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Erythrocyte repopulation after major ABO incompatible transplantation with lymphocyte-depleted bone marrow

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Summary:

Forty-four out of 258 allogeneic BMT were performed across the major ABO barrier. Donor erythrocyte repopulation could be evaluated in 30 cases. Fifty-eight patients transplanted with an ABO compatible or minor incompatible graft served as the control group. All patients received a marrow graft depleted of lymphocytes by counterflow centrifugation. Less than 10^8 residual erythrocytes were present in the graft. Cyclosporin A was used as immunoprophylaxis after transplantation. Erythrocyte repopulation was measured using a fluorescent microsphere method. An adapted transfusion policy was applied. Eight out of 30 patients (27%) with major ABO incompatibility had no detectable donor erythrocytes 2 months after BMT. Up to 3 months after BMT donor erythrocyte repopulation was significantly delayed in the ABO incompatible group (P = 0.03). Significantly more erythrocyte transfusions were required in the ABO incompatible group (P < 0.001). Six patients with blood group O (20%) developed pure red cell aplasia which resolved in five without therapeutic intervention. In these six patients anti-A antibody titers were persistently high the first 3 months after BMT. This was in contrast with 22 patients with timely recovery of erythropoiesis in whom anti-A and anti-B antibody titers showed a steady decrease after BMT. The incidence of immunohematological complications in these patients who received a lymphocyte depleted major ABO incompatible graft is similar (20%) to the incidence reported in the literature. Serious morbidity related to major ABO incompatibility did not occur.

Keywords: erythrocyte repopulation; ABO incompatibility; lymphocyte depleted; BMT

Major ABO incompatibility between recipient and donor occurs in about 10–15% of HLA matched allogeneic bone marrow transplantations. Acute hemolysis by anti-A or anti-B antibodies of recipient origin at the time of infusion of the donor marrow can be prevented by reduction of the antibody titers in the recipient or by removal of erythrocytes from the graft.1–5 Studies by Bensinger et al7 and Buckner et al7 have demonstrated that major ABO incompatibility is no obstacle to successful outcome after BMT. No increased risk of graft rejection, graft-versus-host disease (GVHD) or mortality related to ABO incompatibility have been observed. Several reports have described delayed hemolytic anemia, delayed onset of erythropoiesis, pure red cell aplasia (PRCA) and increased post-transplant transfusion requirements after major ABO incompatible BMT.8–13

In contrast to the previous studies all patients transplanted in our center received marrow grafts depleted of lymphocytes by elutriation. Donor erythropoiesis and transfusion requirements were evaluated in 30 patients who received a major ABO incompatible graft and compared to an ABO compatible or minor ABO incompatible control group of 58 patients. Delayed onset of erythropoiesis occurred in eight patients who received a major ABO incompatible graft. The clinical course after BMT of these patients is described in more detail. The pretransplant titers and the post-transplant course of ABO antibodies in these patients were compared to those of the other 22 patients transplanted with a major ABO incompatible graft.

Subjects and methods

Patient groups

From 1981 to 1994, 285 allogeneic bone marrow transplantations were performed in adults. In 44 cases (15%) major ABO incompatibility existed between patient and donor. In 14 out of 44 patients donor erythrocyte repopulation could not be evaluated for the following reasons: early transplant-related mortality within 1 month after BMT in three, early relapse within 6 months after BMT in five, graft failure and autologous recovery in three and no available data in three patients. The remaining 30 patients were transplanted for acute myeloid leukemia (AML) (n = 6), acute lymphoid leukemia (ALL) (n = 8), chronic myeloid leukemia (CML) (n = 14), severe aplastic anemia (SAA) (n = 1) and eosinophilic syndrome (n = 1). Twenty patients with blood group O received either a blood group A graft (n = 19) or a blood group B graft (n = 1). A B marrow was transplanted to three patients with blood group A and one patient with blood group B. Three patients with blood group A received a blood group B graft and three patients with blood group B received a blood group A graft.

