MALAYSIAN JOURNAL OF SCIENCE
MJS
ISSN 1394 - 3065

MAHSA International Medical Sciences and Technology Conference (Mi-Med) 2024

Special issue

Malaysian Journal of Science 44 (Special Issue 1): 39-42 (December 2025)

https://mjs.um.edu.my

A Patient with Platelet Transfusion Refractoriness

Wint Wint Thu Nyunt[1a*], Rabeya Yousuf[2b] and S Fadilah S Abdul Wahid[3c]

Abstract: Platelet transfusion refractoriness is a less-than-expected increase in platelet count following platelet transfusions. We report a case of platelet transfusion refractoriness with identification of anti-HLA class I alloantibody. In patients with thrombocytopenia, even when multiple established aetiologies are present, it is essential to recognise platelet transfusion refractoriness and to perform further laboratory investigations, including platelet immunology test. This approach enables identification of additional contributing factors to thrombocytopenia and clarification of the underlying causes of platelet refractoriness, thereby guiding appropriate therapeutic strategies.

Keywords: Alloantibody, platelet immunology test, platelet transfusion refractoriness, thrombocytopenia.

1. Introduction

Platelet transfusion refractoriness is characterized by a less-than-expected increase in platelet count after platelet transfusions (Cohn, 2020). We report a case of platelet transfusion refractoriness with identification of anti-HLA class I alloantibody in a patient with relapsed B-cell acute lymphoblastic leukaemia (B-ALL) post-transplant.

2. Case Report

In May 2017, a 39-year-old woman presented with anaemia, leucocytosis, and thrombocytopenia (platelets 29 x 10^9/L) and was diagnosed with B-ALL. She was married with two children. After receiving chemotherapy, she achieved complete remission.

In April 2018, she underwent allogeneic haematopoietic cell transplantation (allo-HCT) (human leucocyte antigen (HLA)-matched brother donor; both blood group B+). Secondary graft failure occurred on day +36 post-transplant. She received a second stem cell infusion in May 2018 and achieved complete remission. However, since allo-HCT, she had persistent thrombocytopenia and mild leucopenia.

In July 2021 (3 years+ post-allo-HCT), her disease relapsed. In September 2021, she was admitted for autologous chimeric antigen receptor T cell (CAR-T) therapy. She experienced febrile neutropenia and grade 1 cytokine release syndrome. Her platelet count prior to CAR-T therapy (day -6) was 53 x 10^9/L. During her hospital stay for CAR-T therapy, platelet counts displayed a decreasing trend (Figure 1).

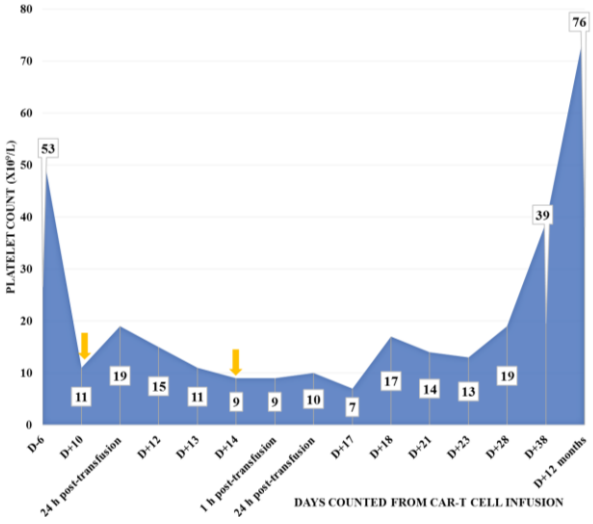

Figure 1. Trend of platelet counts in our patient. (Yellow arrow indicates platelet transfusion)

At day +10 post-CAR-T therapy, her platelet count dropped to 11 x 10^9/L, but she had no bleeding manifestations. Since she was a hospitalized patient with febrile neutropenia, she received platelet transfusion. The platelet count at 24 hours post-transfusion was 19 x 10^9/L, which did not meet the expected increment (Table 1; Figure 2).

