Platelet transfusion refractoriness cases referred to NHSBT Filton for human platelet antibody (HPA) investigations: 2020-2021

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Introduction

Platelet transfusion refractoriness (PTR) is the failure to increment to random ABO blood group donor platelets within 24 hours on two separate occasions. A number of adverse clinical conditions are associated with PTR, such as increased bleeding time and decreased patient survival.

Approximately, 80% of PTR cases are caused by non-immune factors[1] e.g. sepsis or disseminated intravascular consumption. Up to 50% of PTR cases are due to immunological factors[1] caused by alloantibodies directed against the human leukocyte antigens (HLA) class I, human platelet antigens (HPA) or both.[1] However, antibodies to HPA in isolation are rare and equate to <1% of PTR cases.[2]

Methods

HLA antibody testing was performed by Luminex bead-based assay using LSM12 screening and LS1A04 single antigen class I identification kits (One Lambda). HPA antibody identification were carried out using the platelet immunofluorescence test (PIFT), monoclonal immobilisation of platelet antigen assay (MAIPA) and the Luminex bead-based assay PakLx (Immucor). All results are immunoglobulin G (IgG) class.

Aim

In this audit we aim to define the number of HLA class I and HPA antibody specificities detected in this patient group.

Table 1. Results for PTR Patient Referrals

	Total	% Total	Female	% Female	Male	% Male
HLA class I Antibody Positive	**118**	**48.6**	76	66.0	42	32.8
HLA class I Antibody Negative	**125**	**51.4**	39	34.0	86	67.2
HPA Antibody Negative	**226**	**92.2**	103	89.5	123	94.6
HPA Antibody Positive:	**19**	**7.8**	12	10.4	7	5.3
- **Anti-GPIIb/IIIa**	**6**	**2.4**	3	2.6	3	2.3
- **HPA-1b**	**6**	**2.4**	4	3.4	2	1.5
- **Anti-GPIb/IX**	**2**	**0.8**	0	0	2	1.5
- **HPA-1a**	**1**	**0.4**	1	0.8	0	0
- **HPA-1b & 2a**	**1**	**0.4**	1	0.8	0	0
- **HPA-5b**	**1**	**0.4**	1	0.8	0	0
- **HPA-15a**	**1**	**0.4**	1	0.8	0	0
- **HPA-1b, 2b & 5b**	**1**	**0.4**	1	0.8	0	0

Results

Overall, 256 referrals were received between February 2020 and February 2021. Thirteen samples were not tested or inconclusive and were therefore excluded. False positive HLA antibody specificities were observed by Luminex (e.g. HLA-A80, B37, B57, B58, B73) and reported as negative. Following these exclusions, 243 (HLA) and 245 (HPA) referrals were analysed (table 1), HLA class I antibodies were found in 118 (48.6%) patients whereas 125 (51.4%) were HLA class I antibody negative. HPA antibodies were found in 19 (7.8%) patients, conversely 226 (92.2%) were HPA antibody negative. The most common platelet specific antibodies were isoantibodies to glycoprotein (GP) IIb/IIIa and HPA-1b, n=6 (2.4%). Only two referrals (0.8%) were HPA antibody positive in the absence of HLA class I antibodies.

Discussion

These data further highlight the rarity of HPA antibodies in PTR. HPA alloimmunisation is usually in addition to HLA antibodies. In accordance with previous reports[2,3], HPA antibodies without HLA class I antibodies in this cohort were extremely rare (n=2, 0.8%)**.** This evaluation reinforces the practice of HLA testing preceding HPA testing, apart from in exceptional clinical circumstances, where investigations can be initiated simultaneously. The transfusion of HLA and/or HPA selected platelets is an established and effective treatment strategy in PTR patients, improving clinical outcomes including bleeding frequency, severity, morbidity or mortality.[3] Where both HLA class I and HPA antibodies are present, HPA matching should be prioritised. One of the more common platelet specific antibody detected in this cohort was anti-GPIIb/IIIa to which it is not possible to provide matched platelets due to it's expression on platelets. Whereas, it is possible to provide HPA platelet matched units for patients with HPA-1b antibodies because approximately 85% of the White population possess the HPA-1a1a phenotype.

Key references

1. Brown C. Guidelines for the Management of Platelet Transfusion Refractoriness. Accessed on 15/12/2020. https://nhsbloodandtransplant.sharepoint.com/:w:/r/sites/ControlledDocumentsLibrary/_layouts/15/Doc.aspx?sourcedoc=
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