Case Report

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Management of Allosensitisation in Allogeneic Haematopoietic Stem Cell Transplantation: A Case Report

Transfusion Medicine Section

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ABSTRACT

In partially matched Stem Cell Transplantation (SCT), the presence of Donor-Specific Anti-HLA antibodies (DSAs) is a critical factor contributing to graft rejection. This is particularly challenging for patients with restricted donor availability who need rapid access to transplantation. Managing DSAs before transplantation is essential to improve engraftment success and overall transplant outcomes in these high-risk individuals. The use of partially HLA-mismatched donors is increasingly favoured in transplantation, particularly in cases where fully matched donors are scarce or when time-sensitive procedures are required. However, the presence of DSAs has emerged as a major barrier to effective engraftment, posing a threat to transplant viability. This case describes the application of a desensitisation protocol in a highly sensitised patient with DSAs exceeding 5000 Mean Fluorescence Intensity (MFI). The approach included alternate-day Plasma Exchange (PLEX), rituximab and Intravenous Immunoglobulin (IVIg), all administered before proceeding with a partially matched stem cell transplant. Post-transplant, neutrophil engraftment was achieved on day 17 and platelet engraftment on day 23, both slightly delayed relative to expected norms. Other than mild to moderate gastrointestinal and febrile symptoms, which were managed medically, no acute complications such as primary graft failure or Graft-versus-Host Disease (GvHD) were observed. At six-month follow-up, the patient demonstrated stable trilineage haematopoiesis with no evidence of relapse, graft failure, or chronic GvHD, highlighting the potential utility of desensitisation in overcoming DSA-mediated barriers to successful transplantation

Keywords: Desensitisation, Donor-specific anti-HLA antibodies, Partially matched stem cell transplantation, Mean fluorescence intensity

CASE REPORT

A 31-year-old male who was diagnosed with Acute Myeloid Leukaemia (AML) underwent numerous chemotherapy and radiotherapy cycles during the course of treatment for the past one year, done in an outside hospital, in addition to transfusion of non-leukofiltered and non-irradiated Packed Red Blood Cells (PRBC) and platelet products (over 20 products each) due to cost constraints. He had no known comorbidities. His blood group was A positive and his body weight was 70 kgs. Patient was advised for allogenic Haematopoietic Stem Cell Transplantation (HSCT). The stem cell donor was his younger sister, whose blood group was also A positive. For allogeneic HSCT, HLA typing was done, which showed a 7/12 match between the patient and donor at high-resolution levels for the HLA-A*, B*, C*, DRB1*, DQB1*, and DPB1* loci, which is a key factor in evaluating suitability for transplant procedures, as shown in [Table/Fig-1].

Pre-transplant Donor Specific Antibodies (DSA) were identified and expressed in terms of Mean MFI. Pre-transplant anti-Human Leucocyte Antigen (HLA) antibody screening revealed a class I panel reactive antibody (%PRA) of 24% and class II PRA of 44%. The highest donor-specific antibody MFI detected was 2895 for HLA class I (B*57:01) and 9359 for HLA class II (DPB1*09:01), as shown in [Table/Fig-2,3]. As the donor-specific antibodies MFI for this patient was above the critical value (>5000 MFI), the desensitisation protocol was followed for this patient.

The DSA desensitisation approach involved performing PLEX on alternate days for a total of three sessions (Days -14, -12 and -10), beginning two weeks before the planned transplant. The apheresis (cell separator) machine used for the procedure was COM.TEC Fresenius Kabi. Each session exchanged approximately 1 to 1.5 times the patient's plasma volume, using a combination of Fresh Frozen Plasma (FFP) and 5% human albumin for replacement,

PATIENT NAME	[redacted]	FIRM	HEMATOLOGY
HOSPITAL NO	[redacted]	METHOD	ILLUMINA NEXT – GENERATION SEQUENCING
REFERENCE NO	[redacted]	SAMPLE	WHOLE BLOOD EDTA
AGE/SEX	31 YRS/MALE	SAMPLE COLLECTED ON	30-09-2024
CLINICAL DIAGNOSIS	AML	TEST DONE ON	03-10-2024

PATIENT TYPING

LOCUS	HLA- A*	HLA –B*	HLA –C*	HLA –DPB1*	HLA -DQB1*	HLA -DRB1*
	A*02:01:01	B*07:06:01	C*06:02:01	DPB1*01:01:01	DQB1*06:01:01	DRB1*10:01:01
	A*11:01:01	B*37:04:02	C*07:02:01	DPB1*04:01:01	DQB1*05:01:01	DRB1*15:01:01
REMARKS	HLA-DPB1*01:01:01+HLA-DPB1*939:01 IS EQUALLY POSSIBLE. HLA-DPB1*04:01:01 +HLA-DPB1*1484:01 IS EQUALLY POSSIBLE. HLA-DPB1*1484:01 +HLA-DPB1*939:01 IS EQUALLY POSSIBLE.					

