

# Early Direct Antiglobulin Test Negativity after Bendamustine and Rituximab Treatment in Chronic Lymphocytic Leukemia: Two Cases

## Bendamustin ve Ritüksimab Tedavisi ile Erken Direkt Antiglobülin Testi Negatifliği Elde Edilen İki Kronik Lenfositik Lösemi Olgusu

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University of Health Sciences, İstanbul Training and Research Hospital, Clinic of Hematology, İstanbul, Turkey

### To the Editor,

Autoimmune hemolytic anemia (AIHA) can emerge at any stage of chronic lymphocytic leukemia (CLL); furthermore, patients can present with AIHA before diagnosis [1]. Although direct antiglobulin test (DAT) positivity is one of the hallmarks of AIHA, it was also demonstrated to be associated with advanced disease [2] and poor prognosis [3] independent of hemolytic anemia in CLL patients [3]. Here we present two CLL patients with AIHA whose DAT results became negative shortly after receiving bendamustine-rituximab (BR) chemotherapy.

### Case 1

A 69-year-old male patient who was being followed without treatment for CLL in Rai stage 2 for 6 months presented with abdominal pain and jaundice. Laboratory tests were as follows: leukocytes: 55,140/ $\mu$ L, lymphocytes: 51,240/ $\mu$ L, hemoglobin: 5.3 g/dL, platelets: 46,000/ $\mu$ L, indirect bilirubin: 2.89 mg/dL, haptoglobin: 2 mg/dL, lactate dehydrogenase (LDH): 1585 U/L, and DAT positive for Immunoglobulin G (IgG) (no titer provided). Imaging studies showed compressing conglomerate lymph node masses in the abdomen. The patient was started on steroid and BR treatments. The hemoglobin value rose to normal levels and DAT became negative after 3 cycles of BR. The patient received 6 cycles of BR chemotherapy and steroids were interrupted at the 5<sup>th</sup> month of treatment. The patient has been followed in remission for 1 year.

### Case 2

A 75-year-old female patient who was being followed without treatment with the diagnosis of CLL in Rai 0 stage for 8 years was admitted due to weakness and fatigue. Laboratory tests were as follows: leukocytes: 78,840/ $\mu$ L, lymphocytes: 67,020/ $\mu$ L, hemoglobin: 6.3 g/dL, platelets: 255,000/ $\mu$ L, indirect bilirubin: 2.58 mg/dL, LDH: 504 U/L, haptoglobin: 1 mg/dL, corrected reticulocyte count: 5.2%, and DAT positive for IgG (4+). The patient was started on steroid treatment and subsequently BR therapy was added due to increased lymphocyte doubling time. After the first cycle, the DAT titer dropped to 3+. Hemoglobin

value rose to normal levels and DAT became negative after 3 cycles of BR. Steroids were ceased at the 7<sup>th</sup> month of treatment; The patient completed 6 cycles of BR and has been followed in remission for 1 year.

While the standard approach in CLL patients with AIHA is steroids, systemic chemotherapy is recommended in refractory cases and in patients requiring treatment for CLL [1]. Although first-line therapy in CLL patients is the fludarabine-cyclophosphamide-rituximab regimen, the wide use of BR chemotherapy, especially in advanced-age patients, has brought up the application of this combination in patients with AIHA [4,5]. In a recent study including 26 CLL patients who had AIHA and received BR, the response rate was 81% for AIHA and 77% for CLL [4]. Similarly, our patients also responded well in terms of CLL and AIHA. The most striking point was that DAT became negative in a short period of time (after 3 cycles of BR).

In conclusion, in addition to being a plausible option in advanced-age CLL patients, BR seems to be an important treatment of choice in terms of eliminating the poor prognostic factor of DAT positivity and assuring safe cessation of steroid treatment due to rapid achievement of DAT negativity.

