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LETTER TO THE EDITOR

Successful cord blood transplantation for a paroxysmal nocturnal hemoglobinuria complicated with Budd-Chiari syndrome and myelodysplastic syndrome

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Paroxysmal nocturnal hemoglobinuria (PNH) is a rare acquired disorder of hematopoietic stem cells. The disease is characterized by hemolytic anemia, bone marrow failure, and thrombosis [1]. Allogeneic hematopoietic stem cell transplantation (Allo-HSCT) is the only curative treatment for PNH, but it has a disadvantage of high incidence of treatment-related death. Therefore, the indication is currently limited [2].

A 37-year-old male who visited our hospital with complaint of abdominal pain was diagnosed with classic PNH with 22.4% of $CD55^{-}CD59^{-}$ red blood cells.

Bone marrow analysis showed no evidence of myelodysplastic syndrome by morphological and cytogenetic examination. Ultrasound examination showed extremely narrowed inferior vena cava and hepatic vein. He was diagnosed as PNH complicated by Budd-Chiari syndrome. Eculizumab was not given due to financial reasons.

At 18 months after diagnosis, pancytopenia progressed and bone marrow analysis revealed increased blasts (5.2%), dysplastic changes in all lineages, and cytogenetic abnormality (monosomy 7), leading to a diagnosis of MDS RAEB-1, which progressed to RAEB-2 at 19 months. Since HLA-matched donors were not available, he received CBT using 5/6 HLA-matched cord blood unit with 1.44×10^5/kg CD34-positive cells and 1.93×10^7/kg nucleated cells. Conditioning regimen consisted of fludarabine 30 mg/m^2/day for 6 days, i.v. busulfan 3.2 mg/kg/day for 2 days, and melphalan 40 mg/m^2/day for 2 days. Tacrolimus and short-term methotrexate were used for graft-versus-host disease (GVHD) prophylaxis. For sinusoidal obstruction syndrome (SOS) prophylaxis, ursodeoxycholic acid and dalteparin were administered. Neutrophil and platelet engraftment were achieved successfully. Bone marrow aspiration performed at day 32 showed no evidence of MDS by cytogenetic examination. Regarding regimen-related toxicity, hepatotoxicity including SOS was not seen. He developed grade II acute GVHD and mild chronic GVHD of the skin, which was controlled with steroid ointment treatment. At 3.5 years after CBT, hepatic vein lumen was easily identifiable by ultrasound examination. At present, he is doing well 4 years after transplantation without recurrence of MDS, PNH, and thrombosis.

The primary indications for allo-HSCT for PNH were cytopenia, life-threatening thrombosis, and hemolysis. Considering the efficacy of eculizumab, thrombosis alone is currently not a rationale for allo-HSCT; however, MDS is still the indication for allo-HSCT [3–5]. There are few reports of allo-HSCT for PNH [2, 5–8]. It was suggested that reduced-intensity conditioning (RIC) might be superior to myeloablative conditioning (MAC) [6, 7]. It was very difficult to select the conditioning regimen for the present case. RIC should be preferable for Budd-Chiari syndrome, which is a significant risk factor of transplant-related mortality (46%) [7]. On the other hand, for MDS with high-risk cytogenetics, sufficient antitumor effect is needed to reduce the relapse rate. In addition, his donor source was cord blood for which the standard regimen has not been established.

Recently, Yamamoto et al. reported promising outcome of conditioning regimen for CBT consisting of fludarabine, busulfan, and melphalan [9]. For the present case, we modified this regimen with the dose reduction of busulfan to 6.4 mg/kg, due to Budd-Chiari syndrome, and achieved a successful transplant with disease free for 4 years after transplant. The treatment strategy we chose may be informative for PNH cases with similar status.

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Compliance with ethical standards

All the authors have read the manuscript and have approved this submission.

The patient has provided permission to publish these features of his case, and the identity of the patient has been protected.

Conflict of interest The authors declare that they have no conflicts of interest.

Ethical approval All procedures performed in this report were in accordance with the ethical standards of the institutional and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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