Miller-Fisher syndrome associated with acute motor axonal neuropathy: Clinic-immunological correlation

Síndrome de Miller-Fisher asociado a neuropatía axonal motora aguda: correlación clínico-inmunológica

Sir,

Miller-Fisher syndrome (MFS) is an extremely rare, autoimmune, axonal polyradiculoneuropathy which takes place during childhood. It is characterised by the clinical triad of ataxia, ophthalmoplegia and areflexia. The annual incidence of Miller-Fisher syndrome is 0.09 cases per 100,000 inhabitants. The few published series that exist with children account for approximately 9% of the total of acute polyradiculoneuropathy cases. As in the case of Guillain–Barré syndrome, it is often triggered by certain strains of Campylobacter jejuni that induce the formation of anti-GQ1b antiganglioside, although there have also been cases described involving Haemophilus influenzae and Mycoplasma pneumoniae. Anti-GQ1b antibodies are elevated in 90–97% of Miller-Fisher syndrome cases. These antibodies recognize epitopes that are expressed specifically in the nodal regions of the oculomotor nerves, in the dorsal root ganglia and in the cerebellar neurons. All these structures are responsible for the symptoms of Miller-Fisher syndrome.

Occasionally, Miller-Fisher syndrome and Guillain-Barré syndrome in its demyelinating, acute, motor axonal and acute sensorimotor variants may have an overlapping clinical spectrum, depending on the immunopathological cause. Moreover, motor axonal forms generally respect cranial nerves and present a predominantly distal involvement. Very few cases of this type of presentation have been studied in the light of current knowledge, improved antibody detection techniques and purification of new antigens from the nervous system. We present a study of a patient suffering from Miller-Fisher variant associated with an acute peripheral case of acute motor axonal neuropathy (AMAN). We analysed the antiganglioside antibody pattern and its correlation with the symptoms, as well as the evolution and response to treatment with intravenous immunoglobulin.

The patient was a boy aged 4 years and 9 months, who was admitted to our hospital due to generalised weakness with inability for ambulation, gait instability and palpebral oedema with right ptosis. These symptoms had a progressive clinical evolution of 2 weeks. The patient had suffered an episode of gastroenteritis of unknown aetiology 15 days earlier.

On examination at admission the patient was prostrate, with sensation of acute illness, highlighting a mild bilateral palpebral oedema with right ptosis. At the neurological level, he was conscious, alert, and responsive, with a clear sensory spectrum. He also presented ophthalmoplegia affecting the third, fourth and sixth cranial nerves, inability for vertical and horizontal visual tracking and bilateral facial paresis. In addition, he suffered generalised hypotonia with proximal predominance, inability to sit and walk, decreased strength which was especially marked in the lower limbs, and a slightly asymmetrical balance of the right leg over the left, 1/5 and 2/5, respectively. He also presented universal areflexia, with seemingly preserved thermo-algesic and proprioceptive sensitivity. No cerebellar signs, tremor, dysmetria or dysdiadochokinesia were identified. There were no meningeal signs.

Complementary tests highlighted albumino-cytological dissociation in the cerebrospinal fluid with protein levels of 0.8 g/l and 5 mononuclear cells per mm³. Neuroimaging tests (cervical and thoracolumbar MRI scans) showed no morphological changes or signal alterations in the brain, brainstem, spinal cord or cauda equina in T-1, T-2 or FLAIR weighted sequences.

In the initial neurophysiological study, the electromyograms of the upper limb (deltoid, biceps and extensor digitorum muscles) and lower limb (rectus femoris, anterior tibialis and gastrocnemius muscles) revealed a neurogenic pattern. There was spontaneous denervation activity with fibrillations and positive waves, highly deficient evoked motor conduction pathways that were more pronounced in the proximal muscles of the upper limb being examined, and motor unit potentials of long duration and great amplitude, with an increased proportion of polyphasic motor unit potentials. The electroneurogram presented impaired motor conduction with reduced amplitude. Distal latency and conduction velocity remained at normal parameters at the level of both facial nerves, right median nerve, right ulnar nerve and both peroneal nerves. Sensory conduction
was within normal limits in both speed and amplitude and was, therefore, compatible with motor axonal polyradiculopathy.

