Antigen-positive platelet transfusion in neonatal alloimmune thrombocytopenia (NAIT)

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Neonatal alloimmune thrombocytopenia (NAIT) is a fetomaternal incompatibility most commonly induced by maternal anti–HPA-1a, IgG alloantibodies against a polymorphic epitope of the glycoprotein IIb/IIIa complex in approximately 97.5% of white patients. Current guidelines recommend transfusion of immunologically compatible platelets to prevent cerebral hemorrhage, the most severe complication in affected newborns. Such platelet concentrates, however, are often not readily available. In a retrospective analysis in German and Canadian centers, 27 newborns with NAIT were identified who received platelets from random donors. Unexpectedly, 24 of 27 newborns showed an increase above a threshold of 40 \( \times 10^9 \) platelets per liter, with moderate \((n=8)\) or significant \((n=16)\) platelet count increments (more than 80 \( \times 10^9/\text{L} \)). We conclude that transfusion of platelet concentrates from random donors is an appropriate strategy in the management of unexpected, severe NAIT predominantly in first pregnancies, pending the availability of compatible platelets. (Blood. 2006;107:3761-3763)

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HPA-1a have been transfused with random donor platelets, and in some cases unexpected high platelet increments have been observed.\textsuperscript{14-17} To study more systematically the effect of HPA-1a–incompatible platelet transfusions in severe NAIT, we initiated a review of newborns with severe NAIT who received random donor platelet concentrates.

\subsection*{Study design}

In this retrospective analysis we enrolled 1 Canadian (Hamilton) and 6 German (Berlin, Bonn, Düsseldorf, Giessen, Greifswald, Rostock) university hospitals and 1 German Red Cross transfusion laboratory (Dresden). Each center identified platelet transfusions in NAIT patients who fulfilled the following criteria: (1) laboratory-confirmed HPA-1a antibodies in maternal-blood samples, (2) transfusion of platelet concentrate(s) from random donors, and (3) a period of observation of 4 days or longer with documented platelet counts. Platelet transfusions and other therapeutic interventions aimed at preventing bleeding complications, platelet counts, and response to platelet concentrate transfusions were retrieved from each patient’s file. Platelet antibodies were detected using GP-specific assays.\textsuperscript{18}

\subsection*{Results and discussion}

Twenty-seven neonates (11 female, 16 male) born to mothers with serologically confirmed HPA-1a antibodies were identified (Figure 1) who received at least 1 HPA-1a–positive (patient nos. 1-3, 5, 8-11, and 13) or random platelet concentrate. Maternal antibody status was known in 5 of 27 cases. The median gestational age was 39 weeks; 25th quartile, 37.5 weeks; 75th quartile, 39.5 weeks. Thirteen of 26 newborns were born to primiparous women. In all but 3 patients (nos. 7, 20, and 24) platelet counts increased above \(40 \times 10^9/L\) following 1 or 2 random platelet transfusions, a value above the threshold of \(30 \times 10^9/L\) considered relevant in the prevention of cerebral hemorrhage.\textsuperscript{8} After the first 1 or 2 transfusions, significant increments (more than \(80 \times 10^9/L\)) were observed in 16 of 27 patients (nos. 1-3, 5, 6, 10-15, 17, 21, 23, 25, and 26), and less pronounced but still sufficient increments were seen in patients 4, 8, 9, 18, and 19. Even patient 16, the second of 2 siblings with severe NAIT, who was born with a platelet count of \(6 \times 10^9/L\) and who showed a minor increment, still did not require further transfusion. Response to 4 random platelet transfusions was highly variable in patient 22. There were 3 exceptions in this series of patients: in patients 7, 20, and 24 random donor platelets were clearly without effect, and further HPA-1a–negative platelet transfusions were required in patients 7 and 20. Ten patients also received IVIG (nos. 1, 6, 7, 13, 16, 20-22, 24, and 25), and 4 patients were treated with corticosteroids (nos. 4, 7, 19, and 22). In none of the patients were adverse effects related to random donor platelet transfusions (eg, disseminated intravascular coagulation [DIC] or increased hemorrhage) observed. Cerebral hemorrhage occurred prenatally in patients 1 and 6, and in patient 5 hydrocephalus of unknown etiology was diagnosed at birth, underscoring the severity of NAIT.
The cause for the relative effectiveness of immunologically incompatible platelet transfusion in NAIT is not entirely clear. Potentially a sufficiently large dose of antigen-positive platelets might adsorb circulating alloantibodies and thus enhance recovery of megakaryocytes and thrombopoiesis. This could explain the observation of a delayed rise in platelet counts in some patients. From an immunologic perspective, a newborn who has been sensitized by alloantibodies as result of passive transplacental transfer may react more favorably when transfused with antigen-positive platelets than an actively immunized subject. The likely explanation is that the incompatible transfusion in the situation of spontaneous passivation will not enhance the antibody titer.

In our study, we found that in 24 of 27 newborns with unexpected severe NAIT, transfusion of a random platelet concentrate led to an increase in platelet count sufficient for the prevention of spontaneous cerebral hemorrhage. This and the fact that transfused babies experienced no serious adverse effects strongly indicate that immediate transfusion of a random platelet concentrate in severe, unexpected NAIT may be associated with fewer risks than waiting for several hours or even days for a HPA-negative concentrate in proven or suspected platelet alloimmunization.

The largest group of patients was contributed by H. Kroll, MD (now located at German Red Cross Blood Transfusion Service, Dessau, Germany).

Acknowledgment

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