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Pathogenesis of nephrotic syndrome after hematopoietic stem cell transplantations

Sergio Dellepiane,[1] Davide Giuseppe Ribaldone,[2*]

[1]"A. Vercellone" Kidney Transplantation Center, Department of Medical Sciences, University of Torino, Azienda Ospedaliera "Città della Salute e della Scienza- Molinette", Torino, Italy;

[2]Gastroenterology-U, Department of General and Specialist Medicine, Città della Salute e della Scienza, Molinette Hospital, Turin, Italy

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Corresponding author: Davide Giuseppe Ribaldone - Gastroenterology-U, Department of General and Specialist Medicine, Città della Salute e della Scienza, Molinette Hospital, Turin, Italy, C.so Bramante 88 - 10126 Torino – Italy. E-mail: davrib_1998@yahoo.com Tel: +390116335208, Fax: +390116336752.

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TO THE EDITOR: In an interesting letter to the editor Beyar Katz *et al.*[1] reported the incidence of nephrotic syndrome (NS) in patients undergoing allogenic hematopoietic stem cell transplantation (HSCT). The authors found that 6/415 patients (1.4%) developed NS. Of them, four underwent transplant for acute leukemia and two for lymphoma. Acute and chronic graft versus host disease (GVHD) was documented in 5/6 patients. Kidney biopsy revealed membranous glomerulonephritis (MG) and minimal change disease (MCD) in 5; biopsy was not available in one subject. The median onset of NS was 18.5 months post-HSCT. Regarding the treatment, 2/6 responded to corticosteroids, one to tacrolimus and 3 to a combination therapy.

Impressive progresses have been made in the field of stem cells research and their potential applications in human regenerative medicine are increasing. Stem cells from various sources are now moving into clinic[2]. Due to their plasticity, these cells may, in theory, be employed for genesis or regeneration of tissues injured by genetic and degenerative illnesses, like neurological diseases, diabetes, chronic heart failure, end-stage kidney disease, end-stage liver disorders, cancer and others.[3, 4] In haematology, leukaemias are malignancies arising from genetic abnormalities occurring in bone-marrow resident hematopoietic stem cells or in committed lymphoid or myeloid precursors. Two kinds of HSCT are available for leukaemia treatment; autologous HSCs allow the use of myeloablative drugs, do not cause immunological adverse effects but are not curative *per se*. On the other hand, heterologous HSC transplant contributes to malignancy eradication but may induce GVHD. Although renal impairment could affect 50% of patients underwent HSCT, NS is a late-onset uncommon event with an unclear pathogenesis. To address therapies, ameliorate the knowledge of this issue is crucial in the clinical setting. It has been reported that NS could be related to cytomegalovirus infection, radiation, hemolytic-uremic syndrome, and chronic GVHD, which is now considered the main etiological factor. NS has been described as a manifestation of chronic GVHD often occurring after the cessation or tapering of GVHD immunosuppressant therapy. Some studies reported that T helper cells (including

Th1 and Th2 cells) are involved in chronic GVHD; these lymphocytes may suppress immune tolerance and damage the kidney; other authors have found a relationship between CD4+CD25+FOXP3+ regulatory T cells (Tregs) and the pathogenesis of GVHD-related NS. Luo *et al*.[5] have shown that the number of Tregs at day 30, 60, 90, and 180 after HSCT was significantly lower in NS patients than non-NS patients. Conversely, serum levels of interferon-γ (IFN-γ) and tumor necrosis factor-α (TNF-α) were significantly higher in NS patients, and NS post-HSCT was associated with the occurrence of chronic GVHD (P=0.02). Patients with and without NS had similar CD19+ B cell numbers as well as immunoglobulin (Ig) deposits on the epithelial side of glomerular capillaries, but only some patients had increased levels of serum autoantibodies and Ig.

In conclusion, taken together, these results suggest that NS post-HSCT is an immune disorder that may involve immune complex deposition, Th1 cytokines, and Tregs. All these findings should lead clinicians in the choice of the optimal treatment.

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