Twenty-six donors were HLA-identical sibling donors and four donors were HLA-matched unrelated volunteers.
(UPN 168, 199, 226 and 281). Conditioning regimens always included cyclophosphamide (CY) in a total dose of 120 mg/kg. This was followed by total body irradiation (TBI) in two equal fractions with 24 h interval in a total dose of 9 or 12 Gy in 28 patients. Anthracyclines (daunorubicin 156 mg/m² or demethoxydaunorubicin 42 mg/m²) were added in 18 out of 22 patients who received TBI in a dose of 9 Gy. One patient (UPN 281) was conditioned with CY, TBI (9 Gy) and total lymphoid irradiation (TLI) (8 Gy). Another patient was treated with busulphan and CY (UPN 126). In the only patient (UPN 226) transplanted for SAA the conditioning regimen consisted of CY and TLI (12 Gy). Details on the conditioning regimens have been described earlier.\(^1^4,1^5\) Plasma exchange or plasma immunoabsorption to reduce anti-A or anti-B antibody titers before BMT were never applied.

In the same time period, 241 ABO compatible or minor ABO incompatible transplantations were performed. Fifty-eight patients could be used as a control group to study donor erythrocyte repopulation. The remaining patients were considered not to be evaluable mainly because of lack of a donor erythrocyte marker (see below) or because they received unselected transfusions not taking into account the donor marker. Other reasons were early transplant-related mortality, early relapse or graft failure. Indications for transplantation were AML (n = 14), ALL (n = 15), CML (n = 17), low-grade non-Hodgkin lymphoma (n = 5), multiple myeloma (n = 4), SAA (n = 2), and myeloproliferative syndrome (n = 1). Fifty-four donors were genotypically HLA-identical sibling donors and four donors were one locus mismatched siblings. The conditioning regimens always included CY (120 mg/kg). Except for one patient who was treated with TLI, all patients received TBI in a total dose of 9 or 12 Gy. Anthracyclines were added in 35 out of 39 patients treated with TBI in a dose of 9 Gy.

Both in the study and in the control group all marrow grafts were depleted of lymphocytes by density gradient centrifugation followed by counterflow centrifugation.\(^1^6\) Less than 10\(^8\) residual erythrocytes were present in the marrow graft. Cyclosporin A (CsA) was used as immunosuprophylaxis post-transplant in all patients in a schedule, as previously described.\(^1^7\)

**Erythrocyte markers**

Analysis of patient and donor erythrocyte populations in the first months after BMT required an adapted transfusion policy.\(^1^8,1^9\) Before BMT, preferentially before any transfusions were given, a sample for complete red cell phenotyping was drawn from the patient. After phenotyping of the donor, marker antigens, ie antigens present in the donor and absent in the recipient and vice versa, were determined. In case of major ABO incompatibility the A or B antigen was used as a donor marker. In the control group donor marker antigens were C, c, D, E, K, M, N, S, s, Fya, Fyb, Jka, Jkb and Kpa. Erythrocyte transfusions of blood group O lacking the marker antigens were administrated to all patients in both groups.

Measurement of host and donor populations was performed by a fluorescent microsphere method. The sensitivity of this assay is one positive cell per 10,000 negative cells (0.01%).\(^2^0\) Donor erythrocyte repopulation was studied at 0.5, 1, 2, 3, and 6 months after BMT.

**Anti-A and anti-B antibodies**

Anti-A and anti-B agglutinin (IgM) titers were determined by incubating a 3% standard A and B erythrocyte suspension in saline with 2-fold serial dilutions of patient serum at 37°C for 45 min followed by centrifugation and scoring for macroscopic agglutination. Anti-A and anti-B IgG titers were measured by pretreating the patient serum with dithiothreitol at 37°C for 45 min followed by indirect antiglobulin testing with anti IgG serum and scoring for macroscopic agglutination.

Antibody titers were determined before and at least 0.5, 1, 2, 3 and 6 months after BMT.

**Statistical analysis**

The Fisher's exact test was used to compare clinical variables between groups. The Kruskal–Wallis test was applied to compare percentages of donor erythrocytes at different time points after BMT. Within the study group antibody titers were compared using the Mann–Whitney U test.

