Intricacies of GATA-ca, continued

We thank Lemaire *et al.* for continuing the call for attention to the issue of evanescence of red cell alloantibodies in sickle cell disease (SCD). Evanescence of anti-Fy3 is particularly relevant because approximately 68% of people of African descent have a Duffy red cell phenotype of Fy(a–b–) due to the GATA-1 mutation, which is otherwise present in < 1% of most ethnic populations. The risk of developing anti-Fy3 might be reduced by transfusing units that are Fy(a–), a phenotype present in only 34% of Caucasian but in 90% of Black donors. The Lemaire *et al.* cases demonstrate, however, that although production of anti-Fy^a is a risk factor for the development of anti-Fy3, it cannot necessarily be used as a predictive risk factor, since anti-Fy3 may develop in those in whom anti-Fy^a was never detected, possibly due to evanescence or timing of antibody screening. The development of multiple antibodies appears to be the greatest risk for making anti-Fy3. Review of unpublished cases from our laboratory over 10 years, and those in the literature (including the Lemaire *et al.* cohort) reveal a total of 80 cases of patients with anti-Fy3, of which 14 (18%) had only anti-Fy3 reactivity and 66 (83%) had additional red cell alloantibodies; 32 (48%) had no current anti-Fy^a detected. One might suggest that Fy(a–b–) red cells should be used for transfusion of all Fy(a–b–) patients, however this limits the transfusion options to units from minority donors, always in short supply, and G6PD deficiency, which is associated with decreased red cell survival, may be present in up to 20% of such units.[1,2] Unfortunately, it remains unexplained why some patients make anti-Fy3, as these patients have the GATA mutation associated with absence of risk for anti-Fy^b due to loss of expression on red cells, but Fy protein would be expressed in tissues. No genetic difference has been found in the coding region of the gene to explain production of anti-Fy3 (our unpublished observations).

The cases of Lemaire *et al.* also bring attention to measures not yet fully implemented that may improve blood availability and transfusion-related outcomes in patients with SCD. Should SCD patients undergo antibody screening approximately 1 month following transfusion in order to detect all clinically relevant alloantibodies (including anti-Fy3) that may evanesce? Can a universally accessible red cell alloantibody patient registry that maintains privacy compliance be established? Are there alternatives to transfusion for gene therapy support? What can be done to increase recruitment of minority donors, particularly donors of Black African descent? Do blood centers need to find a way to have extended antigen typing on all donors? In order to better preserve transfusion service budget allotment for antigen matching in SCD, can we reduce the use of phenotypically matched units in lower-risk patient populations, such as those on monoclonal antibody treatments like daratumumab?[3,4] Also key is the recruitment and training of technical staff to recognize complex alloantibodies in patients with SCD. We hope for more progress to be made in these areas for our patients undergoing transfusion for SCD in the years ahead.

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