

Allogeneic stem cell transplant in a patient with aplastic anemia with bacteremia and candidemia

Bacteremia ve candidemiası olan aplastik anemili bir hastada allojenik kök hücre nakli

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Allogeneic hematopoietic stem cell transplantation (HSCT) is the definitive therapy for severe aplastic anemia (SAA) [1,2]. The major factors that limit the success of HSCT are graft rejection and graft-versus-host disease (GVHD) [3,4]. Engraftment depends on the conditioning regimen, GVHD prophylaxis, number of donor marrow cells infused and alloimmunization of the patient [3,4]. Taking an aplastic anemia patient with bacteremia and candidemia for transplant is a very high-risk proposition.

A 35-year-old male was evaluated for pancytopenia. His baseline blood counts revealed a hemoglobin of 6 gm%, total leukocyte count of 1200/mm³ with an absolute neutrophil count <500/mm³, platelet count of 15000/mm³, and a reticulocyte count of 0.2%. A bone marrow examination revealed a hypocellular marrow with normal cytogenetics. With these features, he fulfilled the criteria for a diagnosis of SAA. He was admitted with fever of one week's duration (temperature 38-39°C) with vomiting and abdominal pain. As he had features of intestinal obstruction, he was taken for laparotomy under platelet cover. He had intestinal obstruction due to multiple bowel hematomas and underwent jejunal resection with a duodenojejunostomy. Postoperatively he developed bacteremia and candidemia. Blood culture grew *Klebsiella pneumoniae* sensitive to imipenem/meropenem/amikacin and *Candida tropicalis* sensitive to amphotericin/fluconazole. *Staphylococcus aureus* was grown from the wound swab on two occasions, sensitive to vancomycin/teicoplanin. He was treated with imipenem 500 mg q6h, teicoplanin 400 mg od, amphotericin B 1 mg/kg/d,

voriconazole 200 mg bd, and granulocyte infusions for two weeks, after which his blood cultures were negative.

Granulocyte infusions were given on a daily basis for two weeks with an average cell dose of 0.8-1.0 x 10¹⁰ nucleated cells/day. During this time, HLA typing of his sister was done and found to be 6 antigens-matched. During the afebrile period, the patient was started on conditioning with fludarabine (30 mg/m² IV daily on days 2-4), busulfan (4 mg/kg/d q6h on days 5,6) and cyclophosphamide (350 mg/m² IV daily on days 2-4). A peripheral blood stem cell (PBSC) harvest was done from the donor after five days of granulocyte colony-stimulating factor (G-CSF) at 10 mcg/kg/d. A volume of 200 ml was collected with a MNC of 6.6 x 10⁸ cells/kg. The CD 34 cell dose was 4.7 x 10⁶ cells/kg. GVHD prophylaxis was IV cyclosporine (CsA) at a dose of 3.0 mg/kg/d. G-CSF was started from day +7 at 5 mcg/kg/d. CsA was changed to the oral route on day +15. CsA trough levels were measured by microparticle enzyme immunoassay and maintained between 200-400 ng/dl. An absolute neutrophil count >500/mm³ was attained on day +9 and an unsupported platelet count >20000/mm³ was achieved on day +12. Chimerism analysis on day +30 by XY analysis revealed 97% donor cells. The patient was discharged on day +36 and was well at the last follow-up on day +120. The total duration of imipenem was 30 days, teicoplanin 21 days, amphotericin 31 days, and voriconazole 16 days.

Taking a patient with aplastic anemia with sepsis for bone marrow transplant carries a mortality close to 100%. The inci-

dence of proven invasive fungal infections in both adult and pediatric patients undergoing allogeneic HSCT is 13-15%, with cure rates of 40% and a mortality rate of 20% exclusively contributed by fungal infections [5]. Our patient was successfully transplanted using a conditioning regimen, which was not very highly immunosuppressive but enough to achieve engraftment. PBSC was preferred to bone marrow for faster engraftment. Busulfan along with cyclophosphamide has been used for conditioning in SAA [6]. Busulfan is cheaper than total body irradiation and antithymocyte globulin (ATG). Hence, we recommend this conditioning as one option in patients with aplastic anemia, especially those with infection.

References

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