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Long-term administration of immunoglobulin in a patient with anti-SRP immune-mediated necrotizing myopathy

Filipe Oliveira Pinheiro, Pedro Madureira, Maria Seabra Rato, Lúcia Costa

Department of Rheumatology, Centro Hospitalar Universitário de São João, Porto, Portugal

Dear Editor,

Idiopathic inflammatory myopathies (IIMs) are characterized by immune-mediated muscle injury [1]. Immune-mediated necrotizing myopathy (IMNM) is observed in 30% of IIM patients and is characterized by severe proximal weakness and myofiber necrosis with mild lymphocytic inflammation in muscle biopsy [1]. Autoantibodies against signal recognition particle (SRP) or HMG-CoA reductase (HMGCR) may be present [2]. Anti-signal recognition particle (SRP) antibody positive IMNM represents 18% of all IMNMs [3].

Treatment consists of systemic glucocorticosteroids in combination with a steroid-sparing agent [1]. Intravenous immunoglobulin (IVIg) is used in IIMs as a steroid-sparing agent, but prolonged treatment is limited by difficulty of administration, cost, and potential toxicity [4].

We report a case of a 55-year-old female patient, with liver cirrhosis with portal hypertension (variceal hemorrhage, portal hypertensive gastropathy and ascites), and chronic hepatitis B virus infection, admitted in 2011 due to a 2-month history of progressive proximal muscle weakness. At examination, there was evident muscle weakness (Modified Medical Research Council 3 – in neck flexors, deltoid, and biceps, 3 – in wrist extensors and flexors, 2 – in iliopsoas, and 3 – in quadriceps). Laboratory results showed elevated creatine kinase (3,072 UI/ml) and anti-SRP antibody. Thigh magnetic resonance (MR) showed edema and lipomatous atrophy of the hamstrings, adductors, and gluteal muscles bilaterally, right vastus medialis and left quadriceps femoris. A biopsy of the left quadriceps femoris muscle was performed, showing atrophied and necrotic fibers, and moderate adipose replacement; major histocompatibility complex (MHC) class I was expressed in all muscle fibers.

Diagnosis of IMNM was made and the patient received methylprednisolone pulse therapy (1,000 mg i.v. for 3 days), with improvement of muscle strength, and was discharged under therapy with prednisolone 60 mg/day. Due to concerns of hepatitis B reactivation, it was decided to start IVIg as a steroid-sparing agent. A switch from IVIg to azathioprine titrated to a dose of 100 mg/day (1.7 mg/kg) was made, but was soon suspended due to inefficacy, and the patient had to be restarted on IVIg, until remission was achieved.

After stopping IVIg, the patient presented again with worsening of proximal muscle weakness and fatigue, elevated CK (2,251 U/l), without any improvement with an increase in prednisolone to 15 mg/day. It was then decided to restart IVIg and keep IVIg as maintenance therapy, along with further prednisolone dosing to 40 mg/day with slow tapering. During past 7 years the maintenance therapy has been implemented, with a monthly course of IVIg at a dose of 1 g/kg and prednisolone at a dose of 5 mg/day. The patient presented stable CK levels and muscle strength, apart from the instances of missing an IVIg course.

There are no randomized control trials to guide treatment in IMNM, and data to choose the steroid-sparing agent in SRP-positive patients are even scarcer [1]. Additionally, long-term maintenance therapy (more than 6 months) with IVIg is limited because of the high cost and potential side effects [4].

Our case details the management of a complex patient with significant comorbidities, namely cirrhosis and chronic hepatitis B virus infection with complications of portal hypertension (variceal hemorrhage, portal hypertensive gastropathy and ascites). Cases of chronic hepatitis B reactivation have been described with rituximab and other CD20-directed therapies [5]. Despite lack of

Address for correspondence:
Filipe Oliveira Pinheiro, Department of Rheumatology, Centro Hospitalar Universitário de São João, Alameda Professor Hernâni Monteiro, 4200-319 Porto, Portugal, e-mail: filipe.pinheiro92@gmail.com

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evidence of long-term maintenance therapy benefit with IVIg in IMNM, the decision was taken to maintain IVIg due to this safety concern in an immunosuppressed patient. A trial with azathioprine was attempted, which proved to be ineffective, thereby favoring the long-term maintenance with IVIg. Due to the paucity of data and case reports of IVIg in SRP-positive IMNM patients, and because of high cost and adverse events that may be frequent, IVIg is only exceptionally used as maintenance therapy.

As few data exist to guide IVIg therapy for more than 6 months, more studies are needed to confirm its safety and efficacy.

The authors declare no conflict of interest.

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