



LETTER TO THE EDITOR

Methotrexate-associated sexual dysfunction in a female patient with rheumatoid arthritis

Romatoid artritli bir kadın hastada metotreksat kullanımına bağlı cinsel işlev bozukluğu

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To the Editor,

Rheumatoid arthritis (RA) is the most common chronic rheumatologic disease and requires lifelong treatment. RA typically affects the joints, but it can also affect physical, psychological, and sex lives of patients¹. Although RA treatment improves patient quality of life, it can cause sexual problems².

A 39-year-old woman was referred to our hospital. Her main complaints were arthralgia and morning stiffness. At the first visit to our hospital, her height and weight were 160 cm and 62 kg. Her blood pressure, pulse rate, and body temperature were 110/70 mmHg, 72 bpm, and 36.5 °C, respectively. She had tender and swollen metacarpophalangeal and proximal phalangeal joints in the hands. The laboratory findings were as follows: white blood cell count 11000/ μ L, hemoglobin 12.5 g/dL, platelet count 280 000/ μ L, erythrocyte sedimentation rate 40 mm/h, and CRP 30 mg/L (normal range: 0-8). Renal, liver, and thyroid functions were within the normal ranges. Tests for antinuclear antibodies (ANA) and extractable nuclear antigen antibodies were negative. Rheumatoid factor level was 50 IU/mL (normal range: 0-20) and anticyclic citrullinated peptide antibodies were positive. She was diagnosed with rheumatoid arthritis and was started on a regimen of oral MTX at a weekly dosage of 15 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, 4 weeks after the initiation of treatment, the patient began to experience sexual reluctance. The patient consulted with a gynecologist and gynecologic examination was normal. Estrogen and prolactin levels were in normal ranges. Therefore, endocrine causes of sexual problems were ruled out. Her treatment was switched to leflunomide, and within 3 weeks, complete resolution of sexual dysfunction was reported by the patient.

RA is a chronic inflammatory disease and requires long-term treatment. RA medication may cause sexual dysfunction in this patient group³. RA can influence sexual function due to several reasons including pain, joint stiffness and swelling, chronic fatigue, and limitations in activities of daily living⁴. Many women experience problems with sexual function at some point in their lives, and it is estimated that 40% of women in the United States have sexual complaints⁵. Sexual dysfunction prevalence is around 18.4–30% in men and around 25.8–67% in women with RA⁶. Comorbid disease such as diabetes, hormonal disorders and adverse effects of medication, especially with polypharmacy, can also influence patient sexual health⁶.

Methotrexate (MTX) is a potent competitive inhibitor of the enzyme dihydrofolate reductase. MTX is widely used in rheumatology practice for rheumatoid arthritis and many other conditions, including psoriatic arthritis, autoimmune connective tissue diseases, sarcoidosis, and vasculitis. The most

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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 one case of sexual dysfunction during MTX therapy. The exact mechanism of sexual dysfunction as an adverse effect of MTX remains unknown. It was 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, which leads to reduced activity of vascular smooth muscle, may play roles in this effect⁷.

Many sexual dysfunction cases were reported with methotrexate therapy. In our review of the literature, Warren firstly reported sexual dysfunction in three male rheumatoid arthritis patients treated with MTX⁸. Penninga et al. reported sexual dysfunction in a patient with erythroderma treated with MTX⁹. In this case, impotence was noticed 9 months after medical therapy and resolved 2 weeks after discontinuation of MTX. Theodosiou et al. reported sexual dysfunction in two patients with psoriasis treated with MTX¹⁰. These 2 patients reported onset of reduced libido and erectile dysfunction only a few weeks after initiation of MTX. MTX-associated sexual dysfunction was reported in men. All patient symptoms included reduced libido and erectile dysfunction. Our patient was female and shared her experience of sexual reluctance with us. Her treatment was switched to leflunomide and complete resolution of sexual dysfunction was reported by patient.

In conclusion, sexual dysfunction is a problem in both women and men with RA. It is also possible that medication causes sexual problems. As a number of cases of MTX-associated sexual dysfunction have been reported, it will be possible to obtain more detailed information on this issue. Our case report may help to increase awareness about this issue among physicians and patients. Physicians should proactively inquire about sexual health in patients on MTX and consider potential reversible adverse effects of the medication.

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REFERENCES

1. Santos-Moreno P, Castro CA, Villarreal L, Buitrago D. Prevalence of sexual disorders in patients with rheumatoid arthritis and associated factors. *Sex Med.* 2020;8:510–6.
2. El Miedany Y, El Gaafary M, El Arousy N, Youssef S, Ahmed I. Sexual dysfunction in rheumatoid arthritis patients: arthritis and beyond. *Clin Rheumatol.* 2012;31:601–6.
3. Santos-Moreno P, Villarreal L, Ballesteros G, Bello J, Castillo E, Giraldo R et al. Presence of psychological, sexual and sleep disorders in patients with rheumatoid arthritis. *Ann Rheum Dis.* 2016;75:712.
4. Tristano AG. Impact of rheumatoid arthritis on sexual function. *World J Orthop.* 2014;5:107–11.
5. Goldstein I, Clayton AH, Goldstein AT, Kim NN, Kingsberg SA. *Textbook of Female Sexual Function and Dysfunction: Diagnosis and Treatment.* Chichester, Wiley, 2018.
6. Zhao S, Li E, Wang J, Luo L, Luo J, Zhao Z. Rheumatoid arthritis and risk of sexual dysfunction: a systematic review and meta-analysis. *J Rheumatol.* 2018;45:1375–82.
7. Wylie G, Evans D, Gupta G. Reduced libido and erectile dysfunction: rarely reported side-effects of methotrexate. *Clin Exp Dermatol.* 2009;34:234.
8. Blackburn WD Jr, Alarcón GS. Impotence in three rheumatoid arthritis patients treated with methotrexate. *Arthritis Rheum.* 1989;32:1341–2.
9. Penninga EI, Larsen HK, Andersen SE. Impotence caused by methotrexate treatment. *Ugeskr Laeger.* 2008;170:354.
10. Theodosiou G, Svensson Å. Methotrexate-associated sexual dysfunction: two case reports. *Acta Derm Venereol.* 2017;97:1132–33.