**Results**

**Recovery of erythropoiesis in the study and control group**

Because of reasons mentioned earlier it was not possible to form a fully matched control group based on matching for indication for BMT, conditioning regimen, age and acute GVHD. Table 1 shows the comparison of clinical data between the study and the control group.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Comparison of clinical data between the study and the control group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Major ABO incompatible BMT n = 30</td>
</tr>
<tr>
<td>Conditioning regimen</td>
<td></td>
</tr>
<tr>
<td>TBI 9 Gy</td>
<td>22</td>
</tr>
<tr>
<td>Anthracyclines (added to TBI 9 Gy)</td>
<td>6</td>
</tr>
<tr>
<td>Indications for BMT</td>
<td></td>
</tr>
<tr>
<td>Acute leukemia</td>
<td>14</td>
</tr>
<tr>
<td>CML</td>
<td>14</td>
</tr>
<tr>
<td>Others</td>
<td>2</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
</tr>
<tr>
<td>&lt; 40</td>
<td>21</td>
</tr>
<tr>
<td>≥ 40</td>
<td>9</td>
</tr>
<tr>
<td>Donors</td>
<td></td>
</tr>
<tr>
<td>Histocompatible sibling</td>
<td>26</td>
</tr>
<tr>
<td>Others</td>
<td>4</td>
</tr>
<tr>
<td>GVHD (grade)</td>
<td></td>
</tr>
<tr>
<td>0-1</td>
<td>23</td>
</tr>
<tr>
<td>≥ 11</td>
<td>7</td>
</tr>
</tbody>
</table>

No significant differences of clinical variables between the groups were found (Fisher's exact test)
variables between the two groups. No significant differences could be found.

Table 2 shows the means and standard deviations of percentages of donor erythrocytes at various time points after BMT. Significant delay in donor erythrocyte repopulation in the ABO incompatible patient group compared to the control group could be demonstrated up to 3 months after BMT. The difference between the two groups was no longer significant at 6 months after BMT.

To demonstrate delayed donor erythrocyte repopulation in the major ABO incompatible group we compared the relative number of patients without detectable donor erythrocytes (ie < 0.01%) between both groups at various time points early after BMT. In the study group 62% and 33% of the evaluable patients had no donor red cells detectable at 0.5 and 1 month after BMT, respectively. In the control group these percentages were 19% and 0% respectively (P < 0.01).

The median number of erythrocyte transfusions after BMT was 18 (range 6–64) in the ABO incompatible group and 10 (range 2–46) in the control group (P < 0.001).

Leukocyte and platelet recovery did not differ between the ABO incompatible group and the control group (data not shown).

Delayed onset of erythropoiesis of at least 2 months after BMT

Eight patients in the ABO incompatible group (recipients blood group O, grafts blood group A) had no detectable donor erythrocytes up to 2 months after BMT (UPN 70, 83, 100, 126, 199, 253, 281). In this same time period percentages of recipient erythrocytes in the six out of eight patients with a recipient marker (UPN 83 and 281 had no recipient marker) were progressively decreasing. In these eight patients leukocyte counts > 1.0 x 10^9/l were reached at a median of 29 days after BMT (ranging from 19 to 35 days). Patient UPN 199 died of cerebral haemorrhage while hypertensive due to CsA intoxication. At the time of death, 2 months after BMT, the platelet count was still below 20 x 10^9/l. In the remaining patients a platelet concentration of > 20 x 10^9/l without transfusion support was reached at a median of 21 days with a range of 18 to 116 days. Data on these patients are given in Table 3.

UPN 83 developed grade 2 acute GVHD of the skin 3 weeks after BMT. Treatment consisted of addition of corticosteroids to the CsA. While tapering off these drugs she developed limited chronic GVHD of the gut. Two months after BMT a bone marrow aspirate showed active myeloaplasia, absent erythropoiesis and no megakaryocytes. Three months after BMT the percentage of donor erythrocytes was 0.22. At that time point erythropoiesis in the marrow was active but the number of megakaryocytes was still low. She remained erythrocyte transfusion dependent with 0.07% of donor erythrocytes 4 months after BMT. Platelet counts never rose above 50 x 10^9/l. She died of CMV pneumonitis 6 months after BMT.

UPN 100 remained transfusion dependent up to 3 months after BMT. During this period there were no signs of acute GVHD. Bone marrow morphology at 1 and 3 months showed PRCA. At 3 months after BMT no donor erythrocyte percentage was available. At 3.5 and 4 months after BMT these percentages were 4.2 and 19.2, respectively. He is in remission of ALL with 100% donor erythrocytes and no recipient erythrocytes at 6.5 years after BMT.