**Keywords:** Chronic lymphocytic leukemia, Autoimmune hemolytic anemia, Bendamustine, Rituximab

**Anahtar Sözcükler:** Kronik lenfositik lösemi, Otoimmün hemolitik anemi, Bendamustin, Ritüksimab

**Informed Consent:** Informed consent was obtained from both patients.

**Conflict of Interest:** The authors of this paper have no conflicts of interest, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

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Turkish Journal of Hematology, Published by Galenos Publishing House



Address for Correspondence/Yazışma Adresi: Elif SUYANI, M.D., University of Health Sciences, İstanbul Training and Research Hospital, Clinic of Hematology, İstanbul, Turkey  
Phone : +90 212 459 63 04  
E-mail : elifsuyani@hotmail.com ORCID-ID: orcid.org/0000-0002-2516-671X

Received/Geliş tarihi: December 28, 2017  
Accepted/Kabul tarihi: July 09, 2018

DOI: 10.4274/tjh.2017.0464

## Demodicidosis Accompanying Acute Cutaneous Graft-Versus-Host Disease after Allogeneic Stem Cell Transplantation

Allojeneik Kök Hücre Nakli Sonrası Akut Graft Versus Host Hastalığına Eşlik Eden Demodisidoz

İ Pelin Aytan<sup>1</sup>, İ Mahmut Yeral<sup>1</sup>, İ Çiğdem Gereklioğlu<sup>2</sup>, İ Nazım Emrah Koçer<sup>3</sup>, İ Nurhilal Büyükkurt<sup>1</sup>, İ İlknur Kozanoğlu<sup>1</sup>, İ Hakan Özdoğu<sup>1</sup>, İ Can Boğa<sup>1</sup>

<sup>1</sup>Başkent University Faculty of Medicine, Adana Dr. Turgut Noyan Application and Research Center, Clinic of Hematology, Adana, Turkey

<sup>2</sup>Başkent University Faculty of Medicine, Department of Family Medicine, Adana, Turkey

<sup>3</sup>Başkent University Faculty of Medicine, Adana Dr. Turgut Noyan Application and Research Center, Clinic of Pathology, Adana, Turkey

### To the Editor,

A 39-year-old female with acute myeloid leukemia was admitted to our transplantation clinic with face eruption without any pruritus. The eruption had occurred 28 days after she underwent an allogeneic hematopoietic stem cell transplantation (SCT). She was allografted with  $6.12 \times 10^6$  non-manipulated CD34+ cells from a fully matched sibling donor after a conditioning regimen including busulfan (12.8 mg/m<sup>2</sup>), fludarabine (150 mg/m<sup>2</sup>), anti-thymocyte globulin (30 mg/kg), and total body irradiation (400 Gy/day). Graft-versus-host disease (GVHD) prophylaxis comprised methotrexate at 12 mg/day for 3 days and cyclosporine A at 75 mg twice daily. No recent changes had been made to the medication. Neutrophil and thrombocyte engraftment both occurred on day 11. The toxicity related to the regimen was mild, being assigned the first grade for oral mucosa according to the Bearman scale [1]. The findings of the physical examination were patchy and confluent erythema of the face, suspicious for cutaneous acute GVHD. There were no other skin changes except that of the palms and soles. Neither intestinal nor hepatic acute GVHD occurred. Laboratory evaluation revealed a white blood cell count of 12,000/ $\mu$ L, a hemoglobin level of 11.5 g/dL, a platelet count of 158,000/ $\mu$ L, and an absolute

neutrophil count of 8400/ $\mu$ L. A 4-mm skin punch biopsy was performed [2]. There were lymphocytes and polymorphic neutrophils that attacked hair follicles and two Civatte bodies. Histochemically *Demodex folliculorum* was diagnosed with PAS staining within the hair follicles (Figures 1A and 1B). Even with lymphocytes attacking hair follicles and Civatte bodies suggesting GVHD, *Demodex* folliculitis can mimic acute GVHD (Figures 1C and 1D). Demodicidosis was treated successfully with local 1% metronidazole and 5% permethrin. Methylprednisolone was also administered from the beginning of the symptoms and the dosing was reduced by 8 mg every week. The skin eruptions on the face and the neck resolved on day +52.

*Demodex* folliculitis after allogeneic SCT is seen rarely and, as far as we know, our case is the sixth reported case [3,4,5,6]. The most important differential diagnosis of *Demodex* folliculitis within the first 100 days after allogeneic SCT is acute GVHD. The infestation by *Demodex* sp. can be associated with immune suppression. The differential diagnosis of facial erythema after bone marrow transplantation includes acute GVHD, drug eruptions, systemic lupus erythematosus, viral exanthema, toxic erythema of chemotherapy, drug-induced photosensitivity, and photodermatitis [3]. In our case there