. Cerebrospinal fluid analysis revealed an albuminocytologic dissociation. The clinical triad of progressive ophthalmoplegia, areflexia and areflexia alongside albuminocytologic dissociation led to the diagnosis of Miller Fisher syndrome. The patient was commenced on intravenous immunoglobulin and his symptoms showed significant improvement. We use this interesting case to provide context for key learning points about diagnosing Miller Fisher syndrome in children.

Key words: GQ1b ganglioside; Miller Fisher syndrome; Neurology; Ophthalmoplegia; Paediatrics

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Introduction

Miller Fisher syndrome (MFS) is a rare variant of Guillain-Barré syndrome (GBS), an acute autoimmune disease characterised by a clinical triad of ophthalmoplegia, ataxia and areflexia, strongly associated with the presence of anti-GQ1b antibodies. Typically linked to a preceding antigenic trigger such as a recent infection, an accurate diagnosis of MFS entails a good clinical examination and ancillary tests with intravenous immunoglobulin (IVIG) as the primary treatment. Through this case of paediatric MFS, we highlight the diagnostic challenges and clinical pearls in evaluating a child with autism spectrum disorder (ASD) presenting with an evolving ophthalmoplegia.

Case report

A 6-year-old boy with ASD was brought to the Emergency Department by his parents with a 2-day history of new-onset squint and left-sided 'ptosis'. His mother described preceding respiratory tract symptoms including rhinorrhoea and cough that started 5 days prior. His medical history included recurrent urinary tract infections. There was no history of recent vaccinations, travel or family history of squint or neurological disease.

He was apyrexial with normal vital signs. The examination was challenging as he was non-verbal and not fully cooperative. However, power was grossly normal, graded at 5/5, and the patient exhibited ambulation and physical resistance against optical instruments employed during examinations. Light touch and pin-prick sensation of bilateral upper and lower limbs were intact.

Eye examination revealed esotropia (in-turning of the eye) with bilateral abduction paresis. Left-sided ptosis was observed; this was a pseudoptosis (i.e., compensatory attempt to overcome diplopia) since occluding his right eye and showing his preferred cartoon could encourage him to open his left eye (Figures 1,2). Both pupils were mydriatic with

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minimal light response, but slight pupillary constriction to accommodation (light-near dissociation). There were no other cranial nerve deficits. Fundus examination was normal. The absence of optic disc swelling is an important negative finding as abducens palsy can be a false localising sign of raised intracranial pressure (ICP).

His new-onset esotropia with abduction deficit warranted a systemic work-up. Full blood count, urea and electrolytes, creatinine kinase and inflammatory markers were normal. Non-contrast brain magnetic resonance imaging (MRI) and computed tomography (CT) venogram with contrast also ruled out space-occupying lesions and cerebral venous sinus thrombosis.

Cerebrospinal fluid (CSF) analysis showed elevated protein count (0.41 g/L) without pleocytosis (cytoalbuminologic dissociation) and negative anti-GQ1b antibody, a marker for MFS. Lumbar puncture (LP) findings revealed matched oligoclonal band pattern (type 4) in CSF and serum but with no organism growth.

Nerve conduction studies were normal but electromyography (EMG) revealed a somatosensory evoked blink response – an aberrant blink reflex reported in neurological diseases including MFS (Miwa et al, 1995; Cha et al, 1998). His eye movements deteriorated to near-complete ophthalmoplegia at 1-week review (Figure 3). The triad of ophthalmoplegia, ataxia and areflexia led to the diagnosis of MFS, supported by CSF cytoalbuminologic dissociation and EMG finding and was treated with IVIG (2 g intravenously for 5 days).

Upon completion of his IVIG regimen, he showed recovery in gait and ptosis within a week, with resolution of ataxia at 2 months, and ophthalmoplegia at 6 months. His pupils remained moderately mydriatic with sluggish pupillary reaction. This was treated with tinted glasses to mitigate discomfort in bright lights.

