Comments on: Frequency of human platelet antigens in oncohematological patients with thrombocytopenia and the probability of incompatibility to platelet transfusions

Erich Vinicius de Paula

Universidade Estadual de Campinas - UNICAMP, Campinas, SP, Brazil

Platelets share antigens with other cells such as ABH and HLA class I antigens, but also express specific antigens. Platelet specific antigens are identified according to a nomenclature devised by the International Society of Blood Transfusion and are referred to as Human Platelet Antigens (HPA). These include glycoproteins expressed on platelet surfaces such as GPIIb/IIIa, the von Willebrand factor receptor GP Ib/IX, among others. Polymorphisms in the genes that code for these proteins result in different HPA patterns, which can result in the exposure of humans to incompatible HPA during platelet transfusions or pregnancy of an HPA-incompatible fetus. Significant differences in the prevalence of HPA polymorphisms have been described in different populations and HPA polymorphism frequencies in Brazil have been elegantly described in different ethnic groups[1]. Alloimmunization to HPA can result in clinically significant problems such as neonatal alloimmune thrombocytopenia and post-transfusion purpura. The former occurs when an alloimmunized mother gives birth to an HPA-incompatible newborn resulting in neonatal thrombocytopenia. The latter is an extremely rare condition in which the development of anti-HPA antibodies, usually anti-HPA-1a, results in sudden (within 7-10 days after a transfusion), severe and self-limiting thrombocytopenia, with destruction of both autologous and allogeneic platelets. In addition to these two well-recognized HPA-related disorders, HPA alloimmunization is sometimes associated with platelet refractoriness, although the role of HPA antibodies in this context is less straightforward[2].

A report on the prevalence of HPA polymorphisms in a group of multitransfused patients from the Transfusion Outpatient Clinic of *Hospital das Clinicas* (FMUSP) is presented in this issue of the *Revista Brasileira de Hematologia e Hemoterapia* (RBHH)[3]. The study population included 150 patients with aplastic anemia or oncohematological diseases submitted to platelet transfusions at this Institution. In addition to presenting the HPA genotypes of this population, the authors performed a theoretical exercise to estimate the risk of incompatible HPA transfusions by comparing their results with HPA genotype frequencies from a population of blood donors from the same Institution. No significant differences in genotype frequency were observed. The study did not look for the presence of anti-HPA antibodies nor the outcome of transfusions and the authors mostly explored the role of HPA antigens in the development of platelet refractoriness.

The availability of platelet transfusions in 1959 resulted in a dramatic reduction (from 67% to 37%) in the percentage of bleeding-related deaths in leukemic patients[4]. Since this time, several improvements in medical support to oncohematological patients, coupled with improvements in the quality of platelet transfusions, further decreased the morbidity of thrombocytopenia in these patients. Nonetheless, poor response to platelet transfusions or platelet refractoriness remains one of the most dramatic challenges in the management of oncohematological patients.

Platelet refractoriness can be defined as the occurrence of an unexpected increment in platelet count after a platelet transfusion. The frequency of this complication in oncohematological patients varies depending on the study; in a recent analysis of the TRAP (Trial to Reduce Alloimmunization to Platelets) Study, platelet refractoriness developed in 27% of patients with acute leukemia[5]. In Brazil, a single center study published in 2004 describes an extremely high frequency, with 80% of patients developing this complication in the early phase of hematopoietic stem cell transplantation[6]. However, in a more recent study, a 19% frequency of platelet refractoriness, much closer to data of several other studies, was demonstrated among oncohematological patients[7].

Platelet refractoriness can be caused by several non-excluding mechanisms, normally divided into immune and non-immune. Non-immune causes of platelet refractoriness include sepsis, disseminated intravascular coagulation, splenomegaly, fever, medications, among others. Immune causes include alloimmunization to antigens present on platelets due to prior exposure during previous transfusions, transplantation or pregnancy. It is generally accepted that non-immune causes account for about 80% of cases of platelet refractoriness[7].

