Post Transfusion Purpura

1. Background

1.1 Incidence & Clinical Features

PTP is a rare but serious complication of blood transfusion, characterised by the sudden onset of severe thrombocytopenia within 5-10 days of transfusion of blood products[1]. Blood components containing platelets, such as whole blood, red cells in additive solution (SAG-M), red cell concentrates and platelet concentrates have been implicated. An annual average of 10 PTP cases were reported in the first 3 years to the SHOT scheme from 1996/97 to 1998/99. Since the introduction of universal leucodepletion in 1998, the number of reported cases of PTP had fallen progressively to an average of 2 cases per year giving an approximate incidence of less than 1 in 700,000 transfusions[2].

Typically cases of PTP were observed in women with a history of pregnancy, who are most likely to be immunised by a human platelet specific alloantigen (HPA) following pregnancy. PTP can also occur in male patients where primary immunisation must have occurred by an earlier blood transfusion. Due to severe thrombocytopenia, haemorrhage is common and may be fatal. In some cases, the precipitating transfusion has been associated with a nonhaemolytic transfusion reaction[3].

1.2 Pathogenesis

The blood transfusion triggers an anamnestic response in boosting HPA antibodies in an already sensitised person. Thrombocytopenia in PTP is caused by antibody mediated destruction of both donor platelets as well as patient's own platelets. Why HPA alloantibodies destroy both the autologous platelets as well as the platelets of donor origin is not completely understood, although there are several hypotheses. The formation of antibodies which cross react with 'self' during the recall response is one of them. The development of non-specific pan-reacting antibodies against platelet glycoproteins (Gp IIb/IIIa, Ib/IX, Ia/IIa) in addition to the boosting of HPA alloantibody may also be responsible for the autologous platelet destruction in PTP[4,5].

Leucodepletion of whole blood reduces contaminating platelets by 100-fold[6] and in buffy-coat depleted and filtered red cell components, platelets are undetectable (R Cardigan, personal communication). Universal leucodepletion in the UK has resulted in a consistent decrease in haemovigilance reports of PTP[2].

Specificity of platelet antibodies
The most commonly implicated platelet antibody responsible for PTP is anti-HPA-1a in an HPA-1a negative (HPA-1b/1b) patient receiving red cells or platelet concentrates from an HPA-1a positive donor. Cases of PTP due to antibodies with other specificities against HPA-1b, HPA-3a, HPA-3b, HPA-4a, HPA-5a, HPA-5b and HPA-15 have been reported in the literature. An association between IgG3 subclass HPA-1a antibodies and the destruction of autologous platelets has been shown[7].

2. Indications for testing

Unexpected thrombocytopenia in a patient who had received a transfusion of a cellular blood component within the previous 2 weeks should be investigated for PTP.

PTP should not be confused with thrombocytopenia associated with passive transfusion of HPA antibodies. A significant reduction of the platelet count in the first 48 hours after the transfusion of FFP or other plasma containing blood products can occur because of the presence of platelet specific antibodies in the donor's plasma[8,9].

In patients who have received heparin in addition to a blood transfusion, special care must be taken to differentiate PTP associated with purpura from heparin induced thrombocytopenia (HIT), associated with serious thrombotic complications[10,11].

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3. Laboratory investigations

For the laboratory diagnosis of suspected cases of PTP, 6ml of clotted blood and 6 ml of blood in EDTA should be sent to a National Blood Service Histocompatibility & Immunogenetics (H&I) Laboratory, NHS Blood and Transplant, North Bristol Park, Northway, Filton, Bristol BS34 7QH UK. The samples must be accompanied by a correctly completed Platelet Immunology diagnostic reference laboratory request form, giving relevant clinical details. Before the samples are taken, a NHSBT Consultant Clinical Scientist in H&I or a Consultant in Transfusion Medicine should be informed.

4. Out of hours testing

No out of hours testing service is provided because immediate management does not depend on test results. Tests are performed during normal working hours only.

5. Confirmation of PTP

The diagnosis of PTP is confirmed by the demonstration of IgG alloantibodies in the patient's serum against one of the HPA antigens. These antibodies are detected by appropriate HPA antibody detection assays used by H&I. The HPA-1, 2, 3, 5 and 15 genotypes of the patients are determined by a PCR-based testing method.

HLA antibodies do not cause PTP, but they may also be present in the patient's serum.

5.1 HPA antibody Cards

The NHSBT H&I Laboratory at Bristol will issue an HPA antibody card for patients with confirmed PTP for them to keep and show clinicians in case they should require further transfusions.

6. Management

Appropriate treatment should be started as soon as a clinical diagnosis of PTP is made without waiting for the results of laboratory investigations.

The treatment of choice is the infusion of high dose intravenous immunoglobulin (ivIgG), 2g/kg body weight administered in divided doses over 2-5 consecutive days[3]. This should be started immediately even if the patient is bleeding and requires platelet transfusions. About 85% of patients respond to this treatment.

Random platelet transfusions are generally not effective and the survival of platelet concentrates negative for the relevant HPA antigen is also severely impaired during the acute phase of the syndrome (defined as the hospital episode during which the diagnosis of PTP has been made).

Plasma exchange and steroids have been used in the past but an increase in the platelet count is significantly delayed when compared with ivIgG. Plasma exchange should be considered if the patient is refractory to ivIgG therapy.

During the recovery phase of severe thrombocytopenia, the platelet count of the patient should be closely monitored until normal levels are reached because of the possibility of rebound thrombocytopenia.

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7. Transfusion Advice

7.1 In the Acute Phase

In the acute phase of PTP, if severe bleeding occurs before the effect of ivIgG is seen, random ABO and D compatible blood components can be given. Multiple doses of platelet concentrates may be required to treat significant haemorrhage. There is no evidence that the transfusion of red cells or platelets from HPA compatible donors during the acute phase reduces the time of severe thrombocytopenia.

7.2 After recovery

All future elective transfusions of blood and platelets should ideally be obtained from donors negative for the relevant HPA antigen. If this is not possible, the use of standard red cells untyped for HPA should be considered. Standard ABO & D compatible products, unselected for HPA may be administered if the risk of delayed transfusion outweighs the risk of PTP and the platelet count should be monitored.

7.3 Patients with bone marrow failure with HPA-specific antibodies refractory to random platelet transfusion

HPA matched platelets should be transfused to improve incremental counts. Whilst transfusion-dependent following chemotherapy HPA matched red cells are not required.

7.4 Prevention of PTP in patients with HPA-specific antibodies who have had no previous episodes of PTP

Transfusions may be required for mothers who have had a child with alloimmune thrombocytopenia and patients who have been platelet refractory but have since recovered their platelet count and immunity following treatment. The risk of PTP for such patients has been ameliorated by leucodepletion[2,6]. If transfusions of red cells and platelets are required they should be obtained from donors who are negative for the relevant HPA antigen. Untyped or antigen positive blood components should however be given if the risks induced by the delay in obtaining HPA compatible components outweigh the benefits.

8. Reporting to the MHRA and the Serious Hazards of Transfusion (SHOT) Scheme

PTP is one of the most serious non-infectious adverse effects of transfusion and should be reported to both the MHRA and the SHOT scheme. Reporting is the responsibility of the hospital Consultant Haematologist responsible for blood transfusion. The MHRA on-line reporting system, *SABRE*, can be used to report to both the MHRA and SHOT.

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