Authors information:
[a]Department of Medicine, Faculty of Medicine, MAHSA University, Selangor, MALAYSIA. Email: tnwint@mahsa.edu.my[1]
[b]Blood Bank Unit, Department of Diagnostic and Laboratory Services, Hospital Canselor Tuanku Muhriz UKM, Kuala Lumpur, MALAYSIA. Email: rabeya@hctm.ukm.edu.my[2]
[c]Pusat Terapi Sel, Hospital Canselor Tuanku Muhriz UKM, Kuala Lumpur, MALAYSIA. Email: sfadilah@hctm.ukm.edu.my[3]

*Corresponding Author: tnwint@mahsa.edu.my

Received: April 11, 2025
Accepted: July 17, 2025
Published: December 12, 2025

DOI: https://doi.org/10.22452/mjs.vol44sp1.6
Malaysian Journal of Science 44 (Special Issue 1): 39-42 (December 2025)

Table 1. Assessment of platelet increment after platelet transfusions in our patient

Parameter therapy	Value at Day+10 post-CAR-T cell
Body weight	58 kg
Height	157 cm
Body surface area (Du Bois Method)	1.58 m^2
Platelet count before transfusion	11 $x10^9$/L
Platelet count at one hour post-transfusion	-
Platelet increment at one hour post-transfusion	-
Corrected count increment at one hour post-transfusion	-
Platelet count at 24 hours post-transfusion	19 $x10^9$/L
Platelet increment at 24 hours post-transfusion	8 $x10^9$/L
Corrected count increment at 24 hours post-transfusion	4,213

CCI-1h: corrected count increment within 10 minutes to one hour after transfusion. CCI-24h: corrected count increment at 24 hours after transfusion; PC: platelet count; PI: platelet count increment.

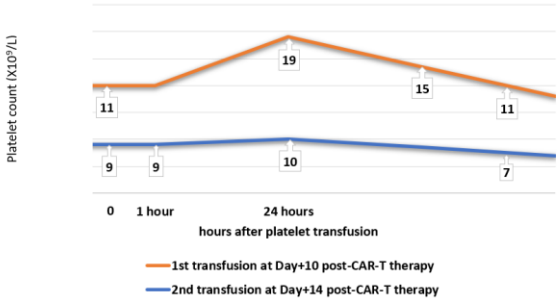

Figure 2. Response pattern to platelet transfusions in our patient.

The lack of the expected platelet count increase following transfusion led to suspicion of refractoriness to platelet transfusion.

Platelet count at day +14 post-CAR-T therapy was 9 x 10^9/L, but she had no bleeding manifestations. Apheresis platelets (one unit) were transfused, but a suboptimal response to platelet transfusion was observed (platelet counts were 9 x 10^9/L at one hour and 10 x 10^9/L at 24 hours after transfusion) (Table 1, Figure 2).

With the recognition of platelet refractoriness, her blood sample was sent to the laboratory to identify the alloimmune cause of platelet refractoriness. Platelet immunology test reported a positive result, with detection of platelet alloantibody with HLA class I specificity when testing the patient's serum against an allogeneic platelet antigen panel. During her hospital stay, she had no bleeding manifestations, and her platelet levels remained stable; hence, watchful observation was adopted with no prophylactic platelet transfusion. Platelet counts gradually increased over time (Figure 1).

Platelet count at day +28 post-CAR-T therapy was 19 x 10^9/L. Disease assessment at day +28 post-CAR-T therapy showed complete remission with incomplete haematologic recovery (CRi) and measurable residual disease (MRD) negativity.

Platelet count at 12 months post-CAR-T therapy was 76 x 10^9/L. Her disease status was complete remission with MRD negativity, and she was well.

3. Discussion

Our patient had pre-existing thrombocytopenia after allo-HCT, despite achieving complete remission. During her hospital stay for CAR-T cell infusion, the possible causes of thrombocytopenia were multifactorial: disease-related (relapsed B-ALL), therapy-related (chemotherapy-induced myelodysplasia, recent leucodepleting chemotherapy, and CAR-T therapy), and platelet refractoriness (anti-HLA class I alloantibody). Anti-HLA class I antibody confirmed an alloimmune cause, although non-immune factors such as fever may also have been present.

3.1 Platelet Transfusion

Prophylactic platelet transfusions are administered to reduce the risk of bleeding in patients with thrombocytopenia, undergoing chemotherapy or haematopoietic cell transplantation for haematologic malignancy, when the platelet count declines to 10 × 10^9/L (McCullough, 2010).

