Thrombotic microangiopathy following organ transplantation

To the Editor: Tsai and Lian [1] and Furlan et al [2] independently demonstrated that a deficiency in the activity of von Willebrand factor-cleaving metalloprotease, ADAMTS-13 or the presence of its inhibitory antibodies causes thrombotic thrombocytopenic purpura. It is unknown whether a similar mechanism occurs in patients who develop thrombotic microangiopathy (TMA) following organ transplantation. We have recently shown that the ADAMTS-13 activity was undetectable in plasma samples obtained from a patient who developed TMA after receiving a cadaveric renal allograft. Deficiency of the protease enzyme occurred in the presence of its inhibitory antibodies. Discontinuation of cyclosporine and daily plasma exchange raised the ADAMTS-13 activity, followed by resolution of the microangiopathic hemolysis and improvement of the graft function [3].

Ruggenenti [4] pointed out in an article recently published in Kidney International that restoration of von Willebrand factor-cleaving protease activity in parallel with disease remission does not necessarily imply that normalization of the protease activity is the determinant of response to plasma. We are curious if this is based on case studies or solely speculations. In our case, we showed that the ADAMTS-13 activity rapidly increased to 50% or higher after two sessions of plasmapheresis. We further showed that the immunoglobulin G (IgG) molecules isolated from the patient’s plasma inhibited the ADAMTS-13 activity in normal plasma. During disease remission, the IgG molecules isolated from the patient’s plasma showed no inhibitory effect on the ADAMTS-13 activity in normal plasma. We speculate that plasma exchange confers its effectiveness by replenishing the missing ADAMTS-13 and/or removal of its inhibitors.

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A prospective trial correlating clinical outcomes with ADAMTS-13 activity levels will clarify the role of replenishing ADAMTS-13 and/or removing inhibitors in determining TMA response to plasma therapy.

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Endothelial chimerism in association with vascular rejection in patients after kidney transplantation

To the Editor: Cell migration from the host to the transplanted organ results in chimerism in the organ [1]. Chimerism may be detected after gender-mismatched organ transplantation with use of fluorescence in situ hybridization [2]. To verify the endothelial chimerism, we studied kidney grafts with immunohistochemistry for ABO blood-group antigens and in situ hybridization for Y chromosome.

Four male recipients had received living kidney transplants from female donors. The blood type of the recipients was type A in all cases, and that of donors were type O in two cases and type B in two cases. Needle biopsies were performed from 2 to 5 months after kidney transplantation and diagnosed as vascular rejection. Endothelial cells stained with CD34 were positive for Y chromosomes, indicating the presence of recipient-type male cells. These endothelial cells were positively stained for recipient-type blood group A. The patients in the present study have shown that replacement of donor endothelium by recipient cells does occur in vascular rejection after kidney transplantation.

Lagaaij et al [3] have recently reported that grafts in which the endothelial cells are damaged by vascular rejection may incorporate host endothelium as part of the repair process. They speculate that host endothelial cells may be recruited from endothelial stem cells in the circulation. Further studies are required to clarify the mechanism of endothelial chimerism in association with vascular rejection after kidney transplantation.

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Risk factors for late kidney allograft failure

To the Editor: We congratulate Ponticelli et al [1] for an excellent paper regarding the evaluation of risk factors for late kidney allograft failure that recently appeared in Kidney International. However, we would like to suggest to the authors to see for the effect of nephron replacement of BMI compared to other categories. It was evident that of the extreme groups the relative risk of chronic allograft nephropathy (CAN) was significantly more in extremes BMI compared to other categories. Meier-Kriesche et al have observed in their study that the relative risk of graft loss death censored and uncensored was more in extremes of BMI compared to other categories. It was evident that of the extreme groups the relative risk of chronic allograft nephropathy (CAN) was significantly more in high BMI group [2]. We have observed in our study and it has been well reported by others that kidneys with insufficient nephron mass for the recipient may be damaged by hyperfiltration injury resulting into proteinuria and CAN [3–5]. Thus we feel that if authors can analyze nephron dosage in addition to other well studied risk factors in this cohort, it would be a significant contribution to the literature.

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