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LETTER TO THE EDITOR

Positive anti-GQ1b Miller Fisher syndrome and *Escherichia coli* infection: A case report

Síndrome de Miller Fisher anti-GQ1b positivo e infección por *Escherichia coli*: reporte de un caso

A 56-year-old man without significant pathological history came to our emergency room in November 2019 with a 9-day history of sudden onset diplopia associated with nausea and vomiting, hands and feet numbness, one day later instability to walk was added, increasing in the following three days, making impossible to stand. Three days later, the patient manifested moderate occipital headache that remitted partially with analgesics. Three weeks before admission, the patient presented with a self-limited episode of nonbloody diarrhea. At admission, the patient had normal vital functions. The general examination was not contributory. In the neurological exam, strength and tone was preserved, osteotendinous reflexes was abolished, superficial cutaneous reflexes were normal with bilateral flexor plantar response, hypoesthesia in the distal region of the four extremities with normal deep sensitivity. Instability for standing, ataxic gait with a widening of the base of support, and inability to perform tandem gait was evidenced, while limb coordination was preserved. Bilateral oculomotor, trochlear, and abducens nerves were compromised. No meningeal signs or abnormal movements was found. Necessary blood tests (hemogram, glucose, urea, creatinine, electrolytes, and liver profile) showed no alterations. The serological tests for Human Immunodeficiency Virus and Syphilis were non-reactive, vitamin B12 (609 pg/ml), and folic acid (14.8 ng/ml) was normal, as the thyroid profile (TSH 2150 u/ml, T4 5.7 IU/dl T3 82 IU/dl). Brain MRI showed no abnormalities. Cerebrospinal fluid was characterized by 4 WBC, glucose 69 mg/dl, and protein elevated to 66 mg/dl; no germs was found in the Gram stain or in India ink stain. On the other hand, the nerve conduction study showed acute axonal sensory polyneuropathy that affected all four extremities (Table 1). IgG and IgM titers for Zika, Chikungunya, and Dengue viruses was not detected, while *Escherichia coli* (*E. coli*) was isolated in routine stool cultures. Finally, serum anti-ganglioside GQ1b antibody was positive (1:12,800). The patient received symptomatic treatment and physical therapy only, regaining gait stability and complete ocular motility 15 days after discharge because of progressive improvement in hospitalization.

Discussion

Miller Fisher syndrome (SMF) is an acute immune-mediated neuropathy characterized by the clinical triad of ophthalmoplegia, ataxia, and areflexia.[1] Although it was first described in 1932 by James Collier, it has been considered a variant of Guillain Barré Syndrome (GBS) since 1956, when Charles Miller Fisher reported three cases with similar findings cerebrospinal fluid.[2]

SMF represents about 5% of Guillain Barré Syndrome cases; however, in eastern populations such as Japan, the incidence reaches 25%, being more frequent in men with a 2:1 ratio.[3] It manifests with diplopia due to paralysis of oculomotor nerves, ataxia due to compromise of sensory roots in the peripheral nervous system, which also explains distal dysesthesias and hypo-areflexia. The involvement of bulbar nerves has been reported less frequently. A study that analyzed the characteristics of patients with Miller Fisher syndrome found 88% seropositive patients for antibodies against GQ1b ganglioside, however, within the seronegative group the IgG antibodies presence against GM1b, GD1c, GalNAc-GM1b and gangliosides complexes have been described.[4] Since the pathogenic mechanisms have not been experimentally demonstrated in humans, hypotheses are still being raised about MFS development. The most accepted theory is ''molecular mimicry'', which suggests the structural carbohydrates of these microorganisms' ''mimics'' components of nerve cells, called gangliosides, containing sialic acid and form part of neuronal membranes.[5] Immunofluorescence studies showed the expression of ganglioside GQ1b in the paranodal myelin of the extramedullary portion of cranial nerves that innervate the extraocular musculature, dorsal root ganglion cells, and muscle spindles so that the antibodies created against some microorganisms cause a cross-reaction against the ganglioside, destroying it and affecting the paranodal region of the myelin sheath.[6] Our patient presented the classic triad of ophthalmoplegia, ataxia, and areflexia; however, it corresponds to a case of atypical MFS due to the overlap with GBS, demonstrated by electromyography, which represents 17% of MFS cases, there may also be ophthalmoplegia without ataxia and ataxic neuropathy without ophthalmoplegia.[7] On the other hand, the albumin-cytological dissociation

Table 1 Sensory and motor nerve conduction study.

