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CASE REPORT

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Erectile dysfunction and reduced libido in a myasthenia gravis patient treated with methotrexate

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Abstract

Patients with myasthenia gravis treated with methotrexate are usually young and sexually active. Therefore, sexual dysfunction associated with MTX treatment should be considered and specifically searched in them as it can be an under-recognized cause of treatment failure or poor compliance

KEYWORDS

methotrexate, myasthenia gravis, sexual dysfunction

1 | INTRODUCTION

Reduced libido and erectile dysfunction are rare adverse effects of methotrexate. Patients with myasthenia gravis treated with methotrexate are usually young and sexually active. Therefore, sexual dysfunction associated with methotrexate treatment should be considered in myasthenic patients as it can be an under-recognized cause of treatment failure.

Methotrexate (MTX) is a folate antimetabolite, irreversibly binding and inhibiting dihydrofolate reductase, leading to inhibition of DNA synthesis, repair, and replication. It is often used in the treatment of neuromuscular diseases, considered as a first-line steroid-sparing agent in idiopathic inflammatory myopathies [1] and as a steroid-sparing agent in patients with generalized myasthenia gravis (MG) who have not tolerated or responded to other medications.[2] Commonest side effects include nausea, fatigue, dizziness, stomatitis, and abdominal pain, while serious adverse effects include hepatotoxicity, pulmonary toxicity, nephrotoxicity, and myelosuppression. Sexual dysfunction is a rare adverse effect of MTX therapy reported to date in patients with psoriasis and/or arthritis.[3-6]

2 | CASE REPORT

This 54-year-old man was evaluated for a poorly controlled MG. His first symptoms appeared at the age of 34 years with dysphagia, head drop, and generalized weakness, and five years later, he was operated for an underlying thymoma. Upon examination, he showed diplopia at all gaze fields, asymmetric blepharoptosis, dysphagia, and proximal upper and lower extremities fixed muscle weakness, graded at 4/5 at the MRC scale. At that time, he was treated with high-dose steroids (40 mg prednizolone qd) and pyridostigmine (120 mg qid). Therapeutic trials with azathioprine and mycophenolate mofetil were deemed unsuccessful due to poor tolerance and adverse effects. A therapeutic trial with methotrexate at a dose of 22.5 mg/wk was initiated, and 4 months later, his presenting symptomatology (Myasthenia Gravis Foundation of America class IIIb, MG activities of daily living [MG-ADL] score 5) resolved and he reached pharmacological remission (MG-ADL score at 0), with adjunctive low-dose prednizolone (5 mg/d) and no need for the use of a cholinesterase inhibitor. At the 6-month follow-up visit, the patient reported that he voluntarily stopped MTX treatment

despite the observed beneficial effect on his MG. He was reluctant to say the reason for this treatment discontinuation, but when explicitly asked, he reported that he experienced erectile dysfunction and reduced libido, 4 weeks following MTX initiation. Despite reaching pharmacological remission under MTX treatment, he chose to discontinue the drug for this reason. His sexual dysfunction resolved within 4 weeks, but three months later, his myasthenic symptomatology reappeared (Myasthenia Gravis Foundation of America class IIIb) and he was once again, placed on high-dose prednisolone (40 mg/d) and adjunctive cholinesterase inhibitor treatment. A thorough urological evaluation was performed and averred normal. Due to the optimal response the patient had on methotrexate treatment, he was re-challenged at a lower dose of 15 mg/week. After a 2-month treatment trial, he reports no sexual dysfunction, but unfortunately, the response of his myasthenic symptomatology is poor with the need of high daily corticosteroid dose.

3 | DISCUSSION

Reduced libido and erectile dysfunction are rare adverse effects of MTX treatment probably related to pituitary dysfunction and reduced nitric oxide production and activity on smooth vascular muscle cells.[6] Patients may be reluctant to report sexual dysfunction to their doctor and, vice versa, doctors often fail to recognize such an adverse effect, as they only seldom discuss about sexual activity of their patients on consultation, so the actual prevalence may be underestimated. As in the present case, it has been reported that decreased MTX doses may lead to improvement of sexual dysfunction, but unfortunately, this comes with a sub-optimal treatment effect.[4] Patients treated with MTX for MG or other neuromuscular diseases are young and sexually active, and therefore, normal sexual function is important to them. Sexual dysfunction associated with MTX treatment should be considered and specifically searched in neuromuscular patients since it can be an under-recognized cause of treatment failure or poor compliance.

CONFLICT OF INTEREST

None of the authors has any conflict of interest to disclose.

AUTHOR CONTRIBUTIONS

CP: wrote the initial draft, collected and interpreted patient's data, reviewed the literature, critically revised the manuscript for important intellectual content, and approved the final version. GKP: reviewed the literature, critically revised the manuscript for important intellectual content, and approved the final version.

ETHICAL PUBLICATION STATEMENT

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

DATA AVAILABILITY STATEMENT

All data relevant to the study are included in the article.

REFERENCES

1. Oddis CV, Aggarwal R. Treatment in myositis. *Nat Rev Rheumatol*. 2018;14(5):279-289. https://doi.org/10.1038/nrrheum.2018.42
2. Narayanaswami P, Sanders DB, Wolfe G, et al. International Consensus guidance for management of myasthenia gravis: 2020 Update. *Neurology*. 2021;96(3):114-122. https://doi.org/10.1212/WNL.0000000000011124
3. Aguirre MA, Vélez A, Romero M, Collantes E. Gynecomastia and sexual impotence associated with methotrexate treatment. *J Rheumatol*. 2002;29(8):1793-1794.
4. Blackburn WD Jr, Alarcón GS. Impotence in three rheumatoid arthritis patients treated with methotrexate. *Arthritis Rheum*. 1989;32(10):1341-1342. https://doi.org/10.1002/anr.1780321029
5. Theodosiou G, Svensson Å. Methotrexate-associated sexual dysfunction: two case reports. *Acta Derm Venereol*. 2017;97(9):1132-1133. https://doi.org/10.2340/00015555-2714
6. Wylie G, Evans CD, Gupta G. Reduced libido and erectile dysfunction: rarely reported side-effects of methotrexate. *Clin Exp Dermatol*. 2009;34(7):e234. https://doi.org/10.1111/j.1365-2230.2008.03082.x

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