Multiple drugs

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Various toxicities: 11 case reports

In a retrospective study of 12 patients with graft failure (GF), who underwent salvage haploidentical hematopoietic stem cell transplantation (HSCT) between 01 January 2012 and 31 July 2020, eleven patients (3 girls and 8 boys; aged: 1.2–14.8 years) were described, who developed various complications during immunosuppressive treatment with alemtuzumab, cyclophosphamide, fludarabine, mycophenolate mofetil, rituximab, tacrolimus, ciclosporin, antithymocyte globulin or treosulfan as a conditioning regimen or for graft versus host disease (GVHD) prophylaxis [*routes and times to reactions onsets not stated*].

The patients were diagnosed with IL10 receptor alpha deficiency (1 patient), myelodysplastic syndrome-refractory cytopenia of childhood (3 patients), severe congenital neutropenia (2 patients), hyper-IgM syndrome (1 patient), haemophagocytic lymphohistiocytosis-Perforin (1 patient), congenital amegakaryocytic thrombocytopenia (1 patient), severe aplastic anaemia (1 patient) and chronic granulomatous disease (1 patient). Subsequently, all patients underwent haematopoietic stem cell transplantation (HSCT). However, all patients developed primary graft failure (7 patients) and secondary graft failure (4 patients). Therefore, salvage haploidentical HSCT was planned, and all patients received conditioning regimen with rituximab 375 mg/m^2 on day -10, alemtuzumab 0.4–1 mg/kg on days -9 to -8, fludarabine 150–160 mg/m^2 on days -7 to -3, treosulfan 20–36 g/m^2 on days -5 to -4 and cyclophosphamide 29 mg/kg on days -3 to -2 (9 patients), rituximab 375 mg/m^2 on day -10, antithymocyte globulin [Thymoglobuline] 5, fludarabine 120 mg/m^2 on days -7 to -3, treosulfan 20 g/m^2 on days -5 to -4 and cyclophosphamide 29 mg/kg on days -3 to -2 (1 patient) and alemtuzumab 1 mg/kg on days -9 to -8, fludarabine 150 mg/m^2 on days -7 to -3, treosulfan 20 g/m^2 on days -5 to -4 and cyclophosphamide 29 mg/kg on days -3 to -2 (1 patient). Subsequently, all patients received unmanipulated bone marrow from HLA-haploidentical father. Afterwards, all patients received GVHD prophylaxis with cyclophosphamide, tacrolimus and mycophenolate mofetil (10 patients) and cyclophosphamide, ciclosporin and mycophenolate mofetil (1 patient). However, all patients developed complications caused by immunosuppressive treatment, which manifested as reactivation of cytomegalovirus and adenovirus infection and BK haemorrhagic cystitis (1 patient), engraftment syndrome, acute respiratory distress syndrome (ARDS), bacteraemia and *Streptococcus mitis* infection (1 patient), adenovirus enteritis (1 patient), reactivation of cytomegalovirus and adenovirus infection and aspergillosis (1 patient), reactivation of human herpesvirus 6 and adenovirus infection and sepsis, toxic nephropathy (1 patient), reactivation of cytomegalovirus infection and sepsis, *Clostridium difficle* colitis (1 patient), reactivation of human herpesvirus 6 and cytomegalovirus infection and Norovirus (enteritis), sepsis, deep skin infection (*Pseudomonas*) (1 patient), reactivation of cytomegalovirus infection and sepsis (*Escherichia coli*), bacteraemia (coagulase-negative *Staphylococcus*) (1 patient), reactivation of cytomegalovirus and adenovirus infection (2 patients), reactivation of cytomegalovirus, BK virus, adenovirus and human herpesvirus 6 infection and BK haemorrhagic cystitis, sepsis (*Enterococcus faecium*), fungal skin infection (*Trichosporon Asahi*) (1 patient).

All patients had resolution of complications. Afterwards, one patient developed idiopathic pneumonitis on day +226, which was treated with etanercept. On day +259, the same patient died due to CLIPPERS syndrome with intracranial bleeding and consecutive hydrocephalus.

Immunosuppressive treatments were stopped on day +56–240 for all patients. At follow-up, 10 patients remained alive.

Albert MH, et al. Salvage HLA-haploidentical hematopoietic stem cell transplantation with post-transplant cyclophosphamide for graft failure in non-malignant disorders. Bone Marrow Transplantation 56: 2248-2258, No. 9, Sep 2021. Available from: URL: http://doi.org/10.1038/s41409-021-01323-9

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