The standard dose of platelets is one unit of apheresis platelets or four to six units of pooled (random) platelets (McCullough, 2010). An apheresis unit contains ~3 x 10^{11} platelets, while a pooled unit contains ~0.55 x 10^{11} platelets (Davis et al., 1999). Transfusion of 1 × 10^{11} platelets in a 70-kg adult increases counts by ~10 × 10^9/L within one hour, and 3–4 × 10^{11} platelets raise counts by ~30–40 × 10^9/L (McCullough, 2010).

3.2 Response Patterns to Platelet Transfusion

For a normal response, platelet count increases after transfusion and gradually declines by approximately three days.

In non-immune refractoriness, an initial rise in platelet count is observed, but transfused platelets are rapidly removed from circulation, causing the count to return to baseline within 24 hours. This indicates normal platelet recovery with reduced survival. A pattern where the initial count rises but then decreases to baseline within 24 hours suggests a non-immune cause.

In alloimmune refractoriness, the platelet count shows little or no increase post-transfusion, indicating alloimmune destruction of transfused platelets. Little or no increase in platelet count after transfusion suggests an alloimmune cause. Our patient showed minimal increment post-transfusion, consistent with alloimmune refractoriness (Figure 2).

3.3 Platelet Transfusion Refractoriness

Platelet transfusion refractoriness is the failure to achieve the expected increase in platelet count after platelet transfusions on at least two consecutive occasions (Cohn, 2020). In our patient, platelet count increments were lower than expected after transfusions on two sequential occasions, and platelet refractoriness was identified.

Causes of platelet refractoriness are classified into alloimmune causes, such as anti-HLA antibodies or anti-HPA (human platelet antigen) antibodies, and non-immune causes, including fever, infection, bleeding, medications (e.g., Amphotericin B), graft-versus-host disease, or splenic sequestration (Cohn, 2020).

DOI: https://doi.org/10.22452/mjs.vol44sp1.6
Malaysian Journal of Science 44 (Special Issue 1): 39-42 (December 2025)

3.4 Evaluation of Platelet Transfusion Refractoriness

Platelet increment (PI) represents a rise in platelet count after transfusion.

PI = post-transfusion platelet count − pre-transfusion platelet count (1)

A PI of < 10×10^9/L on two consecutive transfusions suggests the presence of platelet refractoriness**.**

Corrected count increment (CCI) adjusts for patient body size and the number of transfused platelets (Davis et al., 1999; Cohn, 2020).

If the exact number of transfused platelets is unknown, 3×10^{11} platelets can be used.

$$CCI = PI \times \text{body surface area } (m^2) / \text{Platelets transfused } (\times 10^{11}) \quad (2)$$

In the TRAP study (Trial to Reduce Alloimmunization to Platelets Study Group, 1997), platelet transfusion refractoriness was defined as a ≤4-hour CCI of less than 5,000 following two consecutive transfusions of ABO-compatible platelets, at least one of which had been stored for no longer than 48 hours. Platelet transfusion refractoriness is considered present if two sequential CCIs are both below 5,000. Although most studies adopt a CCI threshold of 5,000, some authors accept a cut-off of less than 7,500 to define refractoriness (Cohn, 2020).

Analysing platelet count within 10 minutes to one hour after transfusion and platelet count at 24 hours after transfusion helps distinguish between immune and non-immune causes of platelet refractoriness. Typically, non-immune causes suggest a normal increase in platelet count immediately after transfusion (CCI-1h above 7,500), but a significant reduction in platelet count by 24 hours (CCI-24h below 5,000). Immune causes often show a lower immediate increase in platelet count (CCI-1h below 7,500) and a continued decrease at 24 hours. Our patient's CCI-1h and CCI-24h after two sequential platelet transfusions were less than 5,000, indicating alloimmune platelet transfusion refractoriness (Table 1).

3.5 Alloimmune Platelet Refractoriness

Alloimmunization involves the development of antibodies against antigens on transfused blood cells. This process can be triggered by prior exposure through pregnancy, blood transfusion, or haematopoietic cell transplantation. The antigens most frequently involved are those of the HLA system, expressed on platelets and leucocytes.

