Received: 22 April 2017 | Accepted: 29 October 2017

DOI: 10.1002/jgf2.145

IMAGES IN CLINICAL MEDICINE

Journal of General and Family Medicine Open Access WILEY

^{18}F-FDG PET-CT in a patient with methotrexate-associated lymphoproliferative disorder

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KEYWORDS: fluorodeoxyglucose, methotrexate-associated lymphoproliferative disorder, positron-emission tomography-computed tomography, rheumatoid arthritis

A 74-year-old Japanese man with rheumatoid arthritis (RA) was referred to our hospital with a 2-month history of fever which had been refractory to antibiotic therapy. He had been treated with methotrexate (MTX; 8 mg/week) and prednisolone (5 mg/day) for 10 years. His physical examination revealed articular deformities and generalized lymphadenopathy. Laboratory examinations showed a lactate dehydrogenase level of 317 U/L; C-reactive protein, 11.14 mg/dL; soluble interleukin-2 receptor, 18 924 U/mL. Positron-emission tomography-computed tomography (PET-CT) demonstrated remarkably increased uptake of ^{18}F-fluorodeoxyglucose (FDG) in the systemic lymph nodes (Figure 1A). Biopsy of the left cervical lymph node was carried out, and its histological findings revealed diffuse large B-cell lymphoma (DLBCL). In situ hybridization for Epstein-Barr virus (EBV)-encoded small RNA was negative. He was diagnosed with MTX-associated lymphoproliferative disorder (MTX-LPD) without EBV positivity. The administration of MTX was terminated. Three months later, his lymph nodes were not palpable and his fever subsided. The uptake of ^{18}F-FDG in the lymph nodes on PET-CT also markedly diminished (Figure 1B). No recurrence has been observed for more than 1 year. His RA is being successfully managed with prednisolone (5 mg/day), salazosulfapyridine (1000 mg/day), and iguratimod (50 mg/day).

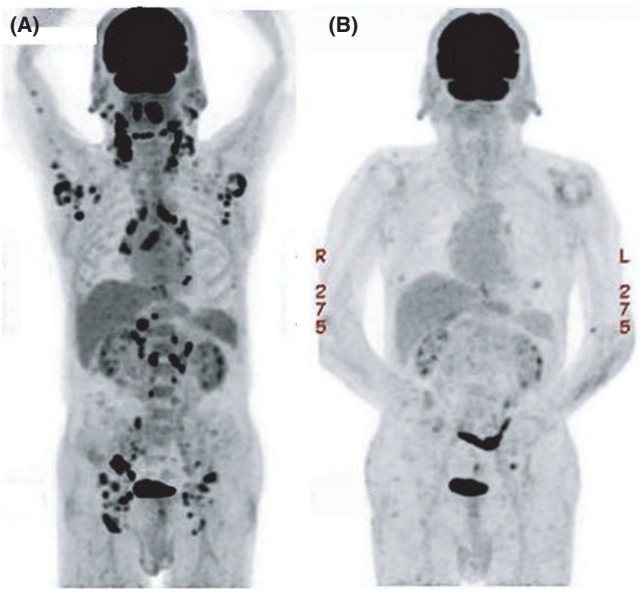

FIGURE 1 Images of ^{18}F-FDG PET-CT at (A) initial examination and (B) 3 months after withdrawal of MTX. A, The increased uptake of ^{18}F-FDG is observed in multiple lymph nodes. B, The uptake of ^{18}F-FDG in lymph nodes markedly diminishes

Methotrexate has been considered an anchor drug and recommended as the first-line therapy for RA. MTX-LPD develops in patients who have been treated with MTX. It was first reported in 1991.[1] The MTX-induced immunosuppressive state is considered to contribute to LPD development.[2,3] EBV reactivation is also thought to play an important role in LPD development.[2] MTX withdrawal and observation for a short time are considered in the initial management of MTX-LPD. It may be a suitable therapeutic option for MTX-LPD with EBV positivity,[3,4] because it was reported that spontaneous regression occurred significantly in patients with EBV positivity and non-DLBCL histological type.[3] In contrast, in MTX-LPD without EBV positivity, the effect of cessation of MTX on disease regression is largely unknown and treatment with chemotherapy might be an option in the early stage. However, physicians should be aware that more than half of the deaths were due to complications

from chemotherapy and other causes except disease progression.[3,4] ^{18}F-FDG PET-CT can detect metabolically active disease in the whole body, including malignant lymphoma in patients who have undergone MTX treatment.[5] However, a clinical role of ^{18}F-FDG PET-CT in MTX-LPD is not fully established.

We report here a case of MTX-LPD, in which disease regression was achieved after withdrawal of MTX. ^{18}F-FDG PET-CT clearly demonstrated the disease activity of MTX-LPD.

CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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How to cite this article: Shimizu H, Nishioka H. ^{18}F-FDG PET-CT in a patient with methotrexate-associated lymphoproliferative disorder. *J Gen Fam Med*. 2018;19:34–35. https://doi.org/10.1002/jgf2.145