The clinical use of leucocyte – depleting filters in the multiply transfused patients – a case report

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Summary
The successful use of bedside leucocyte depleting filters for the transfusion of packed red cells and platelet concentrates in a patient requiring multiple transfusions for the prevention of non-haemolytic febrile transfusion reactions (NHFTR) is described.

Key words: Non-haemolytic febrile transfusion reactions, multiple transfused patients, bedside leucocyte removal filters for packed red cells and platelet concentrates

Introduction
The most frequent cause of non-haemolytic febrile transfusion reaction (NHFTR) is the coincidental administration of leucocytes during the transfusions of blood and blood products resulting in needless patient discomfort and wasted blood.[1] As there is a rising number of patients on multiple transfusions of blood and blood products, there is also a rising number of NHFTR seen, all of which may not be reported for investigations. At the Blood Services Centre, GHKL, the number of NHFTR reported was 118 out of 56976 transfusion cases in 1986, 150 out of 61300 in 1987, 156 out of 74609 in 1988 and 251 out of 88288 in 1989, an increasing trend. However, in 1990 there were 84892 transfusions performed with 211 cases of NHFTR recorded, a decrease in number of NHFTR due to the introduction of leucocyte poor packed red cells and filtered blood for transfusion[2] (Refer to Table I).

Table I
Reported transfusion reactions at the Blood Services Centre GHKL in the last 5 years

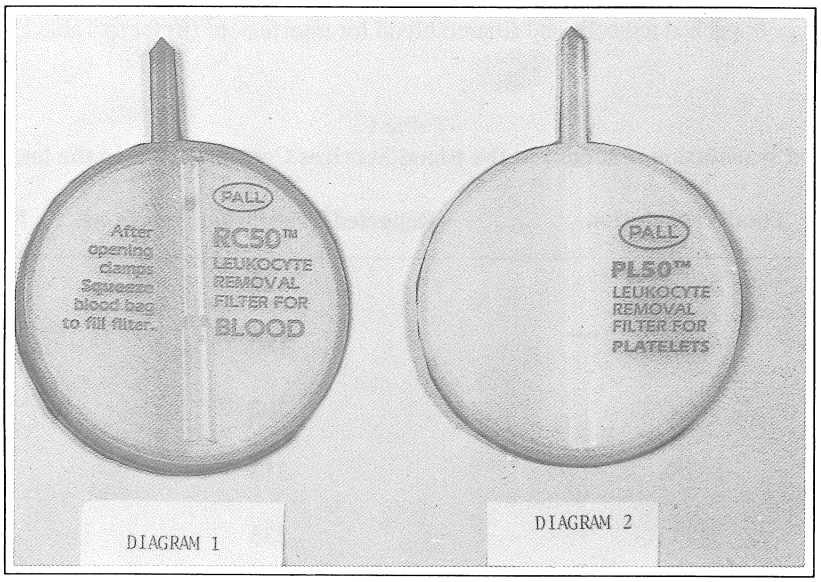
Year	Total Transfusion	Reported Tranfusion Reactions	NHFTR
1986	56976	123	118
1987	61300	180	150
1988	74609	202	156
1989	88288	313	251
1990	84892	233	211

The frequency with which antibodies to leucocytes develop is high and is proportional to the number of exposures.[3] Almost 90% of recipients of multiple transfusions develop either anti-HLA antibodies or antibodies to granulocytes which is usually apparent one week after transfusion and decreases significantly in incidence three months after transfusion.[3,4] Leucocyte depletion is cost-effective in preventing the transfusion of "Passenger" leucocytes and their untoward effects in the recipient such as NHFTR, platelet refractoriness, immunosuppression (eg. reduced disease-free interval after curative resection of colonic carcinoma). graft-versus-host disease and transmission of viruses (eg. Cytomegalovirus).[5]

Case Report

A 72 year old man was diagnosed to have refractory anaemia with excess blasts (FAB classification for Myelodysplastic Syndrome)[6] in August 1990. He had anaemia and thrombocytopenia which required regular supportive transfusions of packed red blood cells and platelet concentrates. On the average, with every admission, he required four units of packed red blood cells and sixteen units of platelet concentrates.

