

Development of myasthenic crisis during new direct-acting antiviral agents (DAAs) treatment for chronic HCV infection: a case report

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ABSTRACT:

— Myasthenic crises can occur spontaneously during myasthenia gravis natural history; they can also be triggered by several factors, such as concomitant infections, pregnancy or drugs. Interferon has been implicated in myasthenic crisis, as well as ribavirin. No data are available about new antiviral drugs for the treatment of hepatitis C virus (DAAs). Here we report the case of a 73-years old man affected by myasthenia gravis and HCV genotype 2a/2c chronic hepatitis, who developed a myasthenic crisis during sofosbuvir and ribavirin treatment. Even if myasthenia gravis is a rare disease, the correlation of myasthenic crises, either direct or indirect, with the use of the new DAAs has to be taken into consideration.

— **Keywords:** HCV, Sofosbuvir, Ribavirin, Myasthenia gravis.

BACKGROUND

Myasthenia gravis is the best defined and the most common chronic autoimmune neuromuscular disorder. It is characterized by a variable combination of ocular, bulbar, limb and respiratory muscles fluctuating weakness¹. Myasthenic crisis is defined as respiratory muscles weakness with respiratory failure and it is a life-threatening condition. A myasthenic crisis can occur spontaneously or can be triggered by several factors, such as concomitant infections, pregnancy or various drugs, in particular antibiotics (aminoglycosides, fluoroquinolones, erythromycin and azithromycin), cardiac drugs (beta-blockers, procainamide, and quinidine), and magnesium². Interferon (IFN) has been implicated in myasthenic crises, as well as ribavirin, even if reports are related to ribavirin/interferon combined treatment^{3,4}. No data are available about new antiviral drugs for the treatment of hepatitis C virus.

CASE REPORT

A 73-years old man affected by myasthenia gravis was referred to our Clinic in 2013 for HCV genotype 2a/2c chronic hepatitis. Anti-HCV treatment was never prescribed before due to interferon contraindication in myasthenia gravis². Furthermore, during prednisone dose increase for the myasthenic crisis, the patient underwent several hepatitis recrudescences. In May 2014, a liver biopsy was performed, resulting a METAVIR fibrosis score 1; in February 2015 transient elastography showed F3 fibrosis (KPa 10.1). Therefore, according to Italian Drug Agency (AIFA) criteria⁵, antiviral therapy with sofosbuvir 400 mg (one tablet) and ribavirin 200 mg (three tablets in the morning and two tablets in the evening, according to weight) was prescribed on February 25th. After 5 days of treatment, the patient presented palpebral ptosis, difficulty chewing and swallowing, limbs weakness, double vision, slurred speech and dyspnea, defining a myasthenic

crisis. He was admitted to Neurology ward on March 2nd with a Myasthenia Score (MS) of 17/30^{6,7}, undetectable HCV-RNA, ALT 48 U/L (nv: 15-47 U/L) and AST 24 U/L (nv: 13-51 U/L). Antiviral therapy was promptly interrupted. Clinical conditions worsened with dysphagia and need of enteral nutrition through a nasogastric tube, respiratory failure and MS equal to 21/30. Intravenous immunoglobulins were prescribed (25 g/die for five days) and prednisone dose was increased (from 5 mg/die to 10 mg/die). In the following days, MS improved (12/30), but liver enzyme remained high: on March 17th: ALT 228 U/L, AST 168 U/L, bilirubin 0.41 mg/dL (nv: 0.3-1.2), PT 86% (nv: 80-120%); on March 23rd: ALT 665 U/L, AST 355 U/L. On March 23rd corticosteroids were gradually reduced to 7.5 mg/die, but a new course of intravenous immunoglobulin was necessary for the worsening of clinical conditions. Successively, during therapy with prednisone and pyridostigmine, clinical conditions finally improved (on April 3rd, MS: 8/30), but liver enzymes persisted high (on April 7th: AST 307 U/L, ALT 439 U/L). The patient was discharged on April 13th continuing follow-up and monitoring.

DISCUSSION

To our knowledge, no data are available about DAAs and ribavirin safety in myasthenia gravis, even if ribavirin treatment has been associated with myasthenic crises in combination with IFN^{3,4}. In the present case, a correlation between DAAs and myasthenic crisis is reported. Whether it is due to a direct or an indirect effect, mediated by im-

munological events triggered by viral clearance, remains unknown. Nevertheless, even though myasthenia gravis is a rare disease, the potential risk of a myasthenic crisis must be taken into consideration.

CONFLICT OF INTERESTS:

The Authors declare that they have no conflict of interests.

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