DONOR TYPING

DONOR NAME	[redacted]	AGE/SEX	28 YRS/FEMALE
HOS:NO	----	RELATIONSHIP	SISTER
REF:NO	[redacted]		

LOCUS	HLA- A*	HLA –B*	HLA –C*	HLA –DPB1*	HLA -DQB1*	HLA -DRB1*
	A*11:01:01	B*07:06:01	C*07:02:01	DPB1*09:01:01	DQB1*06:01:01	DRB1*15:01:01
	A*01:01:01	B*57:01:01	C*06:02:01	DPB1*01:01:01	DQB1*03:03:02	DRB1*07:01:01
REMARKS	HLA-DPB1*09:01:01 +HLA-DPB1*1484:01 IS EQUALLY POSSIBLE.					
COMMENT	7/12 MATCHED AT HIGH RESOLUTION (HLA-A*, B*, C*, DRB1*, DQB1* and DPB1* LOCUS)					

[Table/Fig-1]: HLA typing report of donor and patient.

as shown in [Table/Fig-4]. The replacement fluids during PLEX were selected based on established guidelines and patient safety considerations. No adverse events were noted during all three plasma exchange procedures.

PLEX was followed by Inj. Rituximab 50 mg in 50 mL NS over 1 hour, given as a test dose and Inj. Rituximab 325 mg in 325 mL NS over 5 hours the same day (day -9). A total of Rituxan 375 mg/m^2 was administered. This rituximab dose was selected based on a standard, evidence-based dose in transplant desensitisation protocols, proven to effectively deplete B cells and reduce donor-specific antibody production. One day later (day -8), a single dose of 70 grams of intravenous immunoglobulin (IVIg) was given (1 g/

PATIENT'S DETAIL		DONOR DETAILS	
PATIENT NAME	: [redacted]	DONOR NAME	: [redacted]
HOSPITAL NO	: [redacted]	HOSPITAL NO	: —
REFERENCE NO	: [redacted]	REFERENCE NO	: [redacted]
AGE/SEX	: 31 YRS/MALE	AGE/SEX	: 28 YRS/ FEMALE
CLINICAL DIAGNOSIS	: AML	RELATIONSHIP	: SISTER
FIRM	: HEMATOLOGY	SERUM COLLECTED ON	:30-09-2024

RESULT OF SINGLE ANTIGEN ASSAY PERFORMED ON:02-10-2024

CLASS I : STRONG POSITIVE | CLASS I: %PRA | 24

Donor specific Antibodies- Present

Antibody specificity	Mean Florescence Intensity
A*01:01	2644
B*57:01	2895

Non-Donor specific Antibodies- Present

Antibody specificity	Mean Florescence Intensity	Antibody specificity	Mean Florescence Intensity	Antibody specificity	Mean Florescence Intensity
B*15:12	15485	B*51:01	5515	B*52:01$	1388
B*44:03	14903	B*15:01	4693	B*15:03$	979
B*82:02	13919	B*15:02	4569	B*18:01$	843
B*44:02	13756	B*15:18	4136	B*46:01#	737
B*45:01	13273	B*35:01	3396	C*03:03#	601
B*50:01	10184	B*53:01	3375	B*14:02#	628
B*78:01	7219	B*35:08	3202	B*38:01#	552
B*15:16	6364	B*15:13	3099	C*03:04#	588
B*49:01	5783	B*58:01	1774		

[Table/Fig-2]: Class I antibody detection - donor-specific antibodies identified, with a maximum mean fluorescence intensity of 2895.

PATIENT'S DETAIL		DONOR DETAILS	
PATIENT NAME	: [redacted]	DONOR NAME	: [redacted]
HOSPITAL NO	: [redacted]	HOSPITAL NO	: —
REFERENCE NO	: [redacted]	REFERENCE NO	: [redacted]
AGE/SEX	: 31 YRS/MALE	AGE/SEX	: 28 YRS/ FEMALE
CLINICAL DIAGNOSIS	: AML	RELATIONSHIP	: SISTER
FIRM	: HEMATOLOGY	SERUM COLLECTED ON	:30-09-2024

RESULT OF SINGLE ANTIGEN ASSAY PERFORMED ON:02-10-2024

CLASS II: STRONG POSITIVE | CLASS II: %PRA | 44

Donor specific Antibodies- Present

Antibody specificity	Mean Florescence Intensity
DRB1*07:01$	983
DQB1*03:03	1957
DPB1*09:01	9359

