The beneficial effect of leflunomide on systemic lupus erythematosus: the role of Tregs repopulation?

Comment on: Leflunomide: friend or foe for systemic lupus erythematosus?
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Dear Editor,

We read with great interest the recent article by Wu et al. [1]. They reported the beneficial effects of leflunomide treatment systemic lupus erythematosus (SLE) and speculated that it might suppresses the production of proinflammatory cytokines such as tumor necrosis factor (TNF)-alpha and interleukin (IL)-17, blocks TNF-mediated NF-κB activation and induces inhibition of T cell activation [1]. However, we would like to add another possible mechanism on the beneficial effect of leflunomide on SLE.

It has been reported that regulatory T cells (Treg) play important roles in the induction of peripheral tolerance to self- and foreign antigens [2] and naturally occurring CD4+CD25+ Treg, which express the transcription factor forkhead box protein P3 (Foxp3), have been widely studied as deficiency of Tregs abrogates self-tolerance and causes autoimmune disease, such as SLE [2].

Recently, there have been some reports showing that leflunomide repopulate Tregs [3, 4]. Wang et al. [3] showed that by leflunomide inhibited arthritis by upregulating CD4+CD25+ Tregs, and the active metabolite of leflunomide promoted the differentiation of spleen lymphocytes into CD4+CD25+ Tregs and increased anti-inflammatory cytokine (TGF-beta1) secretion. Also, Baban et al. [4] demonstrated that leflunomide increased FoxP3 Tregs and

IL-10-positive cells but reduced IL-17- and IL-23-expressing cells in both the peripheral blood and kidney cells in the ischemic-reperfused kidney model.

Therefore, there is a possibility that leflunomide might treat SLE by repopulating Tregs in addition to the suppressing inflammatory cytokines. Further studies are necessary to evaluate serial changes of Tregs after leflunomide therapy in SLE and the exact molecular role of Tregs in the pathogenesis in SLE development should be further elucidated in the future.

References

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