The seroimmunological study of antiglycolipid antibodies conducted by enzyme immunoassay (ELISA) detected the presence of IgM antibodies against ganglioside GQ1b at a titre of 1/1500 and IgG positivity against ganglioside GM1 at a titre of 1/500 and IgM against antigen GM2 at a titre of 1/3000. Determination of the remaining antiglycolipid antibodies against GM3, asialo GM1, GD1a, GD1b, GD3, GT1b, sulphatide and globoside were negative.

We performed stool culture for Campylobacter jejuni, which resulted negative. CRP in blood for herpes group viruses was negative. The patient was diagnosed with Miller-Fisher syndrome and associated acute motor axonal neuropathy.

The patient was treated with intravenous immunoglobulin at doses of 2 g/kg (400 mg/kg/day for 5 days) and early motor rehabilitation, with good clinical and neurophysiological response. One month after starting treatment, the clinical examination revealed partial recovery of oculomotor and facial reflexes, unaided sitting, aided standing and paraparetic walking with some aid. In the control neurophysiological study conducted 3 months later, the electroneuromyograms of the orbicularis oculi and the right deltoid revealed an absence of spontaneous activity. Furthermore, voluntary movements at maximum effort were slightly deficient in the orbicularis oculi and without significant deficit in the deltoid. Motor unit potentials were normal. The control electroneurogram showed motor conduction involvement of the right and left facial nerves, with decreased amplitude in both evoked potentials, but predominantly on the left. The only finding in connection with the initial neurophysiological examination was peripheral neuropathy of the facial nerves, predominantly on the left side, possibly at the level of the intrapetrous pathway. However, this had a lesser degree than in the initial examination and the remainder of the neurophysiological study was normal.

Current knowledge of acute polyradiculoneuropathies indicates that these entities are acquired as the result of an aberrant immune response secondary to a triggering event. This event could be infection, vaccination, malignancy or some other autoimmune stimulus. The variety of antibodies formed determines the subsequent pathological outcome. Thus, the presence of anti-GQ1b leads to the involvement of oculomotor nerves since antigen GQ1b is specifically expressed in the nodal regions of the oculomotor nerves, the dorsal root ganglia and the cerebellar neurons. Furthermore, acute neuropathy characterised by cervical—pharyngeal—brachial paralysis or bulbar dysfunctions has been recognised as a variant of Guillain—Barré syndrome. In addition, a recent clinical study has shown that cervical—pharyngeal—brachial paralysis, Miller-Fisher syndrome and Bickerstaff encephalitis form a continuous clinical spectrum. A specific anti-GT1a antibody without GQ1b reactivity is essential for the development of bulbar paralysis in patients with Guillain—Barré syndrome. The glossopharyngeal nerve and vagus nerve contain GQ1b and GT1a, but the presence of GT1a has not been demonstrated in human peripheral nerves. It is likely that specific anti-GD1b antibodies cause ataxia in Guillain—Barré syndrome.
Levodopa-responsive parkinsonism-dystonia due to a traumatic injury of the substantia nigra

Parkinsonismo-distonia unilateral sensible a levodopa por lesión traumática de la sustancia negra

Sir,

The relationship between traumatic brain injury (TBI) and parkinsonism has been established for a long time. However, in exceptionally rare cases there have been reports of parkinsonism secondary to traumatic lesions of the substantia nigra (SN). Case reports of parkinsonism due to SN lesions of vascular origin, either by lacunar stroke or by small mesencephalic haemorrhages, are better known, but also exceptional. Bhatt published a series of 3 patients who started to suffer uncontrolled and involuntary movements of the left limbs, which were more pronounced in the foot. The examination revealed hemidystonia, without any other significant signs. Two months later, in addition to hemidystonia, he suffered akinetic-rigid syndrome characterised by resting tremor, significant cogwheel rigidity and bradykinesia in the affected side of the body. These symptoms had a relatively rapid onset, with severe worsening of parkinsonism within a few weeks. A cranial MRI scan (Fig. 1) conducted at that time showed a right mesencephalic lesion at the level of the SN, with a hyperintense signal on T2-weighted sequences and a hypointense signal in the SN.

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