Platelet refractoriness is identified when a patient exhibits a suboptimal response to platelet transfusions on at least two occasions. When this inadequate response is caused by alloantibodies, it is classified as alloimmune platelet refractoriness.

Not all HLA alloimmunization causes refractoriness to platelet transfusion. Data from the TRAP study (n=530) showed that alloimmunization (HLA class I) occurred in 17% to 45% of patients depending on the platelets transfused. Platelet refractoriness was observed in 7% to 16%, and the subset with alloimmune refractoriness ranged from 3% to 13% (Trial to Reduce Alloimmunization to Platelets Study Group, 1997).

Alloimmunization accounts for a minority of cases of refractoriness to platelet transfusion. In the platelet dose (PLADO) trial, refractoriness to platelet transfusion developed in 14% of patients who received at least two platelet transfusions (102 of 734 patients) (Hess et al., 2016). Alloimmunization was present in only 8% (8 of 102) of documented cases of platelet refractoriness, suggesting that non-immune causes of platelet refractoriness were frequent. In contrast, alloimmunization contributed to platelet refractoriness less commonly (Hess et al., 2016).

Here, we report the occurrence of alloimmune platelet refractoriness with identification of anti-HLA class I alloantibody in a patient with relapsed B-ALL post-transplant.

3.6 Strategies to Prevent Platelet Refractoriness

Interventions to prevent platelet refractoriness include: (1) avoiding unnecessary blood transfusion, (2) transfusing ABO-identical or ABO-compatible platelets, (3) pre-storage leukoreduction of blood components, and (4) treating underlying conditions that contribute to platelet consumption and decreased platelet survival.

4. Conclusion

Even when multiple established causes are identified in patients with thrombocytopenia, it is essential to recognise platelet transfusion refractoriness and conduct further laboratory investigations, including platelet immunology test. This approach supports the identification of additional contributory factors to thrombocytopenia and clarifies the underlying causes of platelet refractoriness.

5. Acknowledgement

We acknowledge the CAR-T UKM research group, led by Prof. S. Fadilah Abdul Wahid, the Director of Plutonet Sdn. Bhd. (the principal sponsor of the CAR-T clinical trials) and his team, as well as the staff of Pusat Terapi Sel, MAKNA, and all haematologists involved, for their excellent teamwork in managing the patient. We thank the patient for providing informed written consent for the use of clinical data.

6. References

Cohn, C. S. (2020). Platelet transfusion refractoriness: how do I diagnose and manage? *Hematology 2014, the American Society of Hematology Education Program Book,* 2020(1): 527-532.

Davis, K. B., Slichter, S. J. & Corash, L. (1999). Corrected count increment and percent platelet recovery as measures of posttransfusion platelet response: problems and a solution. *Transfusion,* 39(6): 586-592.

Hess, J. R., Trachtenberg, F. L., Assmann, S. F., Triulzi, D. J., Kaufman, R. M., Strauss, R. G., Granger, S. & Slichter, S. J. (2016). Clinical and laboratory correlates of platelet alloimmunization and refractoriness in the PLADO trial. *Vox sanguinis,* 111(3): 281-291.

DOI: https://doi.org/10.22452/mjs.vol44sp1.6
Malaysian Journal of Science 44 (Special Issue 1): 39-42 (December 2025)

McCullough, J. (2010). Overview of platelet transfusion. *Seminars in hematology,* 47(3): 235-242.

Slichter, S. J., Davis, K., Enright, H., Braine, H., Gernsheimer, T., Kao, K. J., Kickler, T., Lee, E., McFarland, J., McCullough, J., Rodey, G., Schiffer, C. A. & Woodson, R. (2005). Factors affecting posttransfusion platelet increments, platelet refractoriness, and platelet transfusion intervals in thrombocytopenic patients. *Blood,* 105(10): 4106-4114.

Trial to Reduce Alloimmunization to Platelets Study Group. (1997). Leukocyte reduction and ultraviolet B irradiation of platelets to prevent alloimmunization and refractoriness to platelet transfusions. *New England Journal of Medicine,* 337(26): 1861-1870.

DOI: https://doi.org/10.22452/mjs.vol44sp1.6
Malaysian Journal of Science 44 (Special Issue 1): 39-42 (December 2025)