Conflict-of-interest disclosure:
The authors declare no competing financial interest

Submitted: 3/14/2012
Accepted: 3/15/2012

Corresponding author:
Erich Vinicius de Paula
Universidade Estadual de Campinas - UNICAMP, Rua Carlos Chagas, 450
Cidade Universitária "Prof. Zeferino Vaz"
13083-878, Distrito de Barão Geraldo
Campinas, SP – Brazil
erich@unicamp.br

www.rbhh.org or www.scielo.br/rbhh

DOI: 10.5581/1516-8484.20120043

Platelet antigens associated with alloimmunization can be divided in two groups: HLA and HPA. HLA antigens are believed to be the primary cause of immune platelet refractoriness. HLA class I antigens are synthesized by platelets, which also absorb soluble HLA antigens from plasma, resulting in a relatively higher number of these molecules on the platelet surface compared to granulocytes and red cells[8]. In contrast, platelet-specific antibodies, found in less than 15% of cases of immune-mediated platelet refractoriness, are much less frequently associated with platelet refractoriness and some authors even argue about the clinical significance of this association[2]. It is also important to note that in the context of platelet refractoriness, the mere presence of antibodies does not implicate in a clinically significant effect. In fact, 50% of patients with anti-HLA antibodies do not manifest platelet refractoriness[2]. This observation shows that the link between alloimmunization and its potential clinical consequences are not straightforward, and that other modifiers, many still unknown, determine whether alloimmunization will result in a clinically relevant effect. Therefore, the study presented in this issue of RBHH[3] confirms the HPA genotype pattern described by others, but the implications of these results on the risk of HPA-related disorders and, more specifically, on platelet refractoriness, should be evaluated with much more caution. Nonetheless, it should be regarded as a relevant effort to increase the knowledge in the field of platelet transfusions[9].

References

1. Castro V, Origa AF, Annichino-Bizzacchi JM, Soares M, Menezes RC, Gonçalves MS, et al. Frequencies of platelet-specific alloantigen systems 1-5 in three distinct ethnic groups in Brazil. Eur J Immunogenet. 1999;26(5):355-60.
2. Hod, E, Schwartz J. Platelet transfusion refractoriness. Br J Haematol. 2008;142(3):348-60.
3. Azevedo MR, Jens E, Nukui Y, Chamone DA. Frequency of Human platelet antigens in oncohematological patients with thrombocytopenia and the probability of incompatibility to platelet transfusions. Rev Bras Hematol Hemoter. 2012;34(3):202-5
4. Bayer WL, Bodensteiner DC, Tilzer LL, Adams ME. Use of platelets and other transfusion products in patients with malignancy. Semin Thromb Hemost. 1992;18(4):380-91.
5. Slichter SJ, Davis K, Enright H, Braine H, Gernsheimer T, Kao KJ, et al. Factors affecting posttransfusion platelet increments, platelet refractoriness, and platelet transfusion intervals in thrombocytopenic patients. Blood. 2005;105(10):4106-14.
6. de Paula GG, Novaretti MC, Pozzi DH, Chamone DA. Estudo da refratariedade plaquetária do dia 0 ao 50, em pacientes submetidos a transplante de medula óssea. Rev Bras Hematol Hemoter. 2004;26(1):3-12
7. Ferreira AA, Zulli R, Soares S, Castro V, Moraes-Souza H. Identification of platelet refractoriness in oncohematologic patients. Clinics (Sao Paulo). 2011;66(1):35-40.
8. Lalezari P, Driscoll AM. Ability of thrombocytes to acquire HLA specificity from plasma. Blood. 1982;59(1):167-70.
9. Ferreira AA, Soares S, Castro V, Moraes-Souza H. Platelet transfusion: from empiricism to scientific evidence. Rev Bras Hematol Hemoter. 2010;32(4):335-6

xxx