LETTER TO THE EDITOR

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Daratumumab and Eltrombopag for Pure Red Cell Aplasia Following ABO-Incompatible Allogeneic Hematopoietic Stem Cell Transplant for Acute Lymphoblastic Leukemia

ABO Kan Grubu Uyumsuz Allojenik Hematopoetik Kök Hücre Nakli Olan Hastada Gelişen Saf Eritroid Hücre Aplazisinde Daratumumab ve Eltrombopag Kullanımı

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To the Editor,

ABO-incompatible allogeneic stem cell transplantation (ASCT) has been associated with delayed erythrocyte engraftment and pure red cell aplasia (PRCA) [1,2]. PRCA is seen in 7.5% to 29% of major blood group-incompatible transplants [3,4]. There are rare reports of the use of daratumumab and eltrombopag in the treatment of post-transplant PRCA [5,6,7]. We describe the first case in the literature in which these two new agents, daratumumab and eltrombopag, were used for the same patient and a response was obtained.

A 29-year-old male patient with T-cell acute lymphoblastic leukemia underwent ASCT from a human leukocyte antigen-A mismatched unrelated male donor. Major blood group mismatch occurred (patient: O Rh-positive; donor: A Rh-positive). He received conditioning with fludarabine cyclophosphamide and total body irradiation (myeloablative regimen). Graft-versus-host disease (GVHD) prophylaxis entailed post-transplantation cyclophosphamide, cyclosporin, and mycophenolate mofetil. Due to a high anti-A isohemagglutinin titer (1/512) before ASCT, we applied plasmapheresis for the patient with fresh frozen plasma. After plasmapheresis, the anti-A titer was 1/16. He continued to require red blood cell transfusion support following engraftment once or twice every 2 weeks. The anti-A titer was found to be 1/128 during follow-up. Bone marrow aspiration and biopsy performed on day +45 did not show any erythroblasts, but cells belonging to other series were present (Figures 1A and 1B). During this time, the corrected reticulocyte count was persistently low (0.8%-1.5%). The direct Coombs test was negative and the lactate dehydrogenase level was elevated at 370 U/L (upper limit of normal: 120-246 U/L).

The patient's erythropoietin level was >750 U/L (normal: 4.3-29 IU/L). In the first month, he had 100% donor chimerism. Intravenous immunoglobulin (IVIG) was given at 400 mg/kg/day for 5 days on days +46-50 for PRCA. He did not have any evidence of GVHD; hence, mycophenolate mofetil was stopped on the 35th day and cyclosporine tapering was initiated on day +60. The anti-A antibody titer and reticulocyte value remained unchanged on day +90 subsequent to the cessation of immunosuppressive treatment, rituximab, and IVIG therapy. He was given daratumumab at 16 mg/kg by intravenous infusion once a week for 8 weeks from day +175 to day +252 after ASCT. During daratumumab treatment, 14 units of erythrocyte replacement were required. Following daratumumab therapy, the corrected reticulocyte count was 1.48%, the anti-A titer was 1/16, and the haptoglobin value was 2.03 (Figures 2 and 3). The post-transplant anti-A titer decreased after the 8th weekly dose of daratumumab. Eltrombopag treatment (50 mg/day) was started because of transfusion dependence. During the course of eltrombopag therapy, the patient required 3 units of erythrocyte suspension. On day 12 of treatment, the patient had anti-A negativity, haptoglobin of 2.06, and corrected reticulocyte count of 1.74%. After the 12th day of therapy, he did not need erythrocyte suspensions and his hemoglobin level increased. On the 18th day of treatment, reticulocytosis was detected and bone marrow aspiration and biopsy showed hyperplasia in erythroblasts (Figure 4A and 4B). The decrease in anti-A titer under daratumumab treatment and the subsequent transfusion independence observed following the switch to eltrombopag treatment may be indicative of an additive effect exerted by both agents.

