Oral High Dose Dexamethasone for Pure Red Cell Aplasia Following ABO-Mismatched Allogeneic Peripheral Blood Stem Cell Transplantation: A Case Report

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Abstract Management of pure red cell aplasia following major ABO-mismatched hematopoietic stem cell transplantation is a therapeutic challenge. Various therapeutic modalities have been tried with variable responses, and patient remains transfusion dependent for a long time. We report here the use of pulsed oral high dose dexamethasone for pure red cell aplasia following ABO-mismatched allogeneic transplant with complete recovery.

Keywords ABO-mismatched allogeneic stem cell transplantation · Pure red cell aplasia · Oral pulsed high dose dexamethasone

To the Editor,

Pure red cell aplasia (PRCA) is a known complication following major ABO-mismatched hematopoietic transplantation and various therapeutic modalities have been tried randomly including oral prednisolone, erythropoietin,

rituximab, donor lymphocyte infusion, tapering immunosuppression, intravenous immunoglobulin (IVIG), plasma exchange and injectable high dose dexamethasone [1–6]. Because of variable and unpredictable response of PRCA to these treatment approaches, the patients remain transfusion dependent for a long time, increasing the risk of iron overload and infections [7]. We used oral pulsed high dose dexamethasone in a patient who developed PRCA following ABO-mismatched allogeneic peripheral blood stem cell transplantation (PBSCT) and there was significant improvement in the haemoglobin levels with complete recovery from PRCA without any adverse effects.

A 21-years old male, a case of severe aplastic anemia underwent allogeneic PBSCT from his HLA-matched sibling donor. There was major blood group mismatch with the recipient being O Rh positive and the donor being B Rh positive. Patient had received about 52 packed red blood cell transfusions prior to transplantation. The preparative regimen included fludarabine 30 mg/m² for 6 days, cyclophosphamide 60 mg/kg/day for 2 days and rabbit antithymocyte globulin 3.5 mg/kg/day for 2 days. The total CD 34+ve stem cell dose infused was 5.96 × 10⁶/kg. Graft versus host disease (GvHD) prophylaxis included methotrexate 10 mg/m² on day +1 and 7 mg/m² on days +3 and +6 and cyclosporine 1.5 mg/kg twice daily intravenously, with plasma cyclosporine levels maintained between 150 and 300 ng/ml. Though the patient engrafted on day+10 post PBSCT (absolute neutrophil count >500/μl and unsupported platelet count > 20,000/μl), he continued to be transfusion dependent with pre-transfusion haemoglobin remaining 5–6 g/dl. His retic count was 0.01% and direct Coombs test was negative. There was no acute GvHD and chimerism on day +60 was 100%. Anti-A antibody titers were 1:256 and anti-B antibody titers were 1:128 on day +90. Cytomegalovirus and parvovirus IgM

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and PCR were negative. Bone marrow examination revealed markedly depressed erythroid component (1%) with adequate myeloid and megakaryocytic series suggestive of PRCA. He was given injection erythropoietin 10,000 IU thrice weekly from day +65 for 90 days, followed by oral prednisolone 1 mg/kg/day tapered over 60 days, but there was no response. On day +210 he was given intravenous immunoglobulin (IVIG, 2 g/kg/day for 2 days), but he remained transfusion dependent 30 days post IVIG trial. His cyclosporine dose tapering was started from day +248 but he continued requiring 2 U of red blood cell transfusion every 15 days. Cyclosporine was stopped on day +330. On day +315 patient was given pulsed oral high dose dexamethasone (HDD, 40 mg/day for 4 days). Two weeks following HDD patient's haemoglobin increased from 6.2 to 10.7 g/dl and retic count from 0.01 to 6 %. A second pulse of oral HDD was repeated after 1 month. Patient tolerated HDD well without any side effects. He is now 4 months post HDD with haemoglobin levels remaining above 12 g/dl. His blood group has changed to B Rh positive and anti-B titer reduced to undetectable levels.

PRCA occurs in 10–20 % of ABO-mismatched transplants. Though it does not influence the transplant related mortality or overall survival, it increases the morbidity with transfusion dependency, leading to iron overload and increased risk of infections [6]. Pathophysiology of PRCA following ABO-mismatched allogeneic PBSCT is believed to be due to the persistence of recipient plasma cells which produce antibodies against donor erythroid precursor antigens [1], with the graft being unable to over-ride the recipient's inhospitable plasma cell effect. Various therapeutic approaches have been utilized to deplete the host plasma cells or their effects and have resulted in variable responses [1–6]. Since dexamethasone has significant activity on plasma cells in multiple myeloma [8], and HDD has been successfully used in analogous conditions like immune thrombocytopenia, it can be used to deplete host plasma cells in ABO-mismatched transplants as well. Injectable HDD has been successfully used for treatment of refractory PRCA post major mismatch allogeneic transplantation by Deotare et al. [5]. We reported here successful use of same drug by oral route. This reinforces that dexamethasone can be used for treatment of PRCA post

allogeneic transplantation successfully and without much toxicity. Considering the safety and efficacy of oral HDD [9], other treatment modalities like reduction of immunosuppression or donor lymphocyte infusion which carry a risk of significant GvHD, and IVIG which is more expensive, can be considered later in treatment algorithm for ABO-mismatched post allogeneic transplant PRCA, particularly in resources constrained settings. Notably, HDD can be given by oral route on outpatient basis.

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