

## One case of platelet donor selection for a platelet transfusion refractory patient of the ethnic minority descent

Tiejun Song, Jun Huang, Ying Zhang, Yingjian Wang, Yetao Han, Mengsi Hu, Zhiwei Liu\*

Department of Blood Bank, Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, Hangzhou, Zhejiang 310000, China

### INTRODUCTION

Immunologically mediated unresponsiveness to Platelet(PLT) transfusions mainly results from alloantibodies against human leukocyte antigen (HLA)-A and -B locus antigens, with rates ranging from 7% to 55% after platelet transfusion, depending on different study, patient population, and number and type of transfusions<sup>[1-2]</sup>. Individuals who are HLA homozygous might be expected to be more easily sensitized by exposure to non-self HLA antigens. At the same time, HLA homozygous patients to a great extent tend to be highly alloimmunized patients, making it more difficult to select HLA-matched PLTs. For these patients, the availability of HLA-selected platelets may be crucial. However in China, platelet donor selection by HLA matching is seldom used. In this report, a patient of an ethnic minority descent who is HLA homozygous with acute myeloid leukemia(AML) became refractory to platelet transfusions. By conducting a thorough search for HLA-matched platelet donor, good results were achieved.

### CASE REPORT

A 39-year-old female patient, whose grandmother is of the Hui minority, with a height of 157 cm and a

weight of 48 kg, blood group B, was hospitalized for AML. In the course of induction therapy, her platelet count was below  $20 \times 10^9/L$ . The patient had multiple infusion random donor platelets, however, all occurred refractory platelet transfusion. The platelet-reactive antibody screening result was positive. The patient has 5 times of pregnancy, 9 times of platelet transfusion. The patient had no symptoms of infection, fever, or splenomegaly.

### Platelet donor selection

None negative serological cross match result were found in 52 random donors, then screening was performed among 3 relatives, but none of the three relatives were matched with the patient HLA (**Table 1**). The search was carried out in the platelet gene database of Zhejiang Province Blood Center for this HLA-immunized patients, however only one of more than 3000 HLA-typed platelet donors was found to be HLA identical, together with seven acceptable HLA mismatch donors (**Table 2**). Match classification: according to the American platelet HLA grading standard, "A" indicates HLA identical; "BX" indicates acceptable HLA mismatch donors (with one cross antigens); "B2X" indicates acceptable HLA mismatch donors (with two cross antigens).

**Table 1** Patients and relative's HLA and HPA type

Person detected	HLA type		HPA type							
	HLA-A	HLA-B	HPA-1	HPA-2	HPA-3	HPA-4	HAP-5	HAP-6	HAP-9	HAP-15
Patient	A2,2	B38,40	aa	aa	bb	aa	aa	aa	aa	aa
Mother	A2,11	B27,38	aa	aa	bb	aa	aa	aa	aa	ab
Kinsfolk	A2,11	B27,46	aa	aa	ab	aa	ab	aa	aa	ab
kinsfolk	A11,11	B13,27	aa	aa	bb	aa	aa	aa	aa	ab

\*Correspondence to: Dr. Zhiwei Liu, Department of Blood Bank, Sir RunRun Shaw Hospital, School of Medicine, Zhejiang University, Hangzhou, Zhejiang 310000, China. E-mail: lzwsrrsh@163.com

Conflict of interests: The authors have declared no conflict of interests.

**Table 2** HLA-matched platelet donor searching results

Person detected	Type	Allele A1	Allele A2	Sero A1	Sero A2	Allele B1	Allele B2	Sero B1	Sero B2	classification
Patient	B	02: xx	-	2	-	38: xx	40: xx	38	61	/
Donor-1	B	02xx	-	2	-	38xx	40xx	38	61	A
Donor-2	B	02xx	-	2	-	40xx	-	60	61	BU
Donor-3	B	02xx	24xx	2	24	38xx	40xx	38	61	BX
Donor-4	B	02GDXE	02ENPR	2	-	39xx1	3909	3901	39	BUX
Donor-5	B	02FKXS	02FXXS	2	-	13EMCU	40FNKS	13	60	B2X
Donor-6	B	02xx	24xx	2	24	40xx	56xx	61	56	BUX
Donor-7	B	02xx	24xx	2	24	13xx	40xx	13	61	B2X
Donor-8	B	24xx	24xx	24	-	13xx	40xx	13	61	B2X

### Preparation and transfusion of platelet

Donor 1 underwent two collections; Donor 2 once. Response to platelet transfusions: patients were considered to be platelet refractory if they had a 1-hour post transfusion corrected count increment (CCI) of <7.5. The results are shown in **Table 3**. CCI was calculated as: Platelet Increment\*body-surface area (m<sup>2</sup>)/ platelets transfused (10<sup>11</sup>); body-surface Area was calculated as: 0.006 height (cm)+0.012 8 × weight (kg)-0.152 9.