UPN 70 had no detectable donor erythrocytes up to 3 months after BMT with the picture of PRCA in the marrow aspirate. The patient did not suffer from acute GVHD. Treatment with corticosteroids was started 4.5 months after BMT in an attempt to stimulate donor erythropoiesis. One month later the percentage of donor erythrocytes was 36 and this gradually increased to 100% afterwards. This patient is in complete hematological, cytogenetic and molecular remission of CML 7 years after BMT.

UPN 126 had no detectable donor red cells up to 6 months after BMT reflected by PRCA in the marrow aspirates performed 1, 3 and 6 months after BMT. Cytogenetic analysis of the bone marrow performed 6 months after BMT showed only cells of donor origin. Neither acute nor chronic GVHD occurred. The last erythrocyte transfusion was required 6.5 months after BMT. Nine months after BMT, 78% donor erythrocytes were present. This patient died of marrow and CNS relapse of AML 10 months after BMT while only donor, but no recipient, red cells could be demonstrated.

UPN 162 had PRCA in the marrow aspirate and no detectable donor erythrocytes 3 months after BMT. In these first months he was treated with corticosteroids for acute GVHD grade 1 limited to the skin. From 4 months onwards the percentage of donor cells started to rise to 100% at 1 year after BMT. Cytogenetic relapse of CML occurred 1 year later.

UPN 253, transplanted for eosinophilic syndrome, had no detectable donor erythrocytes until 6 months after BMT at which time point the percentage was 2 and erythropoiesis could for the first time be observed in the marrow aspirate. Acute GVHD did not occur. He died of Aspergillus sepsis complicating de novo chronic GVHD of the liver 9.5 months after BMT.

In UPN 281, transplanted with an unrelated graft for CML in first accelerated phase, donor erythrocytes were never demonstrable during follow-up. She developed acute GVHD grade 1 limited to the skin which was successfully treated by addition of corticosteroids to the CsA. Because of limited chronic GVHD of the skin and gut, treatment with low-dose CsA was continued. Bone marrow mor-

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### Table 2

<table>
<thead>
<tr>
<th>Time (months)</th>
<th>Major ABO incompatible BMT</th>
<th>Control group</th>
<th>P value</th>
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<tr>
<td></td>
<td>% donor erythrocytes</td>
<td>% donor erythrocytes</td>
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<tr>
<td>0.5</td>
<td>n= 26</td>
<td>Mean 0.04</td>
<td>s.d. 0.07</td>
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<tr>
<td>1</td>
<td>30</td>
<td>1.73</td>
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<tr>
<td>2</td>
<td>27</td>
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<tr>
<td>3</td>
<td>25</td>
<td>38.65</td>
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<tr>
<td>6</td>
<td>25</td>
<td>73.93</td>
<td>31.29</td>
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</table>

*Number of evaluations.

*Standard deviation
Table 3  Data on 30 major ABO incompatible patients

<table>
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<tr>
<th>UPN</th>
<th>Pretransplant anti-A or anti-B titers</th>
<th>Leukocytes*</th>
<th>Platelets*</th>
<th>Time to onset of erythropoiesis</th>
<th>Erythrocyte transfusions (no.)</th>
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<tbody>
<tr>
<td></td>
<td>IgM</td>
<td>IgG</td>
<td></td>
<td></td>
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<tr>
<td>Delayed onset of erythropoiesis (n = 8)</td>
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<tr>
<td>70</td>
<td>32</td>
<td>512</td>
<td>30</td>
<td>19</td>
<td>5.5</td>
</tr>
<tr>
<td>83</td>
<td>256</td>
<td>512</td>
<td>33</td>
<td>116</td>
<td>21</td>
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<tr>
<td>100</td>
<td>32</td>
<td>128</td>
<td>19</td>
<td>23</td>
<td>3.5</td>
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<tr>
<td>126</td>
<td>512</td>
<td>16 000</td>
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<td>23</td>
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<tr>
<td>162</td>
<td>64</td>
<td>64</td>
<td>30</td>
<td>21</td>
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<tr>
<td>199</td>
<td>128</td>
<td>1 024</td>
<td>35</td>
<td>---</td>
<td>NE</td>
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<tr>
<td>253</td>
<td>32</td>
<td>128</td>
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<td>19</td>
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<tr>
<td>281</td>
<td>64</td>
<td>2 048</td>
<td>22</td>
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<tr>
<td>Median</td>
<td>64</td>
<td>512</td>
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<td>21</td>
<td>5.5</td>
</tr>
<tr>
<td>Timely onset of erythropoiesis (n = 22)</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>64</td>
<td>16</td>
<td>20</td>
<td>25</td>
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</tr>
<tr>
<td>range</td>
<td>4–512</td>
<td>1–512</td>
<td>10–29</td>
<td>11–50</td>
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</table>

*Days after BMT.
*Months after BMT.
*Until death.
NE = not evaluable, patient died 2 months after BMT.

