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Danger-associated molecular patterns and their effects in graft-versus-host disease

Derya Koyun

Bitlis Tatvan State Hospital, Department of Hematology, Bitlis, Türkiye

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Dear Editor,

Hematopoietic stem cell transplantation continues to be the gold standard treatment option for various blood cancers, and one of its mortal complications is graft-versus-host disease (GVHD). This is due to cell death as a result of tissue damage following chemotherapy and/or radiotherapy during the preparation for transplantation. It is also known that danger-associated molecules liberated during tissue damage after chemotherapy and radiotherapy may be responsible for the development of GVHD. Endogenous and exogenous pathogen-associated molecular patterns trigger a potent danger signal response and it is defined as damage-associated molecular patterns. These danger signals result in cytokine release by activating nuclear transcription factors such as nuclear factor (NF)-κB, early growth response factor (Egr1), and activator protein (AP)-1. These are classified into exogenous and endogenous factors. Endogenous danger-associated molecular patterns include factors such as high mobility group box 1 (HMGB-1), S100 proteins, elastase inhibitors, defensins, cathelicidins, regenerative protein family (Reg), heat shock proteins, heparan sulfate proteoglycans, adenosine triphosphate, and uric acid and induce danger signals almost immediately during unprogrammed cell death [1]. New therapeutic option targeting danger-associated molecular patterns may be a promising alternative for GVHD therapy.

Heparan sulfate is a complex, linear polysaccharide belonging to the glycosaminoglycan familythat shows a diverse interaction with intracellular and extracellular matrices. At the beginning of GVHD, the serum concentration of heparan sulfate rises and correlates with the disease's severity. Studies on experimental models have shown that alpha-1 antitrypsinsignificantly lowers heparan sulfate levels, and this decrease in heparan sulfate is linked to a decrease in the intensity of GVHD. Moreover, alpha-1 antitrypsin reduces inflammatory cytokines like TNF-α and IL-1β. However, it boosts IL-10 production, and promotes Treg expansion [2]. In our center, we also demonstrated that alpha-1 antitrypsin, which affects heparan sulfate levels, plays an important role in resistance to acute GVHD after allogeneic stem cell transplantation in 5 patients [3]. No treatment-related side effects were observed in our patients included. Further studies on different danger-associated molecular patterns, and their efficacy in the treatment of GVHD should be panned.

References

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*Corresponding author:
Email address: deryakoyun11@gmail.com (Derya Koyun)

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