Peer Review File

Article information: http://dx.doi.org/aob-20-63

Reviewer A

Comment 1: This manuscript had a number of minor edits needed to improve its clarity and readability. As someone like myself for whom English was also not their first language, this was a very good effort. Some sections required more editing than others. I have attached a PDF where I have included suggested edits.

Reply 1: Appreciate your guidance and revision. We have improved the English expression of our text according to your revised opinion.

Changes in the text: We have modified our text as advised (see Page1, line 20;Page2, line 46-47,53-54;Page3, line 64,73-77,80; Page4, line 96,101,109-111,114; Page6, line 164-178; Page7, line 186,210).

Comment 2: One correction that I did not always make in the PDF is the term "platelet antibodies", it is better to refer to "HLA and HPA antibodies" than to platelet antibodies because this would suggest to the novice reader that they are only referring to HPA antibodies when in fact they are referring to both HLA and HPA antibodies. Recall that HLA antigens are not specific to platelets but are expressed on all nucleated cells even though "HLA" stands for human leukocyte antigen. In fact, the majority (70% or more) of HLA antigens in the peripheral blood are found on platelets.

Reply 1: We fully agree with your statement about replacing “platelet antibodies” with “HLA and HPA antibodies”.

Changes in the text: We have modified our text as advised (see Page4, line 104-105).

Comment 3: It is important to also mention that patient ABO antibodies can also cause PTR, but rarely unless the ABO antibodies are very high titer due to the much

lower ABO antigen expression on platelets compared to RBCs. This might be less of an issue in China if most of the patients and donors are blood group O, but this might not be the case for some blood donors who are A or B when given to group O recipients, but again this is a very uncommon cause of PTR compared to HLA antibodies.

Reply 1: We fully agree with your opinion about the effect of ABO blood type in compatibility on PTR. Taking into account the low expression of ABO antigen on platelets, and the Technical Manual for Blood Transfusion of China requiring ABO blood type of the patients and donors be same in platelet transfusion, there are few cases of PTR due to incompatible ABO blood type infusion.

Changes in the text: We added a discussion about the effect of ABO blood type incompatibility on PTR (see Page3, line 82-87).

Comment 4: This is a very short but nice review that will introduce the reader to this topic and to be able to look at additional references if they want more information for the care of their patients. It is a large topic! One major omission in this paper is whether or not the authors in their hospital use leukocyte reduced blood for their patients. Also, what percentage of patients with AL develop PTR in their hospital? How does that compare to data in the literature? Are the rates similar?

Reply 1: In our hospital, all AL patients were mostly infused of leukocyte-filtered blood products. In our study, the incidence of immune PTR in AL was 25 %, which was near to N. Agarwal's reports of Indians and higher than C.A. Schiffffer reports of American. Killick, S.B reported that PTR occurred in 15%-25% of patients with thrombocytopenia in British. Differences in the probability of occurrence may be due to ethnic differences and diseases types, AL may has higher incidence of PTR.

Changes in the text: We have added the statement on the use of leukocyte-filtered blood products in our hospital (see Page6, line 167-168)**.** We added the incidence rate of PTR in AL patients of our hospital, and compared them to the data of some literature(see Page4-5, line 120-125)**.**

Reviewer B

Comment 1: The paper needs major English language editing to be suitable for publication.

Reply 1: Appreciate your guidance. We have improved the English expression of our text according to your guidance.

Changes in the text: We have modified our text as advised (see Page1, line 20; Page2, line 46-47,53-54; Page3, line 64,73-77,80; Page4, line 96,101,109-111,114; Page6, line 164-178; Page7, line 186,210).

Comment 2: I think the paper would benefit from a specific introduction to the topic at hand, highlighting the frequency of thrombocytopenia in patients with acute leukemia (at diagnosis and over the course of therapy) and the need for platelet transfusions. This would provide some background before immediately beginning discussion of PTR. The second paragraph of section 1 would mostly suffice for this.

Reply 1: We have added the background on acute leukemia , and pointed out that platelet transfusion was an important support for acute leukemia treatment.

Changes in the text: We have adjusted the background of acute leukemia to the first paragraph of section 1 of our text (see Page1-2, line 28-39).

Comment 3: I found the discussion about CD36 deficiency in section 2 confusing. Can the authors please clarify and explain more how this related to PTR.

Reply 1: Appreciate your guidance. The exposure of type I patients to CD36 antigen, such as multiple blood transfusions, pregnancy, will result in an alloimmune response to develope CD36 antibodies, which can destroy the transfused platelets through antigen-antibody reactions.

Changes in the text: We have added the statements about the relationship between CD36 antigens deletion and PTR (see Page4, line 94-96).

Comment 4: I am not at all convinced by the evidence provided regardingsubtypes of

leukemia and their differential rates of PTR. The authors should discuss the limitations of these studies (small numbers, multiple confounders, no confirmatory studies, lack of mechanistic explanation of why this would be the case)

Reply 1: We looked for more literature, such as Hu Xuelian's retrospective analysis showed that patients with core binding factor AML (CBF-AML) had higher risk to develop HLA-I antibodies and PTR. Indeed, there is not a large amount of literature that shows that the incidence of PTR is different in the subtypes of leukemia. However, most patients who need platelet transfusion in clinical are acute leukemia, our study mainly focuses on acute leukemia. At present, the researches in this field are only some retrospective analysis, in which the sample numbers are small, and the confounding factors are various. The researches of the mechanism of PTR in leukemia patients are also less, We need more in-depth researches.

Changes in the text: We have added the statements about the occurrence of PTR in the subtypes of leukemia (see Page5, line 144-149).

Comment 5: It would be helpful if the authors could provide a bit more information about how one should approach and potentially manage a patient with immunologic PTR. The authors mention steroids, IVIG, etc. It would be nice to expand upon any data for these approaches.

Reply 1: Up to now, there is still less literature of the application of glucocorticoids, high-dose gamma globulin, rituximab and other methods in treatment and management of PTR. We still need more in-depth research on the mechanism of immunological PTR, and find more effective prevention and treatment methods.

Changes in the text: We have added the statements about the treatment and management of PTR (see Page8, line 217-219).