Non-Donor specific Antibodies- Present

Antibody specificity	Mean Florescence Intensity	Antibody specificity	Mean Florescence Intensity	Antibody specificity	Mean Florescence Intensity
DRB1*04:02	15348	DPB1*04:02	7120	DRB1*14:01$	1310
DRB1*04:03	14945	DPB1*18:01	5501	DRB1*12:02$	1157
DRB1*04:04	14525	DRB1*08:01	2295	DRB1*03:01$	1086
DRB1*04:05	14386	DRB1*14:04	2067	DRB1*03:02$	1025
DRB1*04:01	13807	DRB1*08:02	1934	DRB1*03:03$	1024
DPB1*17:01	9453	DQB1*03:02	1812	DRB1*13:01$	1043
DPB1*06:01	7907	DRB1*11:04	1718	DRB1*12:01$	902
DPB1*28:01	7907	DRB1*11:01	1630	DRB1*13:05$	922
DPB1*14:01	7761	DRB1*11:03	1638	DRB1*15:03$	866
DPB1*03:01	7370	DQB1*03:01	1715	DRB1*14:03#	710
DPB1*02:01	7304	DRB1*13:03	1502	DRB3*01:01#	560

Note: The test assesses for specificities belonging to A, B, C, DR, DQ and DP loci.

[Table/Fig-3]: Class II antibody detection - donor-specific antibodies identified, with a maximum mean fluorescence intensity of 9359.

Plasma exchange	Cycle 1	Cycle 2	Cycle 3
Haematocrit (%)	23.8	22.7	26.5
Volume exchanged (mL)	4000 (1.1 PV)	5000(1.4 PV)	4500 (1.3 PV)
Replacement fluids	FFP - 4 5% HA - 3	FFP - 6 5% HA - 4	FFP - 6 5% HA - 4

[Table/Fig-4]: Plasma exchange parameters across three cycles. PV-Plasma volume; HA-Human albumin; FFP-Fresh frozen plasma.

kg). After three alternate-day cycles of PLEX, Inj. Rituximab and IVIg, no DSA was detected against HLA class II antigens of the donor, as shown in [Table/Fig-5,6]. In this case, the patient had an MFI level exceeding 5,000, but C1q testing was not performed prior to transplantation due to logistical challenges. However, following desensitisation treatment, C1q testing was conducted, and the result was found to be zero on screening, as shown in [Table/Fig-6].

Throughout the desensitisation protocol (including plasma exchange sessions, rituximab, and IVIg infusions), the patient was closely monitored for procedure- and drug-related adverse events.

- During plasma exchange: Vital signs (blood pressure, heart rate, respiratory rate, oxygen saturation, and temperature) were

Class II Single Antigen Bead (SAB) + C1q Screen Assay

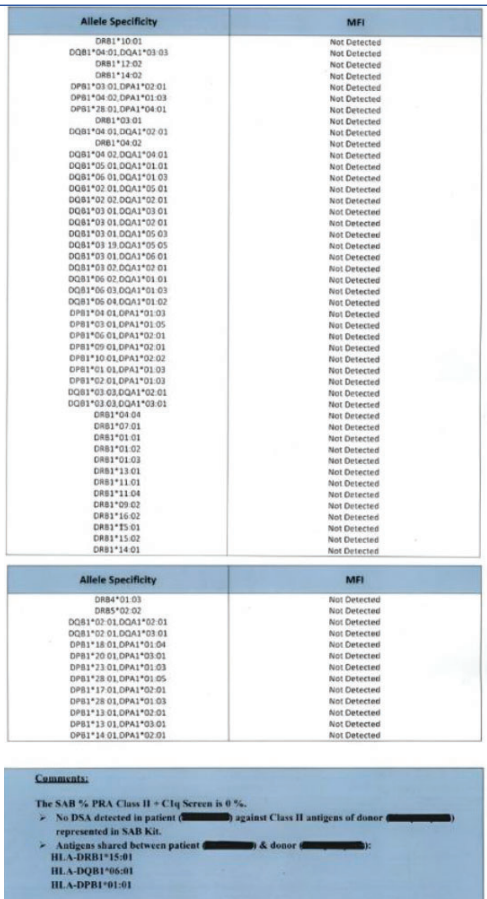
No Donor Specific Antibodies detected against HLA Class II antigens of donor [redacted]

No Antibodies detected against HLA Class II antigens tested with MFI > 1000.

Antibodies detected against HLA Class II antigens tested with MFI < 1000.

