An ulcerating skin tumour in a patient with rheumatoid arthritis

Schenning, L.C.M.; Ottevanger, R.; Quint, K.D.; Tas, S.W.

An ulcerating skin tumour in a patient with rheumatoid arthritis

Laura C M Schenning ,[1] Rosanne Ottevanger,[2] Koen D Quint,[2] Sander W Tas[1]

Handling editor Josef S Smolen

[1]Department of Rheumatology and Clinical Immunology, Amsterdam Rheumatology and immunology Center, Amsterdam University Medical Centres, Amsterdam, North Holland, Netherlands
[2]Department of Dermatology, Leiden University Medical Center, Leiden, South Holland, Netherlands

Correspondence to
Dr Sander W Tas, Department of Rheumatology and Clinical Immunology, Amsterdam Rheumatology and immunology Center, Amsterdam University Medical Centres, Amsterdam, Noord-Holland, Netherlands; S.W.Tas@amsterdamumc.nl

Received 18 December 2023
Accepted 27 January 2024

To cite: Schenning LCM, Ottevanger R, Quint KD, *et al*. *Ann Rheum Dis* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/ard-2023-225436

A 78-year-old white woman was diagnosed in 2010 with IgM-rheumatoid factor negative, anticyclic citrullinated peptide-positive, non-erosive rheumatoid arthritis (RA). Since diagnosis, she had always been treated with methotrexate (MTX), although in different dosages. Our patient presented with an ulcerating tumour (figure 1A) on her left upper leg which developed over the course of 4 months. She did not experience any constitutional symptoms like fever or weight loss. There was no lymphadenopathy at physical examination and no abnormalities in her blood tests.

She was referred to the dermatology clinic, and a skin biopsy was performed. Histological examination revealed a CD20-positive (figure 1F) and Ki-67-positive (figure 1G) diffuse large B cell lymphoma (DLBCL). Epstein-Barr virus (EBV) encoding small RNA's (EBER) staining was negative (figure 1H). A positron emission tomography-CT did not show any signs of systemic involvement, consistent with the clinical presentation of our patient.

Based on histopathological findings, it was not possible to distinguish between a primary cutaneous DLBCL and one related to immunosuppressive medication (ie, MTX). MTX was discontinued immediately, and while awaiting additional investigations, the tumour started regressing without a need for any additional (chemo)therapy. It resolved completely in 5 months' time (figure 1B,C).

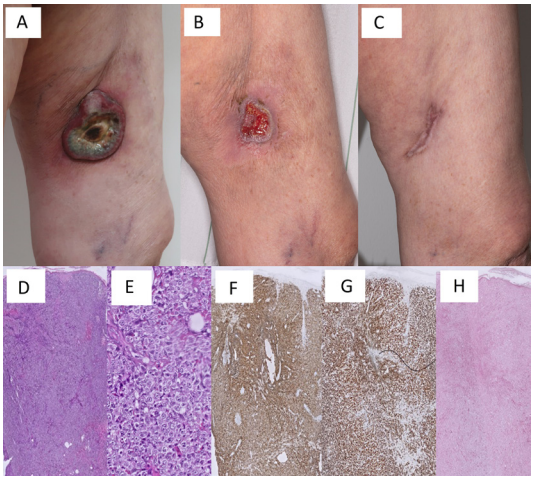

Figure 1 Development over time of cutaneous B cell lymphoma after methotrexate (MTX) cessation including histopathological examination of the skin biopsy of the lesion at baseline. (A) Lesion 1 week after MTX cessation. (B) Lesion 4 weeks after MTX cessation. (C) Lesion 23 weeks after MTX cessation. (D) H&E staining. (E) H&E staining; original magnification: ×60. (F) CD20 staining. (G) Ki-67 staining. (H) EBER staining. D and F–H; original magnification: ×2.

MTX-associated lymphoproliferative disease (MTX-LPD) is rare. It has been described in a cohort of patients with RA to have a 0.69% incidence (over a 3-year observation period).[1] MTX-LPD has the highest incidence in Japan.[1] The most common histological subtype is DLBCL (40%–50%), followed by classic Hodgkin lymphoma (10%–30%).[2] While the exact underlying mechanisms of MTX-LPD remain unclear, it is hypothesised that the immune dysregulation observed in patients with RA, in combination with MTX-related immunosuppression, may play a role in its onset.[3] Most of the MTX-associated DLBCLs resolve after discontinuation of MTX as sole intervention. Remission percentages range up to 81%,[3] dependent on stage at diagnosis. EBV positivity is regarded as a good prognostic factor.

This case demonstrates the rare entity of MTX-LPD. We emphasise the need for immediate discontinuation of MTX when the suspicion of MTX-LPD is raised as this may lead to complete resolution, without the need for chemotherapy.

Contributors LCMS (first author), writing original draft and editing and involved in patient care. RO, visualisation (providing images for figure 1), writing (editing) and involved in patient care. KDQ, writing (editing) and involved in patient care. SWT (corresponding author), writing (editing) and involved in patient care.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Consent obtained directly from patient(s).

Ethics approval Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iD
Laura C M Schenning http://orcid.org/0009-0009-1828-2863

REFERENCES

1 Honda S, Sakai R, Inoue E, *et al*. Association of methotrexate use and lymphoproliferative disorder in patients with rheumatoid arthritis: results from a Japanese multi-institutional retrospective study. *Mod Rheumatol* 2022;32:16–23.
2 Kurita D, Miyoshi H, Ichikawa A, *et al*. Methotrexate-associated Lymphoproliferative Disorders in Patients With Rheumatoid Arthritis: clinicopathologic Features and Prognostic Factors. *Am J Surg Pathol* 2019;43:869–84.
3 Gion Y, Iwaki N, Takata K, *et al*. Clinicopathological analysis of methotrexate-associated lymphoproliferative disorders: comparison of diffuse large B-cell lymphoma and classical Hodgkin lymphoma types. *Cancer Sci* 2017;108:1271–80.