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LETTER TO THE EDITOR

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WILEY

Switching to ixekizumab improves adalimumab-induced interstitial lung disease in patients with psoriatic arthritis: A case report

Dear Editor,

TNF-α inhibitors, including adalimumab (ADA), increase serum Krebs von den Lungen (KL)-6 levels with or without the occurrence of interstitial lung disease (ILD).[1,2] Herein, we report a case of ADA-induced ILD that was successfully controlled with ixekizumab (IXE) in a patient with psoriatic arthritis.

Case: A 60-year-old man with a history of moderate psoriasis presented as an outpatient with an exacerbation of the rash. At the previous hospital, ADA monotherapy had been used as a treatment for 16 months but discontinued because of ILD, which was revealed by computed tomography (CT) and elevated serum KL-6 levels with no history of smoking. At the first visit, psoriatic erythema was seen on both lower legs (Figure 1A), both elbows and trunk. Physical examination showed dactylitis of the middle and ring fingers of the right hand, and we observed increased bone formation and narrowing of the distal interphalangeal joint space of the right ring finger. A skin biopsy from the right thigh revealed psoriasis vulgaris, and chest CT showed ILD (Figure 1B). The patient was therefore given a diagnosis of psoriatic arthritis with ADA-induced ILD. After discontinuing ADA and changing to IXE—an interleukin-17A antagonist—the eruption and the joint symptoms improved (Figure 1C), as did the ILD (Figure 1D). The change

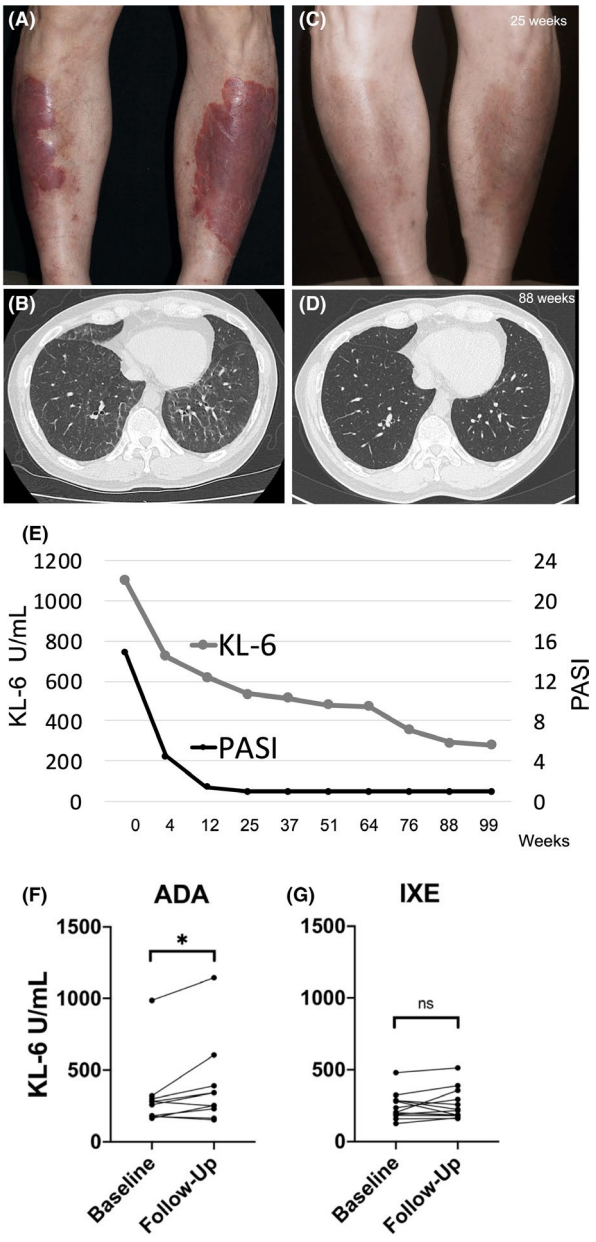

FIGURE 1 A, C, Clinical appearance of the case. Psoriatic lesions are distributed on the lower legs (A), and dermatitis improved with the change from adalimumab (ADA) to ixekizumab (IXE) (C, 25 wk after the start of IXE administration). B, D, Computed tomography scans of ADA-induced interstitial lung disease. The ground-glass opacity in the right middle lobe and both lower lobes (B) disappeared after the change from ADA to IXE (D, 88 wk). E, Changes in serum Krebs von den Lungen 6 (KL-6) levels and Psoriasis Area and Severity Index (PASI) after changing from ADA to IXE in this case. F, G, Serum KL-6 levels before and after treatment in the groups treated with ADA single agent (F) and IXE single agent (G) in our department, for patients with psoriasis vulgaris, psoriatic arthritis, or pustular psoriasis. The data were analyzed using GraphPad Prism version 8 (GraphPad Software Inc). The Wilcoxon matched-pairs signed-rank test was used to assess statistical significance. *$P < .05$; ns not significant

to IXE not only achieved a Psoriasis Area and Severity Index (PASI) of 90, but also reduced KL-6 to reach baseline in 45 weeks (Figure 1E).

Because IL-17A exacerbates pulmonary fibrosis, it was expected that IL-17 inhibitors would not elevate KL-6; it has been reported that increased serum KL-6 levels induced by ADA have been improved by changing to secukinumab (SEC),[3] but SEC has also been reported to both increase and decrease serum KL-6 levels.[4] Here, we reported the case that increased serum KL-6 levels after administration of ADA were improved by changing to IXE; however, there is one report of elevated KL-6 levels being induced by IXE in combination with methotrexate,[5] and careful monitoring during biological treatment is required in this case.

Finally, we have examined the effect of biologics on KL-6 in patients with psoriasis at our hospital. This retrospective chart review was approved by the Ethics Review Board of Hyogo College of Medicine. In the ADA-administered group, serum KL-6 was 313.2 ± 77.0 U/mL (mean ± standard error of the mean) before administration and 387.9 ± 93.7 U/mL (n = 10) after administration, showing a significant increase in KL-6 (Figure 1F), consistent with previously reported results.[1,2] In contrast, with IXE administration, no significant increase in KL-6 was observed, with 234.5 ± 27.3 U/mL before administration and 246.5 ± 31.5 U/mL (n = 12) after administration (Figure 1G). In addition, IXE has not been found to increase the risk of ILD in Phase 3 clinical trials.[6] We therefore consider that changing to IL-17 inhibitors could be useful for patients with psoriasis associated with ADA-induced ILD. However, further study is necessary to draw conclusions, because the paradoxical increase in KL-6 levels being induced by SEC and IXE was reported.[4,5]

DECLARATION SECTION

Approval of the research protocol: N/A.

Informed Consent: Written informed consent was obtained from the patients.

Registry and the Registration No. of the study/trial: N/A.

Animal Studies: N/A.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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