SHORT COMMUNICATION

Methotrexate-associated Sexual Dysfunction: Two Case Reports

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Methotrexate (MTX) is a potent competitive inhibitor of the enzyme dihydrofolate reductase. MTX is widely used in dermatology practice for psoriasis and many other conditions, including bullous disorders, autoimmune connective tissue diseases, pityriasis rubra pilaris (PRP), sarcoidosis, and miscellaneous other dermatoses.

The most common adverse effects of MTX include nausea, fatigue, dizziness, headache, stomatitis and abdominal pain. Serious adverse effects include hepatotoxicity, pulmonary toxicity, nephrotoxicity, myelosuppression and increased risk of lymphoproliferative disorders.

We report here 2 cases of sexual dysfunction during MTX therapy. To the best of our knowledge, there have been only 2 cases in the literature of this rare side-effect in patients with psoriasis treated with MTX (1). There are also some reports of sexual dysfunction in patients treated with MTX for rheumatological conditions (2–4).

CASE REPORTS

Patient 1

A 58-year-old man with a 32-year history of plaque psoriasis was started on a regimen of oral MTX at a weekly dosage of 12.5 mg and folic acid supplement. The patient was otherwise healthy and took no other medications. At the follow-up visit the patient reported that the drug was generally well tolerated. However, 2 weeks after the initiation of treatment the patient began to experience reduced libido and difficulty in obtaining an erection. His treatment was switched to acitretin and, within 4 weeks, complete resolution of the sexual dysfunction was reported.

Patient 2

A 68-year-old man with psoriasis vulgaris, previously treated with narrow-band ultraviolet B (UVB) phototherapy and acitretin, was started on weekly oral MTX 12.5 mg and folic acid 5 mg. The patient had hypertension and diabetes mellitus type 2 and was on losartan and metformin. At follow-up 6 months later, the patient reported loss of libido and erectile dysfunction. The symptoms were noticed 3 weeks after the initiation of treatment. On account of the excellent response to MTX, the patient chose not to discontinue the treatment. Four months later, however, treatment was discontinued due to elevated liver function tests. The patient reported that his sexual dysfunction resolved within 3 weeks on discontinuation of MTX.

Neither of these patients had history of depression or had previously experienced reduced libido or difficulty in obtaining an erection. No signs of depression had been assessed at the initial or follow-up visits.

DISCUSSION

These 2 patients reported onset of sexual dysfunction only a few weeks after initiation of MTX and resolution of the symptoms within 3–4 weeks after discontinuation of the drug, in agreement with the cases reported by Wylie et al. (1). A case of MTX-associated sexual dysfunction has been reported in a patient with erythroderma treated with MTX, where impotence was noticed 9 months after the initiation of the treatment and subsided 2 weeks after discontinuation of MTX. Re-administration of MTX elicited the same symptom 2 months later (5).

The exact mechanism of this adverse effect of MTX remains unknown. It has been assumed that impaired pituitary function, as result of interleukin-1 blockage, as well as an inhibitory effect on the production of nitric oxide by MTX, that leads to reduced activity against vascular smooth muscle, may play a role (1). This type of adverse effect may also be idiosyncratic.

Although reduced libido and impotence are rare side-effects of MTX according to the manufacturers, MTX-associated sexual dysfunction is seldom mentioned in textbooks and rarely reported in the literature. The detection of drug-induced adverse sexual effects is challenging; patients are often reluctant to report sexual dysfunction and there are often several overlapping aetiologies, including cardiovascular disorders, depression or mood disorders. We assume, therefore, that MTX-associated sexual dysfunction may be under-reported.

We report here 2 cases of MTX-induced sexual dysfunction in order to raise the awareness of this adverse effect. Taking into consideration that patients with psoriasis have a higher risk of sexual dysfunction irrespective of treatment, compared with the general population. It is important to make a careful assessment of sexual function both at the initial and follow-up visits (1, 6–9).

The authors declare no conflicts of interest.

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