Discussion

Named after Dr Charles Miller Fisher, MFS is characterised by a triad of ophthalmoplegia, ataxia and areflexia, and affects 1 per 1,000,000 worldwide (Noioso et al, 2023). Miller Fisher syndrome typically follows a monophasic course with an interval between 12 hours and 28 days to clinical nadir (Wakerley and Yuki, 2015). Cerebrospinal fluid cytoalbuminologic dissociation and nerve conduction studies (NCS) showing normal study or sensory nerve involvement are supportive of MFS (Sejvar et al, 2011). Additionally, several studies reported pupillary abnormalities in MFS patients including tonic pupils, mydriasis, absent pupillary reflexes and light-near dissociation (Kaymakamzade et al, 2013; Lee et al, 2021).

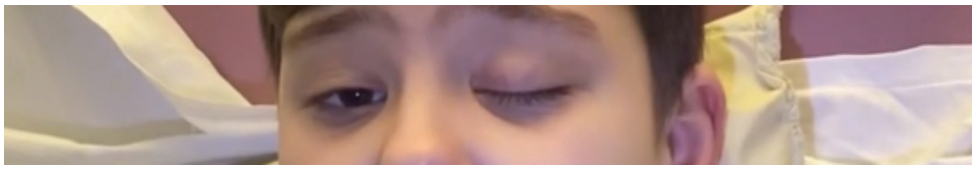

Figure 1. Clinical photograph showing a 6-year-old boy with right esotropia (in-turning of the eye) and apparent left ptosis (droopy eyelid) at primary gaze.

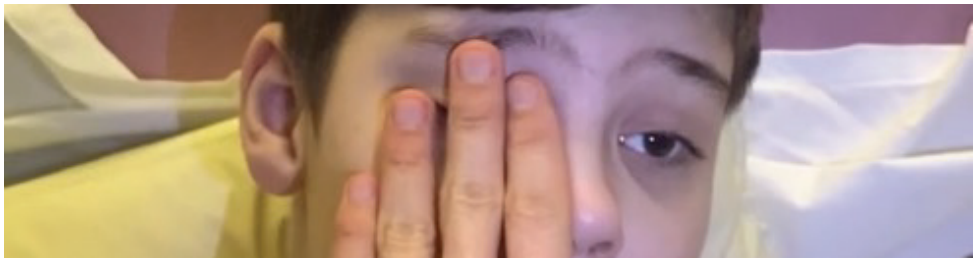

Figure 2. Occlusion of the right eye led to the opening of the left eyelid, indicating the patient's compensatory attempt to overcome diplopia. This patient does not have a true ptosis.