Allele Specificity	MFI
DRB1*04:01	20
DQB1*02:01,DQA1*04:01	Not Detected
DQB1*05:02,DQA1*01:02	Not Detected
DPB1*13:01,DPA1*02:02	Not Detected
DRB3*02:02	Not Detected
DRB4*01:01	Not Detected
DPB1*01:01,DPA1*02:01	Not Detected
DRB1*04:03	Not Detected
DPB1*19:01,DPA1*01:03	Not Detected
DPB1*11:01,DPA1*02:02	Not Detected
DQB1*03:02,DQA1*03:01	Not Detected
DPB1*15:01,DPA1*02:01	Not Detected
DQB1*06:02,DQA1*01:02	Not Detected
DRB1*04:05	Not Detected
DQB1*03:02,DQA1*03:03	Not Detected
DQB1*06:09,DQA1*01:02	Not Detected
DRB1*09:01	Not Detected
DPB1*18:01,DPA1*01:05	Not Detected
DRB1*12:01	Not Detected
DRB1*13:03	Not Detected
DPB1*11:01,DPA1*01:03	Not Detected
DRB3*01:01	Not Detected
DPB1*06:01,DPA1*01:03	Not Detected
DPB1*05:01,DPA1*02:02	Not Detected
DRB1*15:03	Not Detected
DRB1*03:02	Not Detected
DRB5*01:01	Not Detected
DPB1*03:01,DPA1*01:03	Not Detected
DPB1*18:01,DPA1*02:01	Not Detected
DQB1*04:02,DQA1*02:01	Not Detected
DQB1*03:03,DQA1*03:02	Not Detected
DPB1*05:01,DPA1*02:01	Not Detected
DRB1*08:01	Not Detected
DRB3*03:01	Not Detected
DRB1*16:01	Not Detected
DRB1*14:54	Not Detected

[Table/Fig-5]: Class II Single Antigen Bead (SAB) + C1q screen assay.



[Table/Fig-6]: No detectable Donor Specific Antibodies (DSA) in the patient and C1q screening was zero.

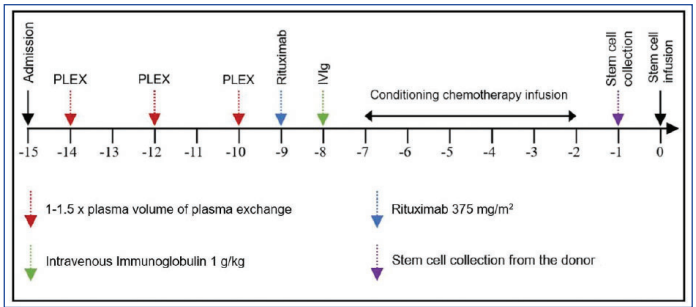
monitored at baseline, every 15 minutes during the procedures, and after completion. The patient was observed for signs of allergic reactions, hypotension, bleeding, electrolyte imbalances (such as hypocalcaemia), and symptoms suggestive of volume overload or transfusion reactions. Pre- and post-procedure laboratory tests included complete blood count, renal function, liver function tests, calcium, and coagulation profile.

- During Rituximab administration: Standard infusion protocols were followed with premedication (e.g., antihistamines and acetaminophen) as per institutional guidelines. The infusion was started at a low rate and escalated as tolerated. The patient was monitored for infusion-related reactions (fever, chills, rash, hypotension, bronchospasm) with continuous vital sign monitoring during and for one hour after infusion.

During IVIg infusion: Infusion was administered at the recommended rate, with close observation for adverse effects such as headache, flushing, hypotension, or anaphylaxis. Vital signs were monitored before, during, and after the procedure.

No adverse events or significant abnormalities were observed during any of the desensitisation steps.

The conditioning regimen was started for 5 days with Inj. Fludarabine 50 mg in 100 mL NS over one hour for five days (Days -7 to -3) and Inj. Melphalan 120 mg in 100 mL NS over one hour given on transplant day -2, as outlined in [Table/Fig-7]. One day before the stem cell transplant, Total Body Irradiation (TBI) was administered twice daily (BD) to the patient as part of the conditioning regimen. The patient was closely monitored for regimen-related toxicity during and following administration of fludarabine, melphalan, and total body irradiation. No severe oral mucositis or gastrointestinal toxicity was observed and no modifications to the conditioning regimen were required due to toxicity.



[Table/Fig-7]: Desensitisation protocol from day -15 to 0.

The specific dosing of fludarabine and melphalan aligns with standard care in allogeneic HSCT, where fludarabine is dosed according to body weight and renal function to optimise immune suppression and engraftment while minimising toxicity. Melphalan dosing is similarly individualised, balancing anti-leukemic potency with the patient's tolerance and organ function. The TBI schedule (twice daily on day -1) was chosen to ensure effective marrow ablation and immunosuppression.

On day 0, Peripheral Blood Stem Cell (PBSC) collection was performed, and a total of 280 mL of stem cell product was harvested. Midway CD34+ cell count in the apheresis product was 2620 cells/µL, as shown in [Table/Fig-8], which is significantly above the typical midway reference range of 100-1000 cells/µL. This indicates excellent mobilisation and a high-yield collection, as midway CD34+ enumeration serves as a valuable intra-procedural quality indicator for estimating product adequacy in real-time. From the total collected volume, 200 mL was selected for infusion, delivering a CD34+ cell dose of 7.4 × 10^6 cells/kg, which is well above the minimum threshold of ≥2 × 10^6 cells/kg and exceeds the optimal target of ≥5 × 10^6 cells/kg for allogeneic transplantation, supporting favourable engraftment. Despite this adequate dosing, neutrophil and platelet engraftment were delayed, occurring on day 17 and day 23, respectively—beyond the typical engraftment windows of day 10-14 for neutrophils and day 14-21 for platelets in peripheral blood stem cell transplants. This delay is likely attributable to the presence of DSAs prior to transplant.