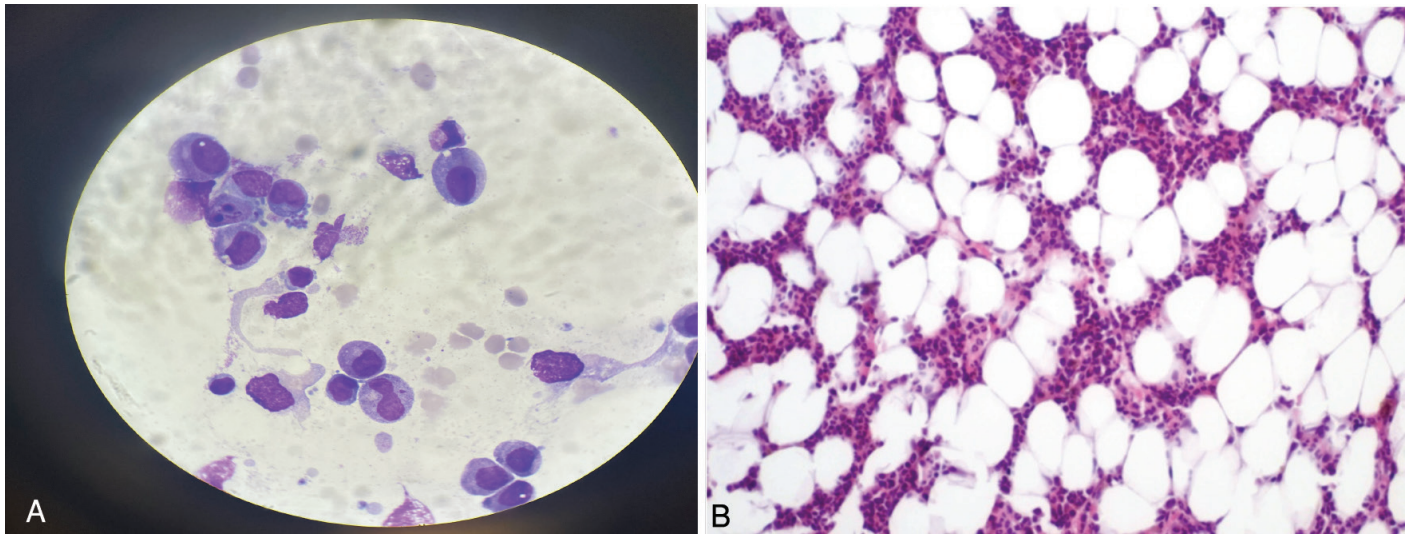

Figure 1. Bone marrow (BM) aspiration (A) and biopsy (B) were performed before treatment with daratumumab. The BM aspirate (A; 100ˣ magnification) and BM biopsy (B; hematoxylin and eosinophil, 200ˣ) findings showed decreased erythroblasts.

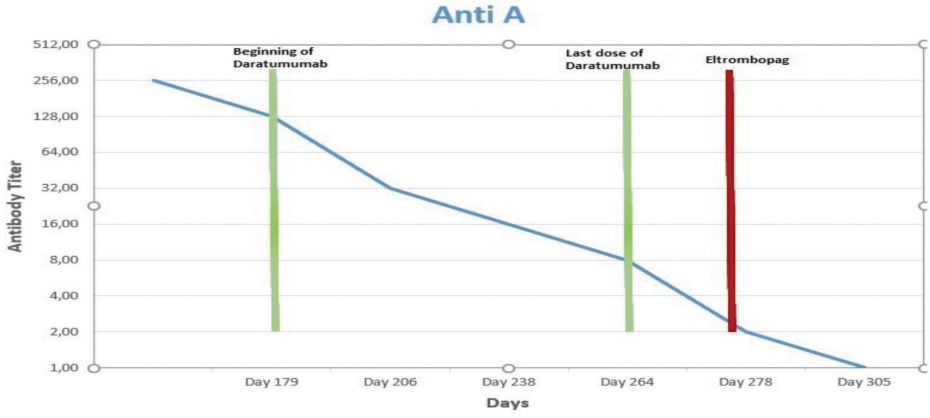

Figure 2. ABO isoagglutinin titer during the course of treatment for pure red cell aplasia following ABO-mismatched allogeneic HSCT. The blue line represents anti-A IgG titers.

HSCT: Hematopoietic stem cell transplantation; IgG: immunoglobulin G.