Sensory NCS				
Nerve/site	Latency (ms)	Peak Ampl (μV)	Distance (cm)	Velocity (m/s)
Right median				
Wrist	0	0	12	0
Left median				
Wrist	0	0	12	0
Right ulnar				
Wrist	2.10	15.2	12	57.1
Left sural				
Calf/Lat malleolus	2.45	5.5	14	57.1
Right sural				
Calf/Lat malleolus	2.65	6.5	14	52.8

Motor NCS				
Nerve/site	Latency (ms)	Peak Ampl (mV)	Distance (cm)	Velocity (m/s)
Right median				
Wrist	4.05	10.4	21	60.9
Elbow	7.50	9.9		
Left median				
Wrist	4.05	5.3	21	51.2
Elbow	8.15	5.3		
Right ulnar				
Wrist	2.65	8.7	22	52.4
Elbow	6.85	7.6		
Right comm peroneal				
Ankle	3.75	8.7	30	48.8
Fib head	9.90	7.0		
Left comm peroneal				
Ankle	4.20	7.3	32	49.6
Fib head	10.65	6.3		
Left tibial (knee)				
Ankle	4.65	9.0	37	43.5
knee	13.15	8.9		

found in this report has been described in 41% of patients with SMF.[8] The favorable evolution without immunomodulatory treatment coincides with the literature. It is known that the prognosis of patients with MFS at 6 months is good (Hughes Functional Grading Scale ≤ 1), even without treatment, mainly because they don't have respiratory compromise.[9,10] Various infectious agents are known to cause the immunopathogenic mechanism associated with MFS. The most frequent is *Campylobacter jejuni*, followed by *Haemophilus influenzae*,[11] *Epstein-Barr virus*, *Cytomegalovirus*, *Streptococcus pyogenes*,[12] *Mycoplasma pneumoniae*, and *Salmonella enteritidis*.[13] Only one MFS case that developed one month after *E. coli* pyelonephritis was reported until now, and the anti-ganglioside GQ1b antibody was not detected.[14] Moreover, *E. coli* is associated with the axonal variant of GBS[15] and recurrence of this disease,[16] the importance of searching for this pathogen.

Conclusion

Therefore, we report for the first time in the literature a case of MFS associated with *E. coli* with the demonstration of anti-GQ1b serum antibody, with favorable evolution despite no immunomodulatory treatment.

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Mild head trauma: Acute encephalopathy trigger in children with RHOBTB2 de novo mutation

Traumatismo craneoencefálico leve: desencadenante de encefalopatía aguda en niños con mutación de novo en RHOBTB2

Dear Editor,

We present a 6 year old girl with microcephaly and epileptic seizures associated with a RHOBTB2 pathogenic variant, who consulted the Pediatric Emergency Department for low consciousness after a mild head traumatism 40 min earlier. The patient had fallen from her own height, neither having presented nausea, vomits, seizures nor immediate conscience loss. Around 10 min after the head trauma, the patient suffered medium disconnection, hypotonia and tendency to fall asleep. At her arrival to the Pediatric Emergency department, the patient had bilateral arreactive and mydriatic pupils as well as a non-sostenible airway. Glasgow scored 3 points. No other signs of intracranial hypertension were present. Orotracheal intubation was conducted and a unique hypertonic saline bolus was administered. Computed tomography (CT) was performed, which did not show structural traumatic injury. Blood tests were normal. Our patient was admitted in the Pediatric Intensive Care Unit, where she remained intubated with propofol perfusion for 24 h. Programmed extubation was performed, with complete neurological recuperation without focal deficits and Glasgow 15 score. Usual treatment was resumed (valproic acid and lacosamide) and the patient was transferred to the general pediatric hospitalization unit, being discharged after 48 h of monitorization and observation.

Rho-related BTB domain-containing protein 2 (RHOBTB2) belongs to an atypical Rho GTPase family whose mRNA levels are high in humans' nervous system. Hence, the important role of normal regulation levels of RHOBTB2 in