During the post-transplant course, the patient received 5 units of irradiated, leucofiltered PRBCs and 7 units of irradiated Single Donor Platelets (SDPs), administered only when platelet counts dropped below 10,000/µL, in order to minimise the risk of alloimmunisation and re-sensitisation. The patient's early post-transplant period was marked by mild-to-moderate gastrointestinal and febrile symptoms, which responded well to standard medical therapy.

INVESTIGATIONS	RESULT
Total WBC count	196,000 cells/µL
Total Mononuclear cells	59%
Viability %	99.4%
Viable CD34 count	2620 cells/µL
CD34 %	1.22%

NOTE: CD34+ cells are isolated and enumerated based on modified International society of Hematotherapy and Graft engineering (ISHAGE) guidelines. Reference given below.

Stem cell dose shall be calculated from the absolute viable CD34 count given in cell per microlitre.

REFERENCE: Sutherland DR, Anderson L, Keeney M, Nayar R, Chin-Yee I. Single platform flowcytometric absolute CD34 counts based on the ISHAGE guidelines. The ISHAGE guidelines for CD34+ cell determination by flowcytometry - International society of Hematotherapy and Graft Engineering.J Hematother.1996 Jun;5(3):213-26.

[Table/Fig-8]: Midway CD34 count.

No major complications such as severe infections, GVHD, or organ toxicity were observed, indicating the safety of the desensitisation and conditioning protocols used. The patient showed steady clinical improvement and was discharged in stable condition one month after transplantation. On long-term follow-up at 6 months, the patient maintained sustained trilineage haematopoiesis, with no evidence of graft failure, GvHD, or disease relapse, and continued to undergo routine surveillance with blood counts, chimerism studies, and viral monitoring.

DISCUSSION

Allogeneic SCT represents a potentially curative treatment for various hematologic cancers. However, the likelihood of locating an HLA-matched sibling donor is limited to around 25%. While global registries of HLA-typed volunteer donors exist, nearly 40% of patients are unable to secure a fully matched donor in time to meet their clinical requirements. In such cases, alternative donor sources such as partially matched unrelated donors, partially matched family members, and umbilical cord blood units are considered [1].

The degree of HLA matching and the existence of antibodies against HLA molecules are closely associated with both graft rejection and patient survival. One major obstacle arises when antibodies specifically recognise and attack donor HLA antigens on the mismatched haplotype, significantly increasing the risk of Primary Graft Failure (PGF) and negatively impacting post-transplant survival. Addressing these alloimmune responses before transplantation is crucial to enhance graft acceptance and improving long-term patient outcomes.

To lower the risk of PGF, several desensitisation strategies have been suggested. One notable protocol, originally introduced by Ciurea SO et al., outlines a comprehensive approach that includes four core strategies: 1) eliminating circulating antibodies through plasmapheresis; 2) suppressing antibody formation by depleting CD20+ B cells using rituximab; 3) neutralising existing antibodies with Intravenous Immunoglobulin (IVIg) and 4) blocking the activation of the complement system. Implementing these combined interventions has shown promise in improving engraftment rates and transplant success among patients with high-risk DSAs [2].

Unlike the Ciurea SO et al., [2] protocol, which incorporates complement blockade as a fourth pillar of desensitisation, blocking

complement activation was not utilised in this case, primarily due to financial constraints. This desensitisation approach focused primarily on the removal of circulating DSAs via plasma exchange, suppression of antibody production through rituximab-mediated B-cell depletion, and neutralisation of residual antibodies with IVIg.

High levels of DSAs, particularly those with an MFI above 5000, are strongly linked to complement activation detected through the C1q assay. This interaction is widely regarded as the leading cause of engraftment failure in patients undergoing allogeneic haematopoietic stem cell transplantation. Monitoring both DSA strength and their ability to fix complement is essential for predicting transplant success and guiding desensitisation strategies prior to transplantation [3]. To highlight the clinical relevance of this challenge, a brief literature review of desensitisation strategies from different studies has been included as shown in [Table/Fig-9] [4-7].

Study	Antibodies	Desensitisation Strategy	Outcome	Key Insight
Yoshihara S et al., [4]	HLA-DSA	Rituximab, plasma exchange, platelet infusion, bortezomib	Delayed engraftment/ failure in high MFI	MFI >5,000 associated with graft failure; lineage-specific rejection
Chang YJ et al., [5]	HLA-DSA	Variable; >80% had no desensitisation	DSAs significantly increased graft failure (3.2% vs. 31.6% vs. 60% for low, moderate, and high DSA levels)	DSAs, especially C1q+, independently associated with graft failure
Barge A et al., [6]	ABO, HLA	Plasma exchange alone	Host anti-donor antibodies can cause marrow failure after BMT, from erythroid hypoplasia to graft failure.	Even weakly reactive anti-HLA can mediate rejection
Ciurea SO et al., [7]	HLA-DSA	Plasma exchange, Rituximab, IVIG, irradiated buffy coat infusion, MFI monitoring	C1q+ → high graft failure risk; improved with desensitisation, >80% engraftment in high-risk	Strong evidence for antibody-directed desensitisation, C1q+/MFI >10,000, require aggressive protocol

[Table/Fig-9]: Brief literature review of desensitisation strategies from different studies [4-7].

