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Case report

A clinical improvement of a idiopathic cervical dystonia in a patient treated with transdermal Rotigotine: a case-report

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Summary. Dystonia is the third most common movement disorder. Cervical dystonia is the most common form of dystonia, a subtype of Primary Focal Dystonia due to the phasic and/or tonic involuntary contractions of different combinations of neck muscles, generally treated with good clinical results with botulin toxin type A or B injection. The etiology of cervical dystonia is still unknown. It was recently proposed that the cervical dystonia is due to malfunctioning of the head neural integrator, that result of impairment in cerebellar, basal ganglia, or proprioceptive feedback. The hypothesis of the existence of an electrical circuit that connects the basal ganglia with the cerebellum and the proprioception feedback, participating in the neural integrator of the head, explains that the damage at any point of the network can lead to motor deficits. Although dystonia is often associated with abnormal dopamine neurotransmission, dopaminergic drugs are not currently used to treat dystonia because there is a general view that they are ineffective. The results from the clinical trials and tests in mice suggest that the coactivation of D1 and D2 dopamine receptors may be an effective therapeutic strategy in some patients. These results support the assumption that dopamine receptors could be considered as targets for treating dystonia. Furthermore, a dopamine agonist-response dystonia in patients with an autosomal recessive L-amino acid decarboxylase deficiency, has been described in the scientific literature. We report a case of focal cervical dystonia successful treated with a dopamine agonist (D3>D2>D1) Rotigotine, a transdermal drug that induces a continuous dopaminergic stimulation. (www.actabiomedica.it)

Key words: cervical dystonia, dopamine, Rotigotine

Introduction

Dystonia is the third most common movement disorder. Cervical dystonia is the most common form of dystonia, a subtype of Primary Focal Dystonia due to the phasic and/or tonic involuntary contractions of different combinations of neck muscles, generally treated with good clinical results with botulin toxin type A or B injection.

The etiology of cervical dystonia is still unknown. It was recently proposed that the cervical dystonia is due to malfunctioning of the head neural integrator, that result of impairment in cerebellar, basal ganglia, or proprioceptive feedback (1).

The hypothesis of the existence of an electrical circuit that connects the basal ganglia with the cerebellum and the proprioception feedback, participating in the neural integrator of the head, explains that the damage at any point of the network can lead to motor deficits.

Although dystonia is often associated with abnormal dopamine neurotransmission, dopaminergic drugs are not currently used to treat dystonia because there is a general view that they are ineffective (2). The results from the clinical trials and tests in mice suggest that the coactivation of D1 and D2 dopamine receptors may be an effective therapeutic strategy in some patients. These results support the assumption that

dopamine receptors could be considered as targets for treating dystonia. Furthermore, a dopamine agonist-response dystonia in patients with an autosomal recessive L-amino acid decarboxylase deficiency, has been described in the scientific literature (3, 4).

We report a case of focal cervical dystonia successful treated with a dopamine agonist (D3>D2>D1) Rotigotine, a transdermal drug that induces a continuous dopaminergic stimulation (5).

Case-report

We report a case of 67 old woman with a forced involuntary and painful contraction of left neck muscles combined with dystonic tremor (Fig. 1). Patient complained also an anxiety depression with insomnia (Beck's Depression Inventory [BDI]=19). Brain MRI, showed no abnormalities. The neck and shoulder muscles RMI showed hypertrophy of the left sternocleidomastoid muscle, compared with the contralateral, without macrostructural alterations or pathological impregnation of gadolinium in the muscle fibers (Fig. 2). The needle EMG argued a typical pattern of co-contraction of agonists and antagonists left neck muscles.

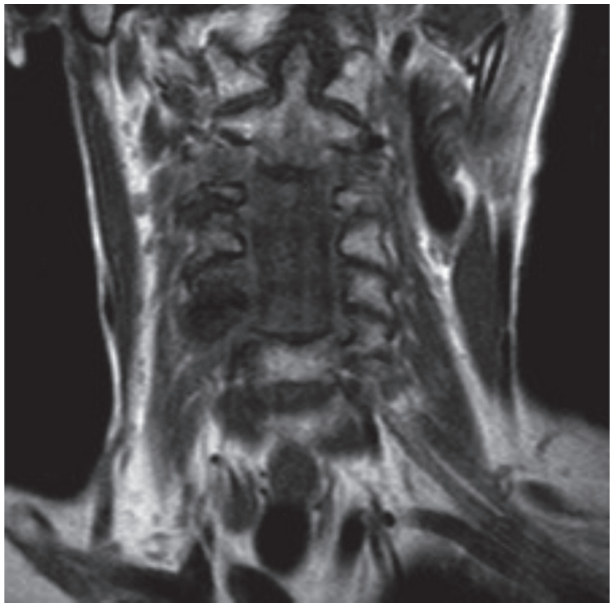

Figure 1.

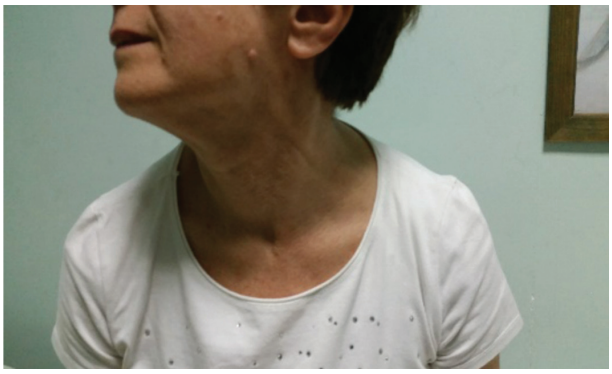

Figure 2.