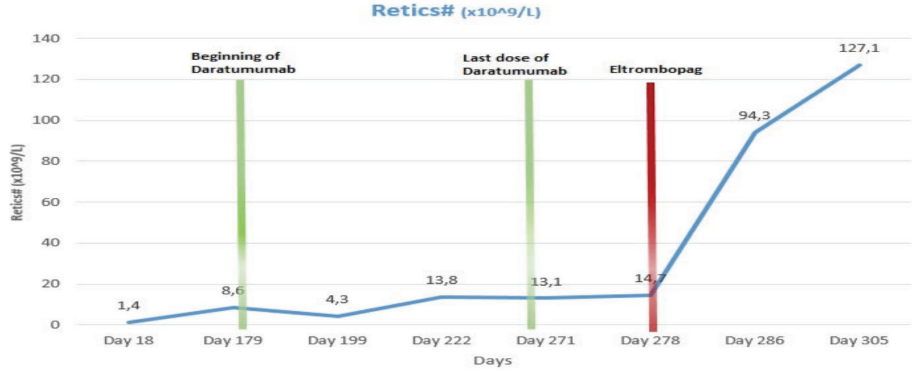

Figure 3. Absolute reticulocyte counts during the course of pure red cell aplasia following ABO-mismatched allogeneic HSCT. The blue line represents absolute reticulocyte counts.

HSCT: Hematopoietic stem cell transplantation.

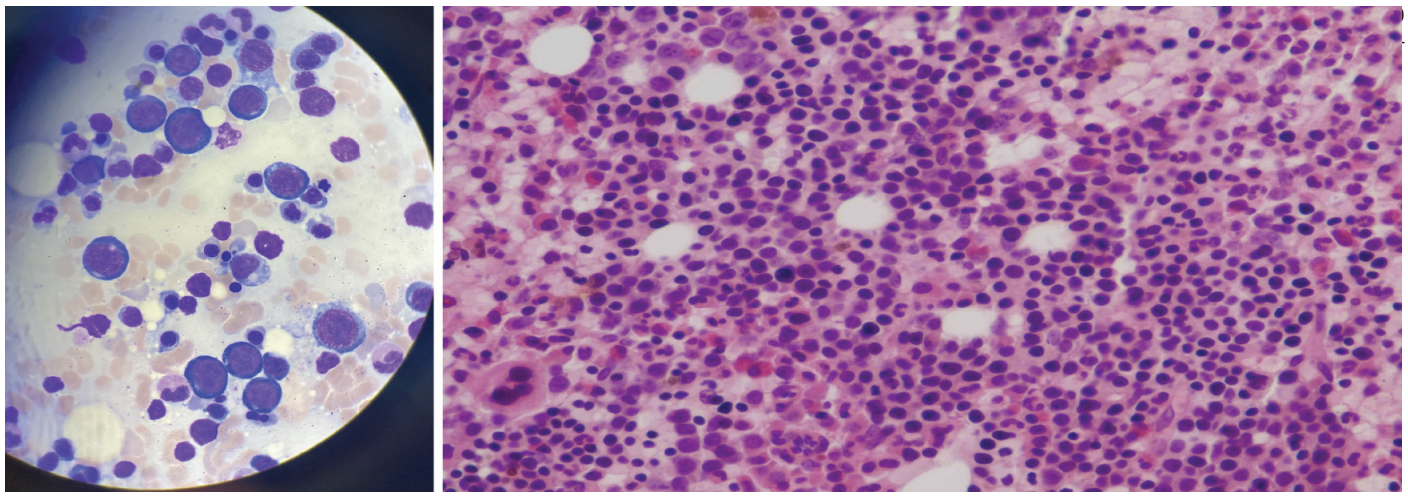

Figure 4. Bone marrow (BM) aspiration (A) and biopsy (B) were performed after treatment with daratumumab and eltrombopag. BM aspirate (A; 100^{x} magnification) and BM biopsy (B; hematoxylin and eosin, 200^{x}) findings showed hyperplasia in erythroblasts.

Keywords: Daratumumab, Eltrombopag, Pure red cell aplasia, Acute lymphoblastic leukemia

Anahtar Sözcükler: Daratumumab, Eltrombopag, Saf eritroid hücre aplazisi, Akut lenfoblastik lösemi

Ethics

Informed Consent: The patient was interviewed and informed consent was obtained.

Footnotes

Authorship Contributions

Data Collection or Processing: A.K., E.Ö.; Analysis or Interpretation: S.D., F.C.; Literature Search: S.D., E.İ., G.K., M.T.A., F.Ö., F.C.; Writing: S.D., E.İ., G.K., A.K., E.Ö., M.T.A., F.Ö., F.C., G.Ö.

Conflict of Interest: No conflict of interest was declared by the authors.

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