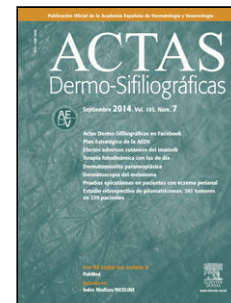


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[[Translated article]]Methotrexate-Induced Gouty Arthritis in Psoriatic Patient

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Carta científico-clínica

Artritis gotosa inducida por metotrexato en un paciente con psoriasis

[[Translated article]]Methotrexate-Induced Gouty Arthritis in Psoriatic Patient

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To the Editor,

Methotrexate (MTX) is a dihydrofolate reductase-inhibiting antimetabolite widely used to treat moderate-severe psoriasis.¹ Owing to its mechanism of action, it can precipitate acute gout flares; although this adverse effect was described long ago,² it is likely underreported given the high prevalence of gout in the general population (2.4% in Spain).³

A 70-year-old man with untreated gout and hyperuricemia and a 30-year history of plaque psoriasis, managed with topical corticosteroids and without a history of psoriatic arthritis, presented with a severe psoriasis flare (PASI 20, BSA 47%). Subcutaneous MTX 15 mg weekly was started. Two months later he presented to the emergency department with arthritis of the right first metatarsophalangeal joint. Given the gout history, a normal radiograph, and a serum urate of 8.1 mg/dL (normal \leq 6.8 mg/dL), the episode was diagnosed as podagra. At dermatology follow-up, MTX was stopped and phototherapy (UVB) initiated. Because psoriasis improved only modestly, subcutaneous MTX was reintroduced at 12.5 mg weekly after 3 months; 15 days later he experienced another gout attack. As this was the second episode after starting MTX, it was

discontinued permanently. The patient's psoriasis is now well controlled on acitretin 25 mg three times per week, with no new gout attacks after 1 year of follow-up.

Gout is a chronic inflammatory arthropathy due to intra-articular deposition of monosodium urate crystals in certain hyperuricemic patients.⁴ It presents with recurrent arthritis flares, most often involving the first metatarsophalangeal joint.⁴ Gout attacks can be precipitated by many factors (drugs, infections, alcohol, fasting, specific foods, physical trauma, etc.) as serum urate levels change—either increase or decrease—and via a synergistic proinflammatory effect of monosodium urate crystals with saturated fatty acids such as stearic acid, activating Toll-like receptor 2 and inducing interleukin-1 β release.⁵

Patients with psoriasis have an increased risk of hyperuricemia and gout.^{6,7} This is partly attributable to the chronic systemic inflammation underlying psoriasis, with involvement of inflammatory pathways shared with gouty arthritis, notably type 1 and type 17 (Th1/Th17) lymphocyte-mediated pathways.⁷ In addition, the high keratinocyte turnover in psoriasis increases urate production from purine metabolism, leading to secondary hyperuricemia.^{2,7,8}

The risk of gout appears even higher in patients with psoriatic arthritis, especially in middle-aged adults (31–50 years).⁷ Monosodium urate crystals are more frequently found in synovial fluid from patients with psoriatic arthritis.⁹ Serum urate levels also correlate with psoriasis severity, and psoriasis treatment seems to reduce them.^{7,10} Consequently, arthritis in patients with psoriasis and hyperuricemia may raise a differential diagnosis between gouty arthritis and psoriatic arthritis, whose main distinguishing features are summarized in Table 1.

Patients with gout have a higher risk of metabolic syndrome and cardiovascular disease.⁷ The high prevalence of hyperuricemia and gout among patients with psoriasis may contribute to the well-known metabolic and cardiovascular comorbidities in psoriasis, although a causal relationship has not been established.⁷

MTX has been used safely in patients with gout. In a recent clinical trial,¹¹ the safety and efficacy profile of MTX in patients with refractory gout treated with pegloticase were evaluated. The MTX–pegloticase group achieved a higher urate response rate than the pegloticase-only group, without significant differences in the number of gout flares. However, MTX can alter serum urate via several mechanisms: inhibition of purine synthesis through dihydrofolate reductase; anti-inflammatory effects mediated by adenosine release and inhibition of T-cell proliferation; and modification of renal excretion.^{2,8,12} However, MTX-induced changes in urate levels may trigger gout episodes in predisposed patients, as in our case.

Some authors have suggested prophylactic colchicine before initiating MTX,² although clinical guidelines provide no specific recommendations. In our view, preventive therapy is not necessary, but a history of gout should be considered to anticipate possible attacks or to enable early intervention should one occur.

