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LETTER TO THE EDITOR

A pediatric case of Miller Fisher syndrome with central involvement

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Dear Editor-in-Chief,

Miller Fisher syndrome (MFS) is a rare condition characterized by external ophthalmoplegia, ataxia, and areflexia, and is considered a clinical variant of Guillain-Barré syndrome (GBS). Reports on MFS with Bickerstaff brainstem encephalitis (BBE) overlapping are also reported and a clear distinction between the two disorders is still debated [1]. Nevertheless, both clinical pictures are characterized in up to 90 % of cases by high titre of serum anti GQ1b antibodies, which have a clear pathogenetic role.

We describe a rare case of pediatric MFS with clinical central involvement, and a good recovery after the second cycle of intravenous immunoglobulin (IVIg), suggesting a therapeutic efficacy of immunomodulatory treatment.

A six-year-old child was referred to our Hospital for acute onset of diplopia, left palpebral ptosis and sixth left nerve palsy associated to gait ataxia. The day after, the patient worsened with drowsiness, ophthalmoplegia, dysphagia and hypopnea that needed mechanical ventilation. Neurological evaluation showed generalized hypotonia and weakness with left predominance, ophthalmoplegia with bilateral ptosis and severe bilateral facial diplegia. Tendon reflexes were absent, while no sensory impairment was noted.

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Cerebrospinal fluid exam, including protein, cell counts, microscopic analysis, polymerase chain reaction for neurotrophic viruses, Lyme antibodies and oligoclonal band research was normal. Blood test analysis was negative for botulinum toxin, neurotrophic viruses, and antiganglioside antibody research, with the exception of serum anti-GQ1b IgG titre obtained using enzyme-linked immunosorbent assay that was high (1:2,560, normal value <1:640).

Cerebral magnetic resonance imaging (MRI) and electroencephalogram did not show any abnormalities.

Limb neurography was normal except H-reflex recorded from soleus muscles that was unelicitable; R1 and R2 responses of the blink reflex were absent bilaterally, and cranial electromyography showed active denervation both in mouth and eye orbicularis muscles bilaterally. Somatosensory evoked potentials (SEP) revealed central impairment (bilateral increased P28 latency: 33.6 ms on the right and 34.3 ms on the left side, normal value <33.1) and brainstem auditory evoked potentials (BAEPs) showed abnormal V/I ratio on the left side (0.39, normal value >0.5).

A diagnosis of MFS with central involvement was made and a first cycle of intravenous immunoglobulins (IVIg) at a standard dose of 0.4 g/kg/die for 5 days was administrated without clinical improvement. More than 1 month after the disease onset, estubation was not feasible for the stable but severe clinical picture, and a second cycle of IVIg at a standard dose was repeated with significative clinical benefit: 7 days after, the child was estubated and discharged from Hospital with mild neurological deficits (mild bilateral facial, left abducens nerve and mild proximal limb paresis); serum anti-GQ1b antibody research became negative.

While MFS is reported in about 5–10 % of GBS forms in adults, in pediatric population is rare, and clinical reports of

central-peripheral involvement in children are anecdotal [2]. Recent data suggest that MFS and BBE conditions are not separate disorders, but rather form a continuous spectrum called the 'anti-GQ1b IgG antibody syndrome' [3] with variable central and peripheral nervous system involvement. Nevertheless, pediatric forms are usually mild, with predominant ocular involvement, even if rarer cases with transient coma or respiratory failure are described [4].

Our patient demonstrated a predominant brainstem (cranial nerve) involvement: peripheral nerves conduction studies were normal except the absence of H-reflex recorded from soleus muscles, whereas cranial motor nerve conduction studies was severely compromised, showing bilateral facial muscle denervation. Although the cerebral MRI did not show any brain damage, the generalized hypotonia and weakness, the mild drowsiness, the ongoing hypopnea, associated to SEP and BAEPs abnormalities, suggested a central involvement probably at the level of spinocerebellar pathways and brainstem.

Immunological studies with monoclonal anti-GQ1b antibodies showed a direct pathogenetic role of the anti-GQ1b in developing MFS symptoms: their binding to paranodal regions of human ocular motor nerves, muscle spindles, dorsal root ganglia and deep cerebellar nuclei may account, respectively, of neuromuscular transmission impairment and functional block leading to ophthalmoplegia, areflexia and peripheral/cerebellar ataxia. The specific compromission of group Ia muscle spindle afferents, supported by the evidence of immunolocalization of GQ1b in human muscle spindles [5], has been proposed as the responsible mechanism for ataxia and areflexia, and correlates with neurophysiological H-reflex absence (mediated by group Ia fibers) and normal sensory conduction (that is carried by group II afferents).

MFS has usually a good prognosis and clinical recovery is often spontaneous. Randomized controlled trials on immunomodulatory treatment in MFS and BEE, are still lacking and a large retrospective study found that, even if immunosuppressive treatment may hasten the amelioration of ophthalmoplegia and ataxia, neither IVIg nor plasmapheresis influence the patients' outcomes, because of the disease natural recovery [6]. Nevertheless, few compromised clinical pictures requiring intubation and mechanical ventilation may need a therapeutic intervention and the remarkable clinical improvement in our patient after the second IVIg cycle suggests the effectiveness of immunomodulatory treatment in severe MFS/BEE.

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