
Infections

Potential role of costimulatory pathways in immune dysfunction in hemodialysis patients

To the Editor:

We read with interest the paper by Mathew et al. who investigated the role of T-regulatory cells in the immune response to HBV vaccination in patients undergoing hemodialysis (HD).¹

This is a very important topic, since response to vaccines is commonly considered an expression of immune status in HD. The authors, in agreement with previous reports, demonstrated that in HD there is a low rate of response to vaccine, but they did not find any significant difference in T-regulatory cell number between healthy controls and HD subjects.

We think that this negative result could depend by the fact that immune dysfunction in HD patients involves alterations of various types of immune cells, including polymorphonuclear leukocytes, monocytes, natural killer cells, B and T lymphocytes^{2,3} and probably the simple study of the number of T-regulatory cells and their subtypes is not sufficient to describe this condition.

Indeed, in this complex picture T cell dysfunction can occur at different levels.

In this regards, in the last years, many studies have demonstrated that co-stimulatory signal alterations may play a role in determining immunodeficiency in HD.⁴

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Costimulatory pathways (CD28, TNF-related, adhesion, and TIM molecules) regulate the interactions between receptors on the T cells and their ligands expressed on several cell types and are essential for the full activation of naïve T cells after antigen-specific recognition.⁵

Girndt et al. found a correlation among the low expression of CD80 and CD86 (CD28 ligands) on monocytes isolated from HD patients, impaired proliferation ability of T cells and reduced response to HBV vaccination.⁶

Similar results were also found analyzing the TNF-related CD40/CD40L pathway, which in HD patients presents a whole imbalance characterized by reduction of CD40 membrane expression associated with elevated levels of the soluble form of CD40 (sCD40).⁷ Interestingly, Contin et al. showed that HD patients with higher serum levels of sCD40, which may act as a natural antagonist of CD40/CD40L interaction, were less responsive to HBV vaccine, whereas sCD40 removal, obtained by the use of polymethylmethacrylate-based dialysis membranes, was associated with a significant improvement of response to vaccination.⁸

All together these evidence suggest that the study of HD-related immunodeficiency should take into consideration the complexity of the different pathways involved and their interaction, also because the comprehension of cellular and humoral mechanisms underlying immune dysfunction could provide new therapeutic targets.

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