In conclusion, we report a patient with MTX-triggered gouty arthritis, to our knowledge the second such case described in the literature. Dermatologists should be aware of this potential adverse effect and suspect it when a plausible temporal relationship exists between a gout flare and MTX initiation. Although MTX was withdrawn in our case per patient preference, the preferred approach is to treat the gout—i.e., anti-inflammatory therapy for the flare and,

especially, urate-lowering therapy—and MTX discontinuation is not necessarily required to prevent further gouty arthritis episodes.

Conflicts of interest

None declared.

References

1. Puig L. Methotrexate: New therapeutic approaches. *Actas Dermosifiliogr*. 2014;105(6):583-589. doi:10.1016/j.ad.2012.11.017
2. Martin JH. Methotrexate in Psoriasis. *Arch Dermatol*. 1967;96(4):431. doi:10.1001/archderm.1967.01610040081015
3. Bustabad S, Díaz-González F. Estudio EPISER 2016. El porqué de un nuevo estudio epidemiológico. *Reumatol Clin*. 2017;13(1):1-3. doi:10.1016/j.reuma.2017.01.003
4. Dalbeth N, Merriman TR, Stamp LK. Gout. *Lancet*. 2016;388(10055):2039-2052. doi:10.1016/S0140-6736(16)00346-9
5. Joosten LAB, Netea MG, Mylona E, et al. Engagement of fatty acids with Toll-like receptor 2 drives interleukin-1 β production via the ASC/caspase 1 pathway in monosodium urate monohydrate crystal-induced gouty arthritis. *Arthritis Rheum*. 2010;62(11):3237-3248. doi:10.1002/art.27667
6. Merola JF, Wu S, Han J, Choi HK, Qureshi AA. Psoriasis, psoriatic arthritis and risk of gout in US men and women. *Ann Rheum Dis*. 2015;74(8):1495-1500. doi:10.1136/annrheumdis-2014-205212
7. Hu SCS, Lin CL, Tu HP. Association between psoriasis, psoriatic arthritis and gout: a nationwide population-based study. *Journal of the European Academy of Dermatology and Venereology*. 2019;33(3):560-567. doi:10.1111/jdv.15290
8. Smoleńska Ż, Kaznowska Z, Zarówny D, Simmonds HA, Smoleński RT. Effect of methotrexate on blood purine and pyrimidine levels in patients with rheumatoid arthritis. *Rheumatology*. 1999;38(10):997-1002. doi:10.1093/rheumatology/38.10.997
9. Oliviero F, Scanu A, Galozzi P, et al. Prevalence of calcium pyrophosphate and monosodium urate crystals in synovial fluid of patients with previously diagnosed joint diseases. *Joint Bone Spine*. 2013;80(3):287-290. doi:10.1016/j.jbspin.2012.08.006
10. Isha, Jain VK, Lal H. C-reactive protein and uric Acid levels in patients with psoriasis. *Indian J Clin Biochem*. 2011;26(3):309-311. doi:10.1007/s12291-011-0132-4
11. Botson JK, Saag K, Peterson J, et al. A Randomized, Placebo-Controlled Study of Methotrexate to Increase Response Rates in Patients with Uncontrolled Gout Receiving Pegloticase: Primary Efficacy and Safety Findings. *Arthritis and Rheumatology*. 2023;75(2):293-304. doi:10.1002/art.42335

12. Lee JJ, Bykerk VP, Dresser GK, et al. Reduction in Serum Uric Acid May Be Related to Methotrexate Efficacy in Early Rheumatoid Arthritis: Data from the Canadian Early Arthritis Cohort (CATCH). *Clin Med Insights Arthritis Musculoskelet Disord*. 2016;9:37-43. doi:10.4137/CMAMD.S38092
13. Gladman DD. Clinical, radiological, and functional assessment in psoriatic arthritis: is it different from other inflammatory joint diseases? *Ann Rheum Dis*. 2006;65(suppl_3):iii22-iii24. doi:10.1136/ard.2006.058453

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Table 1. Differential clinical and radiologic findings between psoriatic arthritis and gouty arthritis

| | Gouty arthritis | Psoriatic arthritis |
|--|---|--|
| Distal interphalangeal joint involvement | Occasional | Very common (characteristic) |
| Axial involvement | Rare | Common |
| Dactylitis | Rare | Common |
| Enthesitis | Uncommon | Common |
| Nail disease | No | Common |
| Ankylosis | Rare | Common (characteristic) |
| Periostitis | Uncommon | Common |
| Symmetry | Uncommon | Occasional |
| Erosions | Rare; sclerotic overhanging edge erosions | Common: marginal and paramarginal erosions in the proximal phalanx; marginal "mouse-ear" periostitis at the distal interphalangeal joint |

Source: Adapted from Gladman¹³.



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