This report describes the experience with desensitisation treatment in a partially matched SCT patient with DSA, conducted at a tertiary care hospital in India, using the treatment protocol described by Ciurea et al.

Despite the detection of high-level donor-specific antibodies (MFI >5000) against the intended haploidentical sibling donor, alternative donor options were limited in this patient due to the absence of fully matched related or unrelated donors and the urgency to proceed with transplantation for refractory AML. The decision to use the haploidentical sibling donor was guided by:

- The donor's good health, ABO compatibility, and availability for mobilisation and collection.
- The feasibility of applying an established desensitisation protocol (PLEX, Rituximab, and IVIg) with close post-procedure monitoring.
- Literature evidence supporting acceptable engraftment rates in DSA-positive haploidentical transplants when DSA levels are reduced below clinically significant thresholds pre-transplant.
- Institutional experience and multidisciplinary consensus (haematology, apheresis, transfusion medicine, and transplant teams) favouring timely transplantation over prolonged donor search, which could risk disease progression.
- The combined approach of targeted desensitisation, high-dose stem cell infusion, and intensified monitoring helped achieve complete DSA clearance prior to conditioning and successful engraftment, despite initial immunological risk.

Donor-specific antibodies (DSAs) are now widely acknowledged as a leading contributor to primary graft rejection, affecting outcomes in both solid organ transplants and allogeneic haematopoietic stem cell transplants, particularly those with HLA mismatches. Initial findings from the MD Anderson Cancer Centre established a clear link between the presence of DSAs and the risk of PGF in patients receiving partially matched transplants [2,3]. Since then, various studies have reaffirmed this link and implicated DSAs in the failure of engraftment in both partially matched and other HLA-mismatched stem cell transplant settings. These discoveries underscore the importance of early detection and management of DSAs to improve engraftment and overall transplant success in mismatched donor scenarios [2-5].

In a landmark study by Ciurea et al., involving 122 recipients of partially matched stem cell transplants, a clear connection between DSA presence and PGF was established. Among the participants, 18% had detectable DSAs, and nearly one-third of them (32%) experienced PGF, compared to only 4% in those without DSAs. Moreover, engraftment was delayed in DSA-positive patients, averaging 19 days versus 18 days for those without antibodies [3]. This case reflected similar findings, with neutrophil engraftment on day 17 and platelet engraftment on day 23, highlighting the impact of DSAs on the engraftment timeline. This pattern of delayed haematopoietic recovery suggests that even in the absence of outright graft failure, DSAs can significantly prolong the engraftment phase and delay haematologic recovery.

Defining DSA positivity often involves using an MFI cutoff of 1,000, though this threshold can vary across labs. While rejection may occur with any detectable DSA, the likelihood of PGF increases significantly when MFI levels exceed 5,000. For example, patients with DSAs below this level face a 9% rejection rate, whereas this risk escalates to 32% in those with higher MFI values. [3]. A strong correlation has also been found between high MFI DSAs and complement-binding activity. This indicates that patients with high antibody levels may benefit from additional evaluation with the C1q assay [3,4]. In this case, although initial C1q testing was not possible, post-desensitisation results showed no complement-binding activity. Incorporating complement-binding assays into routine evaluation of DSAs may enhance risk stratification and inform tailored desensitisation approaches.

The IVIg dosing was chosen based on its established role in DSA desensitisation protocols, where a single high dose (1-2 g/kg) can rapidly block Fc receptor-mediated antibody effector functions, neutralise circulating alloantibodies, and modulate B-cell activity [2-4]. In this case, 1 g/kg was deemed sufficient to achieve post-PLEX immune modulation while minimizing potential volume overload and thromboembolic risks in the peri-transplant period.

Yoshihara and colleagues conducted a study involving 79 partially matched HSCT patients, discovering that 20.2% had anti-HLA antibodies, with 11 individuals exhibiting donor-specific reactivity. These patients showed significantly lower rates of neutrophil (61.9% vs. 94.4%) and platelet engraftment (28.6% vs. 79.6%). Importantly, multivariate analysis identified DSA levels exceeding 5,000 MFI as the only independent predictor of graft failure [4]. This case similarly involved a patient whose pre-desensitisation DSA level surpassed 9,000 MFI, corresponding with delayed engraftment. These results highlight the predictive value of DSA intensity and support MFI thresholds as a practical marker for risk stratification in partially matched HSCT candidates.