Discussion

Delayed onset of donor erythropoiesis and persistence of anti-A or anti-B hemagglutinins are well known phenomena after major ABO incompatible BMT.5,10 After red cell depletion of the graft Sniecinski et al5 observed delayed onset of erythropoiesis > 40 days after BMT and persistence of anti-A and anti-B antibodies > 120 days in 10 out of 66 (15%) major ABO incompatible transplantations. In a later study on major ABO incompatibility these complications occurred in nine out of 58 (16%) patients while the overall incidence of immunohematological complications was 21%. Serious associated morbidity was not observed however and erythropoiesis became normal in all but one
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Figure 1: Course of ABO antibody titers IgM (a) and IgG (b) after major ABO incompatible BMT. (a) shows the mean course of antibody titers (IgM) in 22 patients with timely recovery of donor erythropoiesis after major ABO incompatible BMT (bold line); the eight patients with delayed onset of erythropoiesis are shown separately; (b) shows the same course for IgG.

patient. In a study by Gmür et al. three out of 15 major ABO incompatible transplants (20%) developed PRCA lasting 5 to 8 months. In our study erythropoiesis was delayed in the 30 patients who received a major ABO incompatible graft compared to an ABO compatible or minor ABO incompatible control group. In eight out of 30 patients, donor erythrocytes were still undetectable 2 months after BMT. Six out of eight patients developed the clinical picture of PRCA lasting from 3.5 to 9 months after BMT. Except for a transient positive direct antiglobulin test in UPN 70 no clinical or laboratory signs of hemolysis were observed at the beginning of erythrocyte production in five of the six PRCA patients. In one patient donor erythrocytes were never detectable after BMT. UPN 83 had 0.22% of donor erythrocytes 3 months after BMT. Major ABO incompatibility may have played a role in the delayed onset of erythropoiesis in this patient but GVHD and recurrent viral infections can not be ruled out as additional causative factors.

All patients with delayed onset of donor erythropoiesis were blood group O which was significantly more often than in the major ABO incompatible patients with timely onset of erythropoiesis. Most cases of PRCA after BMT reported in the literature involve patients with blood group O and donors with blood group A or B, although two cases of a recipient with blood group A and a donor with blood group B and vice versa have been described.

Twenty-two patients in the major ABO incompatible group had detectable donor erythrocytes within 2 months after BMT. Pretransplant IgM anti-A and anti-B antibody titers were identical and IgG titers were significantly lower compared to the eight patients with delayed onset of erythropoiesis. Various reports in the literature did not agree on a correlation between pretransplant ABO antibody titers and the number of days post-transplant before onset of erythropoiesis.

In the 22 patients antibody titers decreased immediately after BMT and were undetectable or present in low titers at 3 months after BMT. This is in agreement with the data of Gmür et al. in 11 patients with timely recovery of erythropoiesis after major ABO incompatible BMT. They described a progressive decrease and titers persistently \( \leq 16 \) from day 32 onward. The course of ABO antibodies after BMT was clearly different in seven out of eight patients in our study with delayed onset of erythropoiesis. An early rise or persisting high titers (IgG more than IgM) were observed in this group. A correlation between delayed onset of erythropoiesis and post-transplant rise or persistence of high (above 16) antibody titers was also described in recipients of a non-lymphocyte-depleted major ABO incompatible graft.

Extraordinary antibody titers decreases were also described in recipients of a major ABO incompatible graft. Only after a substantial reduction in these titers to a level of four to 16 erythrocyte production began. Delay in erythropoiesis can be explained by the interaction of anti-A or anti-B antibodies with donor erythroid precursors expressing the A and/or B antigens.

A study comparing the course of anti-donor ABO antibodies after BMT between recipients of elutriated and non-elutriated major ABO incompatible grafts was performed by Bär et al. Although the number of patients studied was small, no evidence for prolonged persistence of anti-donor antibodies in the elutriated group was found.