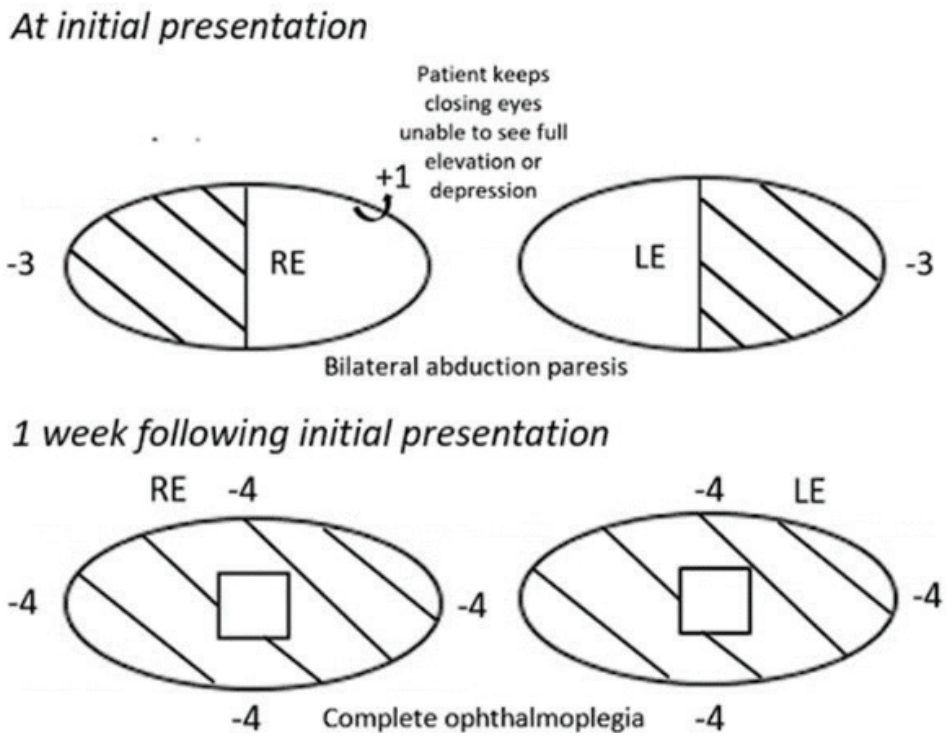

Figure 3. Ocular motility diagram of the patient's evolving ophthalmoplegia at initial presentation vs 1 week following initial presentation. LE: Left Eye; RE: Right Eye. Figure was created with BioRender.com (version, 2024) (Toronto, ON, Canada).

The diagnosis of MFS in children clearly require a multidisciplinary approach involving paediatrics, neurologists, and ophthalmologists. In this case, ophthalmologists helped to form the differential diagnoses and direct investigations. The initial presentation of apparent 'ptosis' with dilated pupil would raise concerns of third nerve palsy; however, the cover test excluded true ptosis. The findings of esotropia and bilateral abduction deficits led to neuroimaging as the commonest non-traumatic cause of abducens nerve palsy is neoplasm in children as opposed to microvascular in adults (Kalita et al, 2022). However, serial eye examinations confirmed the progression of ophthalmoplegia, in keeping with MFS. This led to further investigations including a lumbar puncture (LP), NCS and EMG by paediatricians and neurologists.

The significance of anti-ganglioside antibodies in paediatric MFS cases is unclear (Koga et al, 2012). Rates of anti-GQ1b positivity in paediatric MFS are much lower (22–66%) than in adult MFS (up to 89%) (Masahiro et al, 2001; Jang et al, 2020) – consistent with our GQ1b-seronegative MFS case. Hence, clinicians should not use a negative GQ1b test result to exclude MFS. In keeping with Brighton's case definition for MFS, anti-ganglioside antibodies (anti-GQ1b and anti-GT1a) are supportive but not necessary for diagnosis (Sejvar et al, 2011). While immune dysregulation has been described in ASD (Robinson-Agramonte et al, 2022), there is a paucity of evidence supporting an association between MFS and ASD.

Intravenous immunoglobulin or plasmapheresis is a gold standard treatment for MFS (Sejvar et al, 2011). Corticosteroid therapy is not efficacious and is linked to poor outcomes (Sejvar et al, 2011).

Ophthalmic examination in autistic children requires a tailored and patient-centred approach. Assessing visual acuity, binocular vision, and ocular motility involves tools and techniques accommodating the child's sensory preferences while avoiding overstimulation. Building rapport through communication during examination is crucial for the child and parent/guardian. Considering the sensory sensitivities often present in ASD, clinicians should modify their approach to establish a comfortable assessment environment through incorporating familiar objects to enhance engagement and providing breaks during instances of distress. By understanding the individual needs of children, clinicians can optimise the accuracy of examinations.

Learning points

- When examining paediatric patients with ASD, incorporate children-friendly items (cartoons) to improve engagement.
- A patient's compensatory attempt to overcome diplopia may be misinterpreted as ptosis. Occlude the contralateral eye to check for this pseudoptosis.
- Abducens nerve palsy (unilateral or bilateral) can be a false localising sign.
- Miller Fisher syndrome presents with ataxia, evolving ophthalmoplegia and areflexia. Cerebrospinal fluid, NCS and EMG results are helpful to improve diagnostic certainty.
- Anti-GQ1b is supportive but not necessary for MFS diagnosis. The rate of anti-GQ1b positivity is much lower in paediatric MFS (22–66%) than in adult MFS (up to 89%).

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Availability of data and materials

Anonymised data presented in this article are available on reasonable request from the corresponding author and approval by Barking, Havering and Redbridge University Hospital NHS Foundation trust. Data are not publicly available due to parts of the data containing confidential patient information.

Authors contributions

BJC and AR contributed to collecting clinical data and drafting the article. RD, AK and MP contributed to the data analysis and critical revision. All authors contributed to important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics approval and consent to participate

Informed written consent was obtained from the patient's next-of-kin to publish the case study, in accordance with the ethical standards of the Declaration of Helsinki.

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Conflict of interest

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