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INVITED COMMENTARY

Systemic inflammation in kidney transplant candidates: a hidden threat?

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Kidney transplant recipients are at higher risk for cardiovascular morbidity and mortality than general population. Besides atherosclerosis risk factors, other, less-studied conditions have been suggested to play a role as well. Among those, systemic inflammation, typical for CKD5 patients, has been discussed [1]. While the role of TNF-α or IL-6/CRP axis in the initiation of systemic inflammation is well recognized, recently described autoantibodies to cytokines were found to impair immune reactions, which may result in the increased risk of cancer and autoimmunity [2]. Interestingly, autoantibodies to cytokines with known regulatory function may increase the risk of infection and aggravate systemic inflammation. In this issue of Transplant International, Lund and colleagues [3] show that major cardiovascular events (MACE) at 5 years after kidney transplantation are associated with increased pretransplant levels of naturally occurring cytokine-specific autoantibodies against regulatory cytokine IL-10. To prove this, authors used a large biobank of sera obtained just before kidney transplantation to measure several cytokines and their autoantibodies and Danish National Registry to evaluate the cardiovascular outcomes in 619 kidney transplant recipients. Moreover, authors showed the association of pretransplant levels of TNF-α, IL-6, hsCRP, and IL-10 with all-cause mortality after kidney transplantation. Of note, study results are quite robust because authors observed also patients with MACE before transplantation to have lower levels of autoantibodies against TNF-α.

Lund's observation is of interest, and based on study results, a protective effect of circulating IL-10 can be hypothesized. It remains unclear how naturally occurring autoantibodies against IL-10 aggravate systemic inflammation involved in the atherosclerosis pathogenesis.

In transplantation immunology, IL-10 is a well-studied cytokine with multiple, pleiotropic, effects in immunoregulation and inflammation. It downregulates the expression of Th1 cytokines, MHC class II antigens, and costimulation, while it enhances B-cell survival, proliferation, and antibody production. Among other cell types, IL-10 is produced by B cells, which are known as regulatory B cells (Bregs). Those cells were shown to be involved in the maintenance of immune tolerance [4]. Therefore, naturally occurred IL-10 autoantibodies at transplantation might theoretically influence the balance between effector and regulatory

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tools of adaptive immunity toward increased alloresponse. Authors collected data on acute rejection within the first post-transplant year, but they were not able to show any associations between rejection and pretransplant IL-10 autoantibody levels. However, they found an association with delayed graft function (DGF) and they speculate that systemic inflammation might be involved in DGF development. Systemic inflammation is typical for patients who have been undergoing the long-term dialysis treatment, and, in a significant proportion of them, malnutrition inflammation atherosclerosis (MIA) syndrome is detected [5]. Similarly, patients who stay longer on dialysis experienced more frequently DGF, which is well-known risk factor for acute rejection and premature graft loss [6]. Therefore, it is likely that systemic inflammation before kidney transplantation represents the hidden threat for mid-term cardiovascular complications and kidney graft outcome, and as such, it needs to be taken seriously.

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Conflict of interest

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