European Journal of Case Reports in Internal Medicine

Multiple Sclerosis-Related "Spasticity-Plus Syndrome" May Benefit from Early Nabiximols Treatment

Silvia Miante, Marco Puthenparampil, Monica Margoni, Francesca Rinaldi, Paolo Gallo, Paola Perini

The Multiple Sclerosis Center, University Hospital of Padova, Padova, Italy

Conflicts of Interests: Silvia Miante reports travel grants from Novartis, Almirall, Biogen Idec, Sanofi Genzyme, Teva, outside the submitted work. Marco Puthenparampil reports grants and personal fees from Novartis, grants and personal fees from Almirall, grants and personal fees from Biogen Idec, grants and personal fees from Sanofi Genzyme, grants from Teva, outside the submitted work. He served as an advisory board member for Novartis, Biogen, and Sanofi Genzyme. Monica Margoni reports grants from Genzyme Sanofi, Merck Serono, Biogen Idec, grants and personal fees from Novartis. Francesca Rinaldi served as an advisory board member of Biogen Idec and has received funding for travel and speaker honoraria from Merck Serono, Biogen Idec, Sanofi-Aventis, Teva and Bayer Schering Pharma outside the submitted work. Paolo Gallo reports grants and personal fees from Novartis, grants and personal fees from Almirall, grants and personal fees from Biogen Idec, grants and personal fees from Sanofi Genzyme, grants and personal fees from Teva, grants and personal fees from Merck Serono, grants from University of Padova, grants from Italian Ministry of Public Health, grants from Veneto Region of Italy, grants from Italian Association for Multiple Sclerosis, outside the submitted work. Paola Perini reports grants and personal fees from Merck Serono, grants and personal fees from Biogen, grants and personal fees from Genzyme Sanofi, grants and personal fees from Teva, grants and personal fees from Bayer Schering, grants and personal fees from Novartis, outside the submitted work.

Funding: Almirall SA provided funding for the project but did not participate in the conception, writing or decisions taken.

Acknowledgements: Editorial assistance was provided by Francesca Cappellini, PhD and Aashni Shah (Polistudium SRL, Milan, Italy). This assistance was supported by Almirall.

ABSTRACT

We present the case of a 42-year-old woman affected by relapsing-remitting multiple sclerosis who presented an extensive involvement of the spinal cord during the disease course. After a trial on first-line treatment, which she discontinued due to poor compliance, she was switched to intravenous ocrelizumab 600 mg every 6 months. At 10 years from the disease onset, as a result of the extensive spinal cord involvement, she began to complain of progressive and rapid reduction in ambulatory performance due to spasticity of the right leg, instability and severe fatigability, together with overactive bladder symptoms. The early introduction of nabiximols positively impacted on the patient's symptoms and on the neurological examination, as well as on her quality of life.

KEYWORDS

Spasticity, nabiximols, multiple sclerosis, fatigues

LEARNING POINTS

- The early introduction of nabiximols may positively impact "spasticity-plus syndrome"-related symptoms.
- Treatment with nabiximols should be considered earlier in young MS patients with low disability (EDSS <4) since it can represent a comprehensive approach to a broad spectrum of symptoms.
- Nabiximols is well tolerated in young MS patients, with a reduced risk of discontinuation.

INTRODUCTION

Spasticity is a very frequent and disabling symptom of multiple sclerosis (MS), affecting approximately 60% of patients and almost all patients with a progressive form of the disease[1]. Recently, the concept of a "spasticity-plus syndrome" has been defined to include all of the spasticity-related clinical manifestations that share common features and possibly an inclusive therapeutic approach[2]. Nabiximols treatment is safe, effective and well tolerated and it could be considered early in the disease course.

CASE DESCRIPTION

We present the case of a 42-year-old woman with relapsing-remitting MS who experienced inferior limb spasticity early in the disease course. The first clinical manifestation of MS was in 2010, when the patient presented right retrobulbar optic neuritis. She underwent brain MRI, which showed multiple inflammatory lesions disseminated in space suggestive of MS; cervical MRI disclosed an inflammatory lesion at the C2–C3 level (*Figs. 1 and 2*). Lumbar puncture revealed the presence of IgG oligoclonal bands in the cerebrospinal fluid. MS was diagnosed and the patient was started on glatiramer acetate, which was stopped after a few months due to a cutaneous reaction. The patient was therefore switched to IFN-β1a (Avonex). After 3 years, in a setting of clinical and neuroradiological stability, she decided to interrupt the treatment. In April 2014, the patient developed a spinal relapse characterized by weakness in the right leg, Lhermitte's sign, paraesthesia and allodynia of the trunk with D10 level. She was treated with high-dose steroids for 5 days with regression of symptoms and Avonex was restarted. In 2016, the patient started to complain of motor fatigability and a reduced performance in walking, still possible for more than 1 km (Expanded Disability Status Scale; EDSS 2.0). Over the following years she experienced a progressive worsening in ambulatory performance

DOI: 10.12890/2021_V8Sup2

DISCUSSION

Spasticity-related symptoms in young MS patients can determine long-standing disability and can have a great impact on the patient's quality of life. In a recent paper, a group of authors proposed the term "spasticity-plus syndrome" to define a new and broad concept which encompasses a cluster of symptoms sharing a common aetiology and possibly a common therapeutic approach. Spasticity and other related symptoms, namely gait disturbances, fatigue, pain, ataxia, overactive bladder, sleep and mood disorders, may all be considered as a whole, and thus, be managed with the same therapeutic approach[2]. Here, we report a real-life case of a young MS patient who developed a broad spectrum of symptoms (right leg stiffness, instability, fatigue, overactive bladder symptoms) well comprised within a "spasticity-plus syndrome", which presented early in the disease with great impact on the patient's quality of life. The early introduction of nabiximols allowed the initiation of comprehensive treatment of the patient's symptoms. This was confirmed by the noteworthy improvement both in EDSS and FSS scores. A recent Italian study retrospectively evaluated a group of MS patients treated with nabiximols in order to analyze predictors of sustained treatment persistence over long-term follow-up[3]. Carotenuto et al. found that EDSS >4 and cognitive impairment predicted treatment discontinuation at follow-up and suggested that nabiximols should be started earlier in the disease course. Our case confirms that the introduction of nabiximols in younger patients with low disability (EDSS >4) is effective and well tolerated, with a reduced risk of discontinuation. We therefore agree that nabiximols should be considered early in the disease course, since it can contribute to improving the quality of life in young MS patients.

REFERENCES

1. Whiting PF, Wolff RF, Deshpande S, di Nisio M, Duffy S, Hernandez AV, et al. Cannabinoids for medical use: a systematic review and meta-analysis. *JAMA* 2015;**313**(24):2456–2473.
2. Fernández Ó, Costa-Frossard L, Martínez-Ginés M, Montero P, Prieto JM, Ramió L. The broad concept of "spasticity-plus syndrome" in multiple sclerosis: a possible new concept in the management of multiple sclerosis symptoms. *Front Neurol* 2020;**11**:152.
3. Carotenuto A, Costabile T, De Lucia M, Moccia M, Falco F, Petruzzo M, et al. Predictors of nabiximols (Sativex®) discontinuation over long-term follow-up: a real-life study. *J Neurol* 2020;**267**:1737–1743.

DOI: 10.12890/2021_V8Sup2