LETTER TO THE EDITOR

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Epstein-Barr Virus-Induced Warm Autoimmune Hemolytic Anemia

Epstein-Barr Virüsü Kaynaklı Sıcak Otoimmün Hemolitik Anemi

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To the Editor,

A 24-year-old male patient was admitted to the intensive care unit (ICU) with high-grade fever, sore throat, skin rash, cough, and shortness of breath for 7 days. On physical examination he had mild pallor, a generalized erythematous and maculopapular rash, and hepatomegaly of 3 cm below the right costal margin but did not have icterus or any palpable lymphadenopathy and splenomegaly. Baseline investigations showed hemoglobin (Hb) of 100 g/L, total leukocyte count of $27x10^9$/L with absolute neutrophil count of $25.6x10^9$/L, and platelet count of $139x10^9$/L. Procalcitonin was elevated at 23.3 ng/mL, but all cultures were sterile. A rheumatology profile revealed negative results for both antinuclear antibody and anti-double-stranded DNA tests. The ICU team administered broad-spectrum antibiotics and best supportive care. His fever subsided and constitutional symptoms improved, but the Hb level gradually declined, as depicted in Figure 1. At this time, the hematology team was consulted regarding anemia. The hematologists advised a reticulocyte count, a direct antiglobulin test (DAT) and extended DAT, Epstein-Barr virus (EBV) reverse transcriptase polymerase chain reaction (RT-PCR) testing, and EBV anti-viral capsid antigen immunoglobulin M (EBV anti-VCA IgM) testing. His reticulocyte count was reported as 10.8%, while the DAT indicated a result of +2 and the extended DAT showed IgG levels at +2. The column agglutination technique (CAT) was used with polyspecific Coombs gel cards (BIO-RAD, Cressier, Switzerland) for the DAT. The monospecific DAT employed gel cards with specific antihuman globulin reagents (IgG, IgA, IgM, C3c, and C3d). An autocontrol alongside the DAT using the CAT showed positive reactivity (+2). Cold acid elution (CAE) on DAT-positive cells revealed autoantibodies causing pan-agglutination with the panel's red blood cells (RBCs). Alloimmunization was ruled out due to the absence of prior blood transfusions. The EBV anti-VCA IgM test was positive and EBV-RT-PCR revealed 55,200 viral copies/mL. The presence of IgG autoantibodies on sensitized RBCs (DAT IgG: +2) and serum autoantibodies reactive solely at

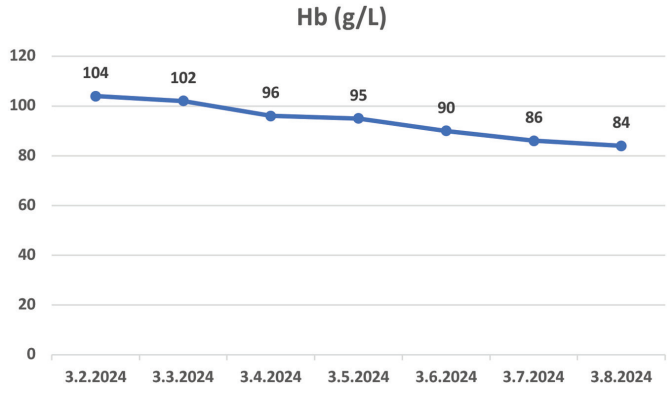

Figure 1. Graph showing a gradual fall in hemoglobin (Hb) prior to treatment with corticosteroids.

37 °C confirmed warm autoimmune hemolytic anemia (wAIHA). CAE on RBCs further revealed autoantibodies optimally reactive at 37 °C. The warm antibody was attributed to EBV infection, not antibiotics, as the positive DAT results persisted for 3 weeks after the antibiotic treatment. He was administered treatment with a 4-day course of pulse dexamethasone at 40 mg/day by injection followed by oral prednisolone at 1 mg/kg/day and supplemented with folic acid, resulting in Hb improvement from 93 g/L to 109 g/L after 1 week. This patient had rare wAIHA secondary to EBV infection. EBV infection causes about 3% of AIHA cases. AIHA associated with infections such as EBV or *Mycoplasma pneumoniae* are usually of the cold type [1]. In cold AIHA, IgM autoantibodies target the i- and I-antigens of RBCs, causing hemolysis [2]. Only three published case reports of wAIHA secondary to EBV infection exist to date and the mechanism of EBV-induced AIHA remains unclear. One possibility is the production of antibodies against EBV that cross-react with RBC membrane antigens, triggering the complement cascade [3,4].

In conclusion, we have reported a case of wAIHA secondary to EBV infection. While EBV is commonly associated with cold

AIHA, the occurrence of warm antibodies secondary to EBV causing AIHA is exceedingly rare. This case underscores the potential for EBV to trigger wAIHA, which typically responds well to corticosteroid treatment [5].

Keywords: Warm autoimmune hemolytic anemia, Epstein-Barr virus, Corticosteroids, Immunoglobulin G autoantibody, Direct antiglobulin test

Anahtar Sözcükler: Sıcak otoimmün hemolitik anemi, Epstein-Barr virüsü, Kortikosteroidler, İmmünoglobulin G otoantikoru, Direkt antiglobulin testi

Ethics

Informed Consent: Informed consent was obtained from the patient.

Authorship Contributions

Surgical and Medical Practices: K.B., C.A., R.S., D.S.; Concept: K.B., C.A., R.S.; Design: K.B., C.A.; Data Collection or Processing: K.B., D.S.; Analysis or Interpretation: K.B., C.A.; Literature Search: K.B., K-C.M.; Writing: K.B., K-C.M.

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