As the patient had botulinum toxin injection treatment contraindications due to adverse effects development, the first-line treatment was transdermal Rotigotine slowly increased until 8 mg/24 h. After 3 weeks of treatment with transdermal Rotigotine (6 mg/24 h), already both painful sensation at the right neck and depression symptoms were improved. After 5 weeks of treatment with transdermal Rotigotine (8 mg/24 h), we observed a reduction of involuntary contraction on the left sternocleidomastoid muscle and the BDI score was 12. After 6 months follow-up during treatment with Rotigotine (8 mg/24 h), the patient had almost complete resolution of the symptoms (Fig. 3).

Currently, after about 3 years, the patient is well and continues the pharmacological treatment with Rotigotina with significant clinical-therapeutic efficacy. The symptom that would seem to respond less to treatment is the dystonic tremor.

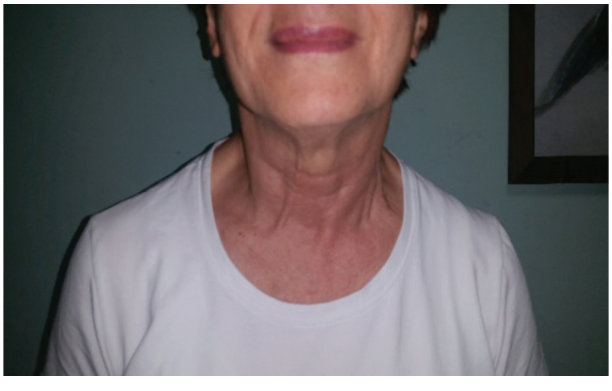

Figure 3.

Conclusion

Cervical dystonia is a common movement disorder with unknown etiology, generally treated with good clinical results with botulin toxin type A or B injection. The side effects related to botulin toxin treatment are generally mild (pain or hematoma at the injection site, fever, skin reaction) and reversible. However, some contraindications such as the use of anticoagulants, the presence of underlying muscular pathologies, or the development of systemic side effects (generalized asthenia, paralysis of the facial nerve, paresthesia, etc.) limit its use in the general population. Moreover, in some patients treated with botulinum toxin type A or B, secondary therapy failure occurs and one of the main causes is the formation of antibodies against A/B T (6).

In this way, since the dopamine agonist-response dystonia (an inherited autosomal recessive disease caused by L-amino acid decarboxylase deficiency) has been described and as rotigotine is a high-potency agonist at human dopamine D1, D2, D3 receptors and a lower-potency agonist at D4 and D5 receptors, we successfully treated our patient with this drug whereby we suggest a wider clinical application of this innovative agonist receptors drug in treatment of cervical idiopathic dystonia.

Although dopaminergic drugs are not currently used to treat dystonia because there is a general view that they are ineffective, the scientific evidence on animal models and clinical experience on humans shows the opposite.

Furthermore, the most modern scientific theories according to which the pathogenetic mechanism of dystonia depends on an alteration of the dopaminergic network, encourages the possibility of successfully using a drug that acts on dopaminergic circuits, particularly improving the D1-D2 interaction at the basal ganglia.

Based on the positive clinical results obtained on this patient affected from idiopathic cervical dystonia treated with Rotigotine, we think that this dopamine agonist, due to its broad receptor profile, can be a valid therapeutic alternative in idiopathic dystonic forms in which botulinum toxin injection is contraindicated or is not very effective following the development of specific autoantibodies or side effects.

Finally, the dopaminergic receptor stimulation induced by Rotigotine, as documented on our patient, gives a natural antidepressant effect. In our opinion, this last clinical data should be taken into consideration as a starting point for future studies in the first-line therapeutic choice in dystonic patients with anxious-depressive syndrome comorbidity.

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

References

1. Sedov A, Usova S, Semenova U, Gamaleya A, Tomskiy A, Crawford JD, Corneil B, Jinnah HA, Shaikh AG. The role of pallidum in the neural integrator model of cervical dystonia. Neurobiol Dis 2019 Jan22; 125: 45-54.
2. Fan X, Donsante Y, Jinnah HA, Hess EJ. Dopamine Receptor Agonist Treatment of Idiopathic Dystonia: A Reappraisal in Humans and Mice. J Pharmacol Exp Ther 2018 Apr; 365(1): 20-26.
3. Mastrangelo M, Caputi C, Galosi S, Giannini MT, Leuzzi V. Transdermal rotigotine in the treatment of aromatic L-amino acid decarboxylase deficiency Mov Disord 2013 Apr; 28(4): 556-7.
4. Wassenberg T, et al Consensus guideline for the diagnosis and treatment of aromatic l-amino acid decarboxylase (AADC) deficiency. Orphanet J Rare Dis 2017 Jan 18; 12(1)
5. Wood M, Dubois V, Scheller D, Gillard MBr Rotigotine is a potent agonist at dopamine D1 receptors as well as at dopamine D2 and D3 receptors J Pharmacol 2015 Feb; 172(4): 1124-35
6. Dressler D. Clinical Features of Antibody-Induced Complete Secondary Failure of Botulinum Toxin Therapy Eur Neurol 2002; 48:26–29

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