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CLADRIBINE IN MYASTHENIA GRAVIS: A CASE URGING FOR PRUDENCE

We read with interest the recent report by Deftereos [1] suggesting patients presenting with hematologic disorders or multiple sclerosis (MS) and co-morbid myasthenia gravis (MG) could be candidates for cladribine treatment, due to cladribine's B and T cell depleting mechanism of action. We present a patient with MS associated with mild ocular MG who developed generalized MG necessitating intensive care unit (ICU) admission and ventilation 2 months after a first treatment course with cladribine.

Our index patient is a 55-year-old male. He was diagnosed with MS in 2011 after 2 relapses and compatible findings on brain and spinal cord magnetic resonance imaging (MRI) and cerebrospinal fluid. Initial treatment with interferon beta-1a was stopped seven years later due to toxic hepatitis and teriflunomide initiated after normalization of his liver tests. Due to a relapse with paraparesis, ascending paresthesias and a new gadolinium enhancing lesion at the T5 level on spinal MRI he was switched to treatment with cladribine. At the time of this relapse he also noted fatigable ptosis without diplopia. The remainder of his neurological examination was normal. Single fiber EMG of the orbicularis oculi muscle and testing for acetylcholine receptor antibodies (anti-AChR-Ab) were negative. No specific treatment for myasthenia gravis was initiated. He received a first course of 1.75 mg/kg cladribine and presented 3.5 months later with fluctuating diplopia rapidly evolving into dysarthria, dysphagia, Medical Research Council (MRC) grade 3 weakness throughout and respiratory insufficiency. He was transferred to the intensive care unit and underwent tracheal intubation. After plasma-exchange (one exchange every other day over 10 days), methylprednisolone (48 mg) and pyridostigmine (60 mg four times a day) he rapidly recovered. Hematological studies showed a lymphopenia at 540 lymphocytes/μL (normal range 1000-3000), low B cells at 73/μL (normal range 100-500), and low T cells (388/μL, lower limit of normal 500). MUSK antibodies were negative. Anti-AChR-Ab were repeated, and were now positive at 18×10^{-10} Mol (reference range 0-5 × 10^{-10} Mol), chest CT did not reveal thymic abnormalities, and brain MRI did not reveal new MS lesions. He developed a thoracic zoster infection and acute septicemia of urinary origin for which he was treated with acyclovir and antibiotics. He was discharged 3 weeks after the onset of this exacerbation on pyridostigmine 60 mg 4 times a day and methylprednisolone 32 mg daily.

A potential role for cladribine treatment in MG was recently suggested in this journal[1] in response to the article of Yi et al.[2] delineating the role of B cells in MG. However, B cell depletion by cladribine[3] is less profound with different kinetics compared to rituximab which, in usual doses, leads to complete suppression of B cell counts. A potential problem with the use of cladribine in MG is the often-long-term lymphopenia induced by this drug[4], making rescue therapy with other immunosuppressive drugs difficult. We recommend caution in treating MG patients with cladribine.

Ethical Publication Statement: We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this letter to the editor is consistent with those guidelines.

Guy Laureys, MD, PhD

Jan L. De Bleecker, MD, PhD

Department of Neurology, UZ Gent, Corneel Heymanslaan 10, 9000, Gent, Belgium

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Correspondence to Guy Laureys; e-mail guy.laureys@uzgent.be