The incidence of immunohematologic complications and PRCA in our study is similar to the incidence reported in the literature. Theoretically one could have expected a higher incidence of immunohaematological complications in our patients. Firstly, all our patients received red cell depleted grafts instead of lowering pretransplant ABO antibody titers in the recipient. In the study by Gmür et al. 14 evaluable patients received an ABO incompatible graft. Seven patients underwent large volume plasma exchange and seven patients received an erythrocyte-depleted graft. Timely recovery of erythropoiesis was observed in all but three patients who had received a red cell depleted graft. Jin et al. however found no difference in erythrocyte transfusion requirements between recipients.
of a red cell depleted graft and patients who had plasma exchange or immunoadsorption before major ABO incompatible BMT. Secondly, all our patients received a lymphocyte-depleted graft in contrast to the patients reported in the literature. Earlier studies in our patient population showed that lymphocyte depletion of donor marrow resulted in a high incidence of mixed chimerism and persistence of host lymphocytes.27,28 However, cytogenetic evaluation of blood and marrow was usually not performed before 6 months after BMT. In the major ABO incompatible patients of the current study cytogenetic analysis of the blood was not performed. Cytogenetic analysis of the bone marrow 6 months after BMT showed no difference in mixed chimerism between the group with PRCA and without PRCA (data not shown). This data suggests that mixed chimerism of the bone marrow does not play a major role in the development of PRCA.

CsA was given as immunoprophylaxis post-transplant in all patients reported in the literature who developed PRCA after major ABO incompatible BMT.10,12,21,22,29,30 In these studies CsA was administered alone or in combination with prednisone or a short course of methotrexate (MTX). PRCA was never observed after the use of only MTX to prevent GVHD. CsA acts primarily as an immunosuppressive agent on T lymphocyte proliferation in response to primary antigen stimulation. In the case of major ABO incompatibility T lymphocytes are re-exposed to the stimulating A or B antigens. In this setting CsA does not inhibit T lymphocyte proliferation. All our patients were treated with CsA. In one patient with PRCA (UPN 100) erythropoiesis began while CsA was still administered. In the other four patients erythropoiesis started 0.5, 1, 2 and 3 months after cessation of CsA according to the treatment protocol. In the three patients with PRCA described by Gmür et al11 erythropoiesis began during CsA treatment in one patient and 10 and 83 days respectively after conclusion of CsA in two patients. Volin and Ruutu21 described one patient recovering from PRCA while still on CsA treatment. In the case study by Ohashi et al29 stopping CsA had no effect on the recovery of PRCA. So, in our opinion CsA only plays a role in the possibility to develop PRCA after allogeneic BMT.

Treatment with corticosteroids for PRCA was not found to be beneficial.10,29,30 In our study UPN 162, 253 and 281 received corticosteroids for GVHD without apparent effect on erythropoiesis. Corticosteroids were administered to UPN 70 4.5 months after BMT in an attempt to treat PRCA. No further erythrocyte transfusions were required. One month afterwards 36% erythrocytes of donor origin were present. Spontaneous recovery can not be excluded as anti-A antibody titers were clearly decreasing before corticosteroid treatment was started.

Treatment successes and failures in PRCA after BMT have been described with plasma exchange10,21,22,32 and erythropoietin (EPO).29,30,33 A patient described by Ohashi et al29 did not respond to EPO alone but erythropoiesis began after the addition of methylprednisolone to EPO. Gamma globulins were not found to be beneficial in two case reports.29,33 In two cases of PRCA treatment with antilymphocyte globulin resulted in restoration of erythropoiesis.22,31 Immuno-hematologic complications did not occur more frequently in recipients of major ABO incompatible marrow grafts, depleted of lymphocytes by counterflow centrifugation, compared to recipients of unmanipulated grafts. Serious morbidity usually did not occur and immunosuppressive intervention was only occasionally necessary.

Acknowledgements
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References
2 Reviron J, Schennetzer C, Bussel A et al. Obstacle to red cell engraftment due to major ABO incompatibility in allogeneic bone marrow transplants (BMT); quantitative and kinetic aspects in 58 BMTs. Transplant Proc 1987; 6: 4618-4622.
13 Klumpp TR. Immunohematologic complications of bone marrow transplantation. Bone Marrow Transplant 1991; 8: 159-170.
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