Ophthalmoplegia due to Miller Fisher Syndrome in a patient with Myasthenia Gravis

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BACKGROUND

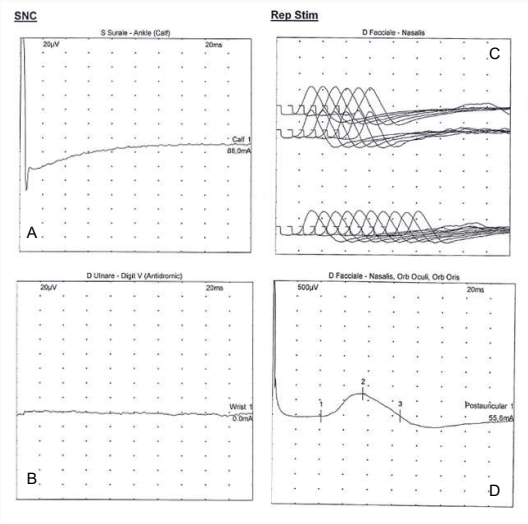
Bilateral acute ophthalmoparesis can be caused by various etiologies, involving brainstem (stroke, tumor, multiple sclerosis, Wernicke encephalopathy), cranial nerves (tuberculous meningitis, Guillain Barrè or Miller Fisher syndrome), cavernous sinus, neuromuscular junction (myasthenia gravis, botulism), muscles (myositis, mitochondriopathies) and orbit (cellulitis, Graves disease).

CASE REPORT

A 79 years old man affected with myasthenia gravis was admitted to our hospital in order to treat rapid worsening of diplopia and fatigue, started a few weeks after flu vaccination and an episode of bronchitis treated with cephalosporin.

Myasthenia gravis (MG) was diagnosed eight years earlier with detection of antibodies against Acetylcholine Receptor (AChR) and Ryanodine Receptor (RyR); clinical symptoms have been so far well controlled by Pyridostigmine, Azathioprine and low doses of steroid; last neurological examination revealed only mild diplopia on left lateral gaze. The patient presented also with a history of mild iatrogenic chronic sensorimotor axonal polyneuropathy due to chemotherapy administred after surgical resection of colon cancer. Oncological follow-up was negative.

During the first days, the patient developed progressive ocular movement abnormalities up to complete external ophthalmoplegia and limb and gait ataxia with inability to walk unsupported. Deep tendon reflexes were absent, except for brachioradialis reflex. Additional features included partial ptosis of the left eye, tingling in the hands, mild proximal weakness in lower limb and dysarthria, nausea, facial asymmetry and mild pupillary abnormalities.



Neurophysiological studies revealed absent sensory action potential (SAP) of sural and ulnar nerve (A-B), increased facial nerve latency (D) and negative repetitive nerve stimulation (C). Ulnar F-wave was not clearly detactable (not shown), while tibial F-wave was normal.

Since not all the symptoms were explainable with the previous diagnosis of myasthenia gravis, other etiologies were investigated.

Serum analysis were unremarkable. Thyroid function, folate and vitamin B12 were normal. Anti-AChR and GQ1b antibodies were analyzed.

Brain MRI did not show any acute cerebral lesion.

Cerebrospinal fluid (CSF) analysis, including virological investigations and oligoclonal bands, was normal and did not reveal albuminocytologic dissociation.

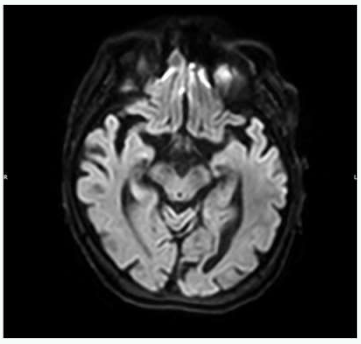
Electromyography showed a pattern of predominantly sensory multiple radiculoneuritis, characterized by increased facial nerve latency and absence of sensory nerve action potentials, ulnar nerve F-wave seemed not clearly detectable.

Repetitive nerve stimulation did not show a decremental response.

Neoplastic markers were normal and full-body CT scan was oncologically negative.

CSF analysis	
Cells	< 1/mmc
Glucose	63 mg/dl
Proteins	24 mg/dl

Serum antibodies		Normal
Anti-AChR	7.2 pmol/ml	< 0.5
GQ1b IgM	1 : 2560	< 1 : 640
GQ1b IgG	1 : 5120	< 1 : 640



Brain MRI revealed only mild chronic cerebrovasculopathy and cortico-subcortical atrophy.

The patient was treated with plasmapheresis with subsequent slow clinical improvement. After two months the patient was able to walk independently and ophthalmoparesis markedly improved.

Antibodies against GQ1b turned out to be positive.

DISCUSSION and CONCLUSIONS

Even if ophalmoparesis can be caused by Myasthenia Gravis, the overall clinical presentation suggested the investigation of an alternative etiology responsible for the current symptoms. The detection of GQ1b antibodies confirmed the diagnosis of Miller-Fisher Syndrome, a rare variant of Guillain-Barrè Syndrome, characterized by ophtalmoplegia, ataxia and areflexia. So far only few cases of MFS overlapping MG have been described.

Since the coexistence of two different autoimmune disorders can occur, it is important to always evaluate possible differential diagnosis even in case of known compatible diseases, especially when some clinical features seem atypical.

REFERENCES

- *Mak et al.* A case of ocular myasthenia gravis and Miller Fisher syndrome. *Hosp Med 2005 Feb; 66(2):116-7*
- *Lau et al.* The co-occurrence of serologically proven myasthenia gravis and Miller Fisher/Guillain Barré overlap syndrome: a case report. *J Neurol Sci. 2009 Jan 15;276(1-2):187-8*
- *Tanaka et al.* Overlap of Myasthenia Gravis and Miller Fisher Syndrome. *Intern Med. 2016;55(14):1917-8*