### DISCUSSION

Alloimmunization to human leukocyte antigens (HLA) remains a major hurdle in achieving successful transplantation and is the primary cause of allo-immune platelet refractoriness<sup>[3]</sup>. The reported prevalence of detectable HLA antibodies in normal male and nulliparous female blood donors ranges from 1% to 17% and increases to 24%~53% in females with prior pregnancy<sup>[4]</sup>. The patient had five pregnancies and a history of nine platelet transfusions, and was

**Table 3** Response to platelet transfusions

Transfusion number	Dose (10 <sup>11</sup> )	Pretransfusion platelet count (10 <sup>9</sup> /L)	Post-transfusion platelet count (10 <sup>9</sup> /L)	CCI (1 h)	Success or not
1	4.75	8	69	18.2	yes
2	4.25	2	44	14.9	yes
3	3.25	7	45	16.6	yes

found platelet-reactive antibody positive. It has been reported that HLA-A \* 11: 0101(25.5%), HLA-A\* 02: 0101(13.5%), HLA-A\* 24: 0201(13.0%), HLA-B\* 40: 0101( 12.5%), HLA-B\* 46:0101( 10.0%), HLA-B\* 58: 01(8.5%) are the most common alleles in Zhejiang Han population<sup>[5]</sup>. The main problem for platelet transfusion in the patient of the ethnic minority descent was that no more than 3% of the population HLA genotype is A02,02 and B38,40. However, following a search for compatible platelet donor's gene pool in blood center, we were able to achieve good result through three platelet transfusions. Due to this it is strongly recommend to provide HLA-matched or compatible PLTs for patients who have developed HLA antibodies. This must however be supported by having an adequate number of HLA-typed platelet donors available to the blood center. In the event of no HLA identical donors being available, HLA-matched or HLA-partial-mismatched PLTs should be selected according to the serological Cross-Reactivity Groups (CREGs) matching strategy, which advocates the use of one or two mismatched

cross antigens as acceptable. Having HLA-matched samples prepared before hand would benefit patients facing and/or receiving frequent platelet transfusions. This would enable them to receive the appropriate platelets without delay, and may also be cost-effective to transfusion departments.

### Acknowledgments and funding

This study was supported by grant from Education Bureau of Zhejiang Province (grant number Y201636005) and grant from Health Bureau of Zhejiang Province (grant number 2016KYB154, 2017KY419).

### References

- [1] Pai SC, Lo SC, Lin Tsai SJ, et al. Epitope-based matching for HLA-alloimmunized platelet refractoriness in patients with hematologic diseases[J]. *Transfusion*, 2010, 50(11):2318–2327.
- [2] Jackman, P R. Low-level HLA antibodies do not predict platelet transfusion failure in TRAP study participants[J]. *Blood*, 2013, 121(16):3261–3266.
- [3] Peña JR, Saidman SL, Girouard TC, et al. Anti-HLA

- alloantibodies in surgical patients refractory to platelet transfusion[J]. *Am J Hematol*, 2014, 89(9):E133–E137.
- [4] Triulzi DJ, Kleinman S, Kakaiya RM, et al. The effect of previous pregnancy and transfusion on HLA alloimmunization in blood donors: implications for a transfusion-related acute lung injury risk reduction strategy[J]. *Transfusion*, 2009, 49(9):1825–1835.
- [5] Dai WJ, Li M. Analysis on HLA I class gene polymorphism of Han population in Zhejiang province[J]. *Chin J Transplant(Electronic Edition)*, 2011, 5(2):142–144.
- (Received 30 May 2018, Revised 07 June 2018, Accepted 10 June 2018)**