The patient's initial four admissions to hospital for supportive transfusion over a period of 12 weeks were uncomplicated. On his fifth admission, he developed spiking temperatures after each transfusion of packed cells with no evidence of heamolysis seen. The patient's direct and indirect Coombs tests were negative and no red cell antibody was detected. Post-transfusion serum of the patient was sent for HLA-antibody studies. The result was negative as the post-transfusion serum was tested against cells from only two donors. The commonest cause of non-haemolytic febrile transfusion reaction is due to the antigen-antibody reaction between anti-leucocyte antibodies in the patient and the corresponding antigen on the allogenic "passenger" leucocytes present in the packed red cells. We then proceeded to filter the packed red cells by the bedside using the PALL RC 50™ leucocytes depleting filter for red blood cells transfusion (refer to Diagram 1). This filter was attached simply via the inlet port directly to the bag of packed red cells and connected by the outlet port directly to the patient's intravenous drip set. A simple, effective and labour saving bedside in-line procedure used at the time of transfusion without requiring formal training of staff nor priming of the filter.



Leucocyte removal filters for blood (Diagram 1) and for platelet concentrates (Diagram 2)

His subsequent admissions for supportive transfusions were free of complications till the tenth admission when he developed spiking temperature of 39°C with chills and rigors after transfusions of platelet concentrates. The febrile transfusion reactions were bad enough for the patient to refuse further transfusion of platelet concentrates. Here again, the febrile reactions were thought to be due to the leucocyte antibodies towards the allogenic "passenger" leucocytes present in the platelet concentrates. Hence, on his eleventh admission, platelet concentrates were transfused through a bedside PALL PL50™ leucocyte-depleting filter for platelets (refer Diagram 2). This filter was set up similarly to the one described earlier for the packed red cells. Using this simple bedside filtration technique, the patient's supportive transfusion of packed cells and platelet concentrates have since been symptom-free.

Discussion

NHFTR is defined as a febrile episode occurring half an hour to two hours after the onset of transfusion, usually lasting between two to twelve hours in the absence of evidence of haemolysis. These NHFTR are due to the action of leucocyte antibodies, developed following exposure to multiple transfusions, on the corresponding antigenic determinants on the allogenic "passenger" leucocytes in the blood and blood components transfused.[3] This antigen-antibody reaction activates complement which in turn causes lysis of granulocytes with liberation of pyrogens and various vasoactive substances, hence a clinical picture of fever, urticaria and, at times, an anaphylactoid reaction.[3] The leucocyte antibodies were typical isoantibodies, showing no activity against the patient's own leucocytes but clumping a wide range of normal donor leucocytes.[7] In order to detect antibodies against the majority of HLA specificities, a large panel of cells for the conventional lymphocytotoxicity test is needed due to the polymorphism of the HLA system.[8] The requirement for a large number of panel donors probably lead to our patient's negative results for the HLA antibody studies done, as our patient's serum was only tested against two donor panels.

The severity of NHFTR depends on the absolute numbers of leucocytes present in the transfused blood, the titre and the type of antibody in the plasma of the recipient, and can be prevented or ameliorated by transfusing leucocyte-depleted blood.[7,10] Only in the late 1980's that attention has been turned to leucocyte depletion of platelets as evidence accumulated that it is the contaminating leucocytes rather than the platelets themselves that are responsible for alloimmunisation against HLA antigens.[9] It has been suggested that the transfusion of less than 0.5×10^9 leucocytes can prevent NHFTR[5] and less than 5×10^6 to prevent alloimmunization in the majority of sensitized patients.[9] The PALL filters for both red cells and platelets, used in our patient, have proved to deplete leucocytes to 5×10^6 or less with a mean platelet loss of 15% from the platelet concentrates transfused.[9] This amount of leucocyte-depletion was apparently sufficient to prevent alloimmunisation[9] and NHFTR as was seen in our patients.

There are many commercially available leucocyte-depleting filters in the market today which requires priming or flushing. The filters used for red cells and platelet concentrates in our patient have the distinct advantage that it does not require priming or flushing and is designed for in-line use at he bedside.[9]

Conclusion

The exact incidence of NHFTR is unclear, however, in the five year period from 1986 to 1990, 84.3% of the transfusion reactions reported to our centre were NHFTR (Refer to Table I).

After reviewing the effects of leucocytes contamination of red cell and platelet transfusion the message is unequivocal: PURE IS BEST.[9] Recognising this, Blood Banks in Malaysia do prepare leucocyte-

poor blood and plasma especially for the transfusions in the multiply transfused and immunocompromised patients. Besides elimination of the effects of leucocyte contamination, the leucocyte-depleting filters have numerous other advantages, including simplicity, low cost, reduction in workload in the blood transfusion service and in the ward, better blood conservation and safer transfusions. As was seen in the successful use of the bedside leucocyte-depleting filters in our patient, its use should be advocated for patients who require multiple transfusions as well as those who are immunocompromised.

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