Chang YJ et al., found a strong association between DSAs and both PGF and poor engraftment in patients receiving unmanipulated

partially matched HSCT. Out of the 345 patients who were evaluated, 87 (25.2%) had anti-HLA antibodies, with 39 (11.3%) having DSAs. Patients with DSA levels measuring an MFI of 2000 or higher were found to have a notably increased risk of poor graft function compared to those with lower antibody levels (27.3% vs. 1.9%) [5]. Here, the patient's DSA level was above this threshold, which corresponded with a delayed recovery of graft function. These findings reinforce that even moderately elevated DSAs may compromise engraftment, supporting the need for intervention well before reaching high-risk MFI levels.

Ciurea SO et al., also reported that anti-HLA antibodies are found in up to 20% of patients undergoing allogeneic HSCT, especially those receiving HLA-mismatched grafts. However, only a subset of these antibodies is donor-specific. Using advanced immunoassays, DSAs have been identified in up to 2% of transplant recipients [8]. Importantly, graft failure occurred in 37.5% of patients with DSAs compared with only 2.7% in those without, highlighting their clinical relevance [8]. Notably, the incidence of DSAs is much higher in women, particularly those with a history of multiple pregnancies, due to sensitisation against foetal HLA antigens [2,3,8,9]. Transfusions further increase this risk by introducing foreign HLA, particularly through leucocyte- and platelet-rich products [4-5]. In this patient, repeated transfusions with unfiltered and non-irradiated products likely contributed to the development of DSAs. These insights highlight the need for preventive strategies, including leukoreduction and irradiation of blood products, especially in heavily transfused patients.

Selecting a donor with no shared HLA antigens targeted by the patient's DSAs is ideal, as antibodies against unrelated HLA antigens do not increase the risk of PGF. However, due to donor availability and time constraints, this option is not always practical. Consequently, a variety of desensitisation protocols have been developed to lower DSA levels and facilitate engraftment even in the presence of incompatibility. Donor selection strategies, although preferred, must often be supplemented with aggressive desensitisation to overcome time-sensitive clinical needs [8,9].

Plasmapheresis remains a cornerstone of desensitisation in both solid organ and haematopoietic transplants. Yet, its use alone has shown limited efficacy in HSCT. For instance, in an early report by Barge A et al., a patient undergoing plasmapheresis alone still experienced graft failure. More recently, combined regimens have gained popularity, such as the MDACC protocol using plasmapheresis, rituximab and IVIg. This approach, used in five HSCT patients with DSAs, aimed to neutralise both class I and II antibodies [6]. Similarly, in this case, immunomodulatory treatments were given to reduce the antibody-mediated rejection.

According to Ciurea SO et al., patients with persistently high DSAs or ongoing complement activation (C1q positive) at transplant time may face unacceptably high risks of graft failure and should either be excluded or considered for alternative therapies [7]. In this case, although the patient was C1q negative, delayed engraftment still occurred, suggesting that DSA-related complications may arise even in the absence of active complement fixation. This underscores the multifactorial nature of engraftment failure, where non-complement pathways and other immune mechanisms may also play significant roles.

Plasma exchange (PLEX) is generally safe but necessitates close monitoring of vital signs, fluid balance, electrolytes, and potential allergic reactions to ensure patient safety during desensitisation before stem cell transplantation. In this case, all sessions were uneventful, underscoring the importance of pre-procedural planning and multidisciplinary oversight.

The choice of replacement fluids was guided by the following considerations:

- **Fresh Frozen Plasma (FFP)** was selected to replenish coagulation factors, particularly in the setting of repeated large-volume exchanges, to minimise bleeding risk before transplantation.
- **5% human albumin** was used to maintain oncotic pressure, reduce the risk of volume overload, avoid unnecessary exposure to additional donor plasma components and lower the risk of allergic/transfusion reactions.

The combination approach aligns with the American Society for Apheresis (AFSA) and British Society for Haematology guidelines, which recommend tailoring fluid replacement based on the patient's clinical status, baseline coagulation profile, total volume exchanged, and anticipated risk of bleeding.

Routine laboratory monitoring of haematologic parameters and DSA levels is crucial to guide treatment efficacy and readiness for transplant. Effective coordination between departments, including Transfusion Medicine, Haematology, and Nursing, was essential for scheduling PLEX, administering Rituximab and IVIg, and aligning with the transplant timeline. Although PLEX comes at a cost, including the consumables, albumins and FFPs (approximately INR 1.5 lakhs inclusive of all three cycles), its role in preventing graft failure justifies the expense, particularly benefits in high-risk sensitised patients [10].

