LETTERS TO THE EDITOR

Interleukin-18 in Adult-onset Still’s Disease: Treatment Target or Disease Activity Indicator?

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To the Editor We read with great interest the recent report by Yoshida et al (1) “Tocilizumab improved both clinical and laboratory manifestations except for interleukin-18 in a case of multiple drug-resistant adult-onset Still’s disease”. They reported that tocilizumab (TCZ) decreased inflammatory markers, such as C-reactive protein (CRP) and ferritin, but did not improve interleukin (IL)-18 in a patient with refractory adult-onset Still’s disease (AOSD). This led them to conclude that IL-18 is located upstream of or at the same level as IL-6 in the inflammatory cascade causing AOSD.

We previously reported a patient with AOSD who was successfully treated with TCZ (2). In this patient, the serum IL-18 level was markedly reduced from 220,000 pg/mL to 7,000 pg/mL after 4 months of TCZ treatment. This finding is quite different from the report by Yoshida et al. Thus, we cannot determine whether IL-18 is located upstream of IL-6 in the inflammatory cascade of AOSD from the results obtained in a couple of patients. Although tumor necrosis factor (TNF)-α is considered to be located upstream of IL-6 in the cytokine cascade provoking AOSD (4), TCZ reduced both TNF-α and IL-18 levels in our patient (2). Our patient discontinued TCZ after 18 doses over 14 months, and has since remained in remission for more than 2 years with no treatment. Just before the 14th dose of TCZ, serum IL-18 was 384 pg/mL. Whether the serum IL-18 level decreases or not is likely to depend on the disease activity of each patient. If serum IL-18 is low, TCZ may be discontinued. Thus, IL-18 shows potential as an indicator of disease activity during TCZ treatment (3).

They also reported that TCZ decreased the serum level of matrix metalloproteinase-3 (MMP-3), as well as CRP and ferritin. However, MMP-3 is not a disease activity marker for AOSD. The decrease of serum MMP-3 was not a direct effect of TCZ, but rather it was due to the reduction of the prednisolone dose. Glucocorticoids increase the serum level of MMP-3, although the mechanism involved is unclear. In fact, the MMP-3 level is increased in any disease by high-dose glucocorticoid therapy (5).

Yoshida et al suggested that drugs targeting IL-18 may be beneficial for the treatment of AOSD. Whether IL-18 is a treatment target for AOSD or merely an indicator of disease activity needs to be elucidated in the future.


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References