HEMATOLOGY, TRANSFUSION AND CELL THERAPY

www.rbhh.org

Scientific Comment

Red blood cell alloantibodies and autoantibodies: different presentation, same physiopathology☆

*Carla Luana Dinardo**

Fundação Pró-Sangue, Hemocentro de São Paulo, São Paulo, SP, Brazil

Alloimmunization is one of the most relevant post-transfusion complications as it is associated with transfusion delays, hemolytic disease of fetus/newborn and hemolytic transfusion reactions, which can be fatal in some cases. The ability of developing red blood cell (RBC) alloantibodies is restricted to a specific group of blood recipients, namely 'immune responders', whose genetics and inflammation background favors the antigen-presenting event and strengthens the Th2 response. Interestingly, multiple cohorts of multi-transfused patients have revealed that the group of immune responders is also prone to the development of RBC autoantibodies, which correspond to approximately 8% of all identified antibodies.[1] In most cases, both alloantibodies and autoantibodies are due to RBC transfusions and the presence of autoantibodies is considered a risk factor for alloimmunization itself, marking the condition of immune responsiveness.[2]

In this issue of Hematology, Transfusion and Cell Therapy, do Valle-Neto et al. describe the alloimmunization profile of a cohort of multi-transfused patients from Minas Gerais, including both sickle cell disease (SCD) and non-SCD patients.[3] The group reported a significant prevalence of autoantibodies within the cohort (6.54%), which was much higher in the group of alloimmunized patients (29.16%) in comparison to the non-alloimmunized group (2.32%). This data elegantly reinforces previous evidence in the literature regarding the high frequency of RBC autoantibodies among alloimmunized patients under chronic transfusion therapy, and highlights that both alloantibodies and autoantibodies are probably formed through similar paths of adaptive immune response.

Taking a close look at the physiopathology of RBC alloimmunization, it is no surprise to find a strong association between autoantibody and alloantibody development. B cells are the cornerstone of autoimmunity and are also key elements in the initiation of alloantibody production. Most of the genetic polymorphisms associated with the risk of post-transfusion antigen sensitization refer to molecules taking part in the antigen-presenting event, some of which have already been linked to a higher risk of autoimmune diseases and their associated autoantibodies.[4] Considering that post-transfusion RBC autoantibodies usually emerge after or concomitantly with alloimmunization, the hypothesis is that the immune response directed against transfused RBCs seems to expand to self-antigens.[5] Thus, an exacerbation of Th2 response plays a central role in both autoimmunization and alloimmunization triggered by transfusion.

The high frequency of autoantibodies among alloimmunized patients sheds light on an important, but still unsolved question concerning how clinically relevant these post-transfusion self-directed antibodies are. While some studies suggest they are quite benign, justifying occasionally mild hemolysis, there are reports of very severe post-transfusion autoimmune hemolysis related to this mechanism.[5] In these dramatic situations, diagnosing the self-directed nature of erythroid destruction may be challeng-

DOI of original article: https://doi.org/10.1016/j.htct.2017.08.001.

☆ See paper by Orsetti Gomes do Valle Neto et al. on pages [107–111].

* *Correspondence to*: Fundação Pró-Sangue - Hemocentro de São Paulo, Av Dr. Enéas de Carvalho Aguiar, 155, Cerqueira César, 05403-000 São Paulo, SP, Brazil.

E-mail address: carlaluana@usp.br

https://doi.org/10.1016/j.htct.2017.09.002

ing, especially because it occurs in previously alloimmunized blood recipients and may resemble hyperhemolysis. Taking into consideration all the evidence related to the physiopathology of post-transfusion RBC autoantibodies, the good news is: preventing alloimmunization also prevents autoimmunization. The enemy to be defeated is still the same.

Conflicts of interest

The authors declare no conflicts of interest.

REFERENCES

1. Aygun B, Padmanabhan S, Paley C, Chandrasekaran V. Clinical significance of RBC alloantibodies and autoantibodies in sickle cell patients who received transfusions. Transfusion. 2002;42(1):37–43.
2. Allali S, Peyrard T, Amiranoff D, Cohen JF, Chalumeau M, Brousse V, et al. Prevalence and risk factors for red blood cell alloimmunization in 175 children with sickle cell disease in a French university hospital reference centre. Br J Haematol. 2017;177(4):641–7.
3. do Valle-Neto OG, Mendonça V, Pereira GA, Moraes-Souza H, Martins PR. Clinical and epidemiological profile of allo and autoimmunized multi-transfused patients against red blood cell antigens in a blood center of Minas Gerais. Hematol Transfus Cell Ther. 2018;40(2):107–11.
4. Oliveira VB, Dezan MR, Gomes FC, Menosi Gualandro SF, Krieger JE, Pereira AC, et al. -318C/T polymorphism of the CTLA-4 gene is an independent risk factor for RBC alloimmunization among sickle cell disease patients. Int J Immunogenet. 2017;44(5):219–24.
5. Sigler E, Shvidel L, Yahalom V, Berrebi A, Shtalrid M. Clinical significance of serologic markers related to red blood cell autoantibodies production after red blood cell transfusion-severe autoimmune hemolytic anemia occurring after transfusion and alloimmunization: successful treatment with rituximab. Transfusion. 2009;49(7):1370–4.