Panel Reactive Antibody (PRA) percentages reflect the overall sensitisation of the patient to a broad panel of HLA antigens [11]. In this case, the patient had a PRA of 24% for Class I and 44% for Class II, indicating moderate sensitisation. However, more importantly, DSAs were identified against the sibling donor's HLA antigens, showing Class I DSA (maximum MFI of 2895) and Class II DSA (maximum MFI of 9359), both strongly positive, indicating a strong alloimmune response against donor antigens. While PRA reflects general sensitisation to a population of antigens, DSA detection is more clinically significant as it directly indicates a risk of graft rejection in transplantation.

This case report is limited by its single-patient design and the absence of pre-transplant C1q testing, which restricted the assessment of complement-fixing donor-specific antibodies at baseline. Additionally, cost-related factors impacted the extent and timing of desensitisation and supportive care, which may affect the generalisability of the findings. These limitations underscore the need for larger, prospective studies with comprehensive immunologic monitoring to refine desensitisation strategies and improve transplant outcomes.

Early identification and comprehensive characterisation of DSAs, including assessment of MFI and complement-binding capacity (e.g., C1q assays), are essential for effective risk stratification in haploidentical stem cell transplantation. Multimodal desensitisation protocols—typically incorporating plasmapheresis, rituximab, and IVIg—have shown efficacy in reducing DSAs and improving engraftment outcomes. In cases with persistent complement-fixing antibodies, complement inhibition may be warranted. Successful implementation of desensitisation strategies requires close interdisciplinary collaboration to ensure safe administration and ongoing monitoring. Importantly, effective DSA management can expand donor options and enable transplantation with partially matched donors.

CONCLUSION

In summary, a comprehensive desensitisation strategy combining plasmapheresis, rituximab and IVIg has proven effective in reducing the risk of DSA-related complications in partially matched haematopoietic stem cell transplantation. This multimodal approach not only improves compatibility between donor and recipient but also enhances overall transplant success and long-term survival. Future advancements in individualised immunologic profiling and early DSA detection may further refine these protocols and optimise patient outcomes in partially matched HSCT.

REFERENCES

[1] Bramanti S, Calafiore V, Longhi E, Mariotti J, Crespiatico L, Sarina B, et al. Donor-specific anti-HLA antibodies in haploidentical stem cell transplantation with post-transplantation Cyclophosphamide: Risk of graft failure, poor graft function, and impact on outcomes. Biol Blood Marrow Transplant. 2019;25(7):1395-406.

[2] Ciurea SO, De Lima M, Cano P, Korbling M, Giralt S, Shpall EJ, et al. High risk of graft failure in patients with anti-HLA antibodies undergoing haploidentical stem-cell transplantation. Transplantation. 2009;88:1019-24.

[3] Ciurea SO, Thall PF, Milton DR, Barnes TH, Kongtim P, Carmazzi Y, et al. Complement-binding donor-specific anti-HLA antibodies and risk of primary graft failure in hematopoietic stem cell transplantation. Biol Blood Marrow Transplant. 2015;21:1392-98.

[4] Yoshihara S, Maruya E, Taniguchi K, Kaida K, Kato R, Inoue T, et al. Risk and prevention of graft failure in patients with preexisting donor-specific HLA antibodies undergoing unmanipulated haploidentical SCT. Bone Marrow Transplant. 2011;47:508-15.

[5] Chang YJ, Zhao XY, Xu LP, Zhang XH, Wang Y, Han W, et al. Donor-specific anti-human leukocyte antigen antibodies were associated with primary graft failure after unmanipulated haploidentical blood and marrow transplantation: A prospective study with randomly assigned training and validation sets. J Hematol Oncol. 2015;8:84.

[6] Barge A, Johnson G, Witherspoon R, Torok-Storb B. Antibody-mediated marrow failure after allogeneic bone marrow transplantation. Blood. 1989;74:1477-80.

[7] Ciurea SO, Malki MMA, Kongtim P, Zou J, Aung FM, Rondon G, et al. Treatment of allosensitised patients receiving allogeneic transplantation. Blood Adv. 2021;5:4031-43.

[8] Ciurea SO, Thall PF, Wang X, Wang SA, Hu Y, Cano P, et al. Donor-specific anti-HLA Abs and graft failure in matched unrelated donor hematopoietic stem cell transplantation. Blood. 2011;118:5957-64.

[9] Ciurea SO, Bayraktar UD. "No donor"? Consider a haploidentical transplant. Blood Rev. 2014;29:63-70.

[10] Padmanabhan A, Connelly-Smith L, Aqui N, Balogun RA, Klingel R, Meyer E, et al. Guidelines on the use of therapeutic apheresis in clinical practice - Evidence-based approach from the Writing Committee of the American Society for Apheresis: The Eighth Special Issue. J Clin Apher. 2019;34(3):171-354.

[11] Tait BD, Süsal C, Gebel HM, Nickerson PW, Zachary AA, Claas FHJ, et al. Consensus guidelines on the testing and clinical management issues associated with HLA and non-HLA antibodies in transplantation. Transplantation. 2012;95(1):19-47.

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