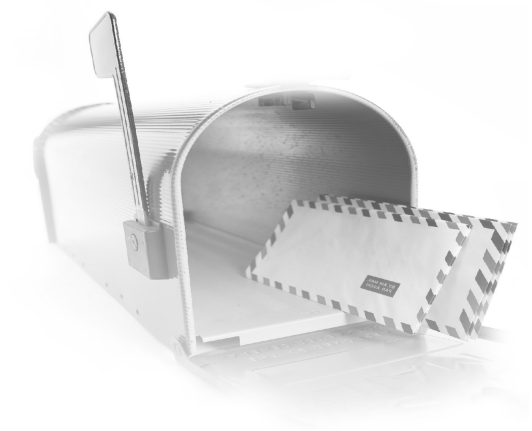

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Letter to the Editor

The role of B cells in acute graft-versus-host disease

TO THE EDITOR: Mounting evidences implicates B cells in the pathogenesis of chronic graft-versus-host disease (GVHD). The body of evidence includes findings such as correlation between chronic GVHD and antibody production against Y chromosome-encoded minor histocompatabilty antigens (mHA) generated after sex-mismatched allogeneic stem cell transplantation (SCT), the clinical response of steroid-refractory chronic GVHD to rituximab, and association between high serum B cell-activating factor (BAFF) levels and chronic GVHD [1]. However, the role of B cells in acute GVHD remains controversial. Some studies that showed the association of high B cell count in the grafts in SCT patients with acute GVHD and beneficial effects of rituximab (used for B cell lymphoma treatment before transplantation) in acute GVHD patients, have suggested the possible role of B cells in the development of acute GVHD.

Kim *et al.* reported that the BAFF level/absolute lymphocyte count (ALC) ratio or that of APRIL (a proliferation-inducing ligand) level/ALC at the time of acute GVHD diagnosis was associated with disease severity [2]. In their study, patients with grade III-IV acute GVHD (6) had higher BAFF level/ALC or APRIL level/ALC ratio than the corresponding ratio observed in patients with grade II acute GVHD (9). These findings suggest that BAFF level/ALC or APRIL level/ALC ratio can help determine the severity of acute GVHD and need to be confirmed in large prospective studies. However, it would be somewhat unreasonable to conclude that B cells may play an important role in the development of acute GVHD on the basis of these findings alone. First, counting the number of B cells should be performed along with measurement of the BAFF or APRIL levels because higher serum BAFF levels may reflect relative B lymphopenia depending on the period after transplantation. Furthermore, comparison of the findings for patients with and without acute GVHD for the same period after allogeneic SCT is essential for investigating the relationship between B cells and acute GVHD.

BAFF has a complex, dichotomous role in immunity, which is mediated by the differential regulation of T cell- and B cell-dependent immune responses [3]. BAFF, a critical regulator of normal B cell homeostasis in mice and humans, also promotes T cell activation and survival [4]; these T cells play a pivotal role in acute GVHD pathogenesis. However, recent studies have also demonstrated the negative regulatory role of BAFF in T cell function [3, 5]. Walters et al. found that BAFF-transgenic mice accepted islet allografts and showed delayed rejection of skin allografts. On the basis of these results, they proposed that BAFF plays an anti-inflammatory role in T cell biology by promoting the expansion of regulatory T cells [3]. We studied the potential protective effect of BAFF against acute GVHD during the peritransplantation period in the setting of allogeneic SCT in humans [5]. Thus, further experimental and clinical studies are needed to elucidate the role of B cells in the development of acute GVHD and gain more insight into the pathogenesis of acute GVHD by studying the association of BAFF with B cells and T cells.

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