Haemopoietic stem cell transplantation is a curative treatment option with minimal transplant-related complications for patients with severe Glanzmann's thrombasthenia

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Aims

Glanzmann's thrombasthenia is a rare autosomal recessive bleeding disorder of platelet function caused by a qualitative or quantitative defect of the platelet membrane glycoprotein IIb/IIIa. For patients with a severe form the condition haemopoietic stem cell transplantation (HSCT) is the only curative option. Since 1985 there have been 19 allogeneic stem cell transplants reported in 18 patients with Glanzmann's thrombasthenia.

We report two successful cases of patients with severe Glanzmann's thrombasthenia with anti-platelet antibodies who had a successful allogeneic HSCT in our centre.

Methods

Patient 1 is a 13-year-old boy who underwent a HSCT after he suffered an intracerebral bleed.

Patient 2 is an 11-year-old girl who had a HSCT when she developed increased frequency of heavy nose bleeds.

Stem cell source: Patient 1 received paternal haploidentical alpha/beta T lymphocyte-depleted granulocyte-colony stimulating factor (G-CSF)-mobilised peripheral blood stem cells.

Patient 2 received 10/10 human leukocyte antigen (HLA)-matched sibling bone marrow.

Conditioning

Conditioning regimes of a combination of fludarabine, thiotepa and treosulfan and antithymocyte globulin (ATG) were used for in both cases:

Patient 1: ATG 2.5 mg/kg for 3 days (day -10 to -8); fludarabine 30 mg/m^2 for 5 days (day -7 to -3); treosulfan 14 g/m^2 for 3 days (day -6 to -4) and thiotepa 5 mg/m^2 bd for 1 day (day -4).

Patient 2: thiotepa 5 mg/m^2 bd for 1 day (day -7); treosulfan for 3 days (day -6 to -4); fludarabine 40 mg/m^2 for 4 days (day -6 to -3); treosulfan for 3 days (day -6 to -4); ATG 2.5 mg/m^2 for 3 days (day -4 to day -2)

Graft versus host disease prophylaxis

Patient 1: ciclosporin 1.5 mg/kg bd from day -1 onwards and methotrexate 15 mg/m^2 on day +1, 10 mg/m^2 on day +3, day +6 and day +11. Ciclosporin was later switched to tacrolimus.

Patient 2: Ciclosporin 1.5 mg/kg bd from day -1 onwards and mycophenolate mofetil 15 mg/kg bd from day -3 to day +35. Ciclosporin was later switched to tacrolimus

Immunosuppression was weaned at 6 months post-HSCT in both patients.

Results

Engraftment

Patient 1 engrafted neutrophils at day +13 and platelets at day +11.

Patient 2 engrafted neutrophils at day +16 and platelets at day +13.

Chimerism

For both patients, 100% donor on all cell fractions at day 28 and on all subsequent tests up to 6 months post-HSCT.

Transplant-related morbidity

Patient 1: Mild gut graft versus host disease which responded to oral prednisolone and budesonide, and switching of immunosuppression from ciclosporin to tacrolimus. He also had cytomegalovirus reactivation which was treated with intravenous ganciclovir and oral valganciclovir.

Patient 2: Ciclosporin induced gum hypertrophy and hirsuitism which responded to switching of ciclosporin to tacrolimus.

At 2-year and 18-month follow up respectively, both patients have no symptoms of Glanzmann's thrombasthenia and no residual complications from stem cell transplant.

Conclusion

Both these cases demonstrate that HSCT can offer curative treatment with minimal transplant-related complications, rapid engraftment, and short duration of neutropaenia in patients with severe Glanzmanns' thrombasthenia. ■

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