LETTERS TO THE EDITOR
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Epstein Barr Virus Induced Warm Autoimmune Hemolytic Anemia

Bilal K. et al: Epstein Barr Virus induced Warm Autoimmune Hemolytic Anemia

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Dear Editor,

A 24-year-old male presented in 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, generalized erythematous, maculopapular rash, hepatomegaly of 3cm below the right coastal margin but did not had icterus, any palpable lymphadenopathy and splenomegaly. His baseline investigations showed a hemoglobin (Hb) of 100 g/L, total leukocyte count of $27x10^9$/L with absolute neutrophil count (ANC) of $25.6x10^9$/L, platelet count of $139x10^9$/L. His Procalcitonin was elevated at 23.3ng/ml, but all cultures were sterile. Rheumatology profile showed negative results for both anti-nuclear antibody (ANA) and anti-double stranded DNA (anti-dsDNA) tests. The ICU team administered broad-spectrum antibioticsand best supportive care. His fever subsided, constitutional symptoms improved, but Hb level gradually declined, as depicted in Figure 1. At this time the haematology team was referred for anemia. The haematologists advised a reticulocyte count, direct anti-globulin test (DAT), extended DAT, Epstein Barr reverse transcriptase polymerase chain reaction (EBV-RTPCR) & EBV anti-viral capsid antigen IgM (EBV anti-VCA IgM). His reticulocyte count measured at 10.8%, while the DAT indicated a result of +2, and the extended DAT showed IgG levels at +2. Column Agglutination Technique (CAT) with polyspecific Coombs gel cards (BIO-RAD, Switzerland) was used for DAT. Monospecific DAT employed gel cards with specific antihuman globulin reagents (IgG, IgA, IgM, C3c, C3d).Autocontrol alongside DAT using CAT showed positive reactivity (+2). Cold acid elution (CAE) on DAT-positive cells revealed autoantibodies causing pan agglutination with the panel RBCs. Alloimmunization was ruled out due to the absence of prior blood transfusions. His EBV anti-VCA IgM was positive and EBV-RTPCR revealed 55,200 viral copies/ml. The presence of IgG autoantibodies on sensitized RBCs (DAT IgG +2) and serum autoantibodies reactive solely at 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 persisted three weeks post-antibiotic treatment. He was initiated treatment with a four-day course of injection pulse dexamethasone at 40mg/day, followed by oral prednisolone at 1mg/kg/day, supplemented with folic acid, resulting in Hb improvement from 93 g/L to 109 g/L after one week.Our patient had rare wAIHA secondary to EBV infection. EBV infection causes about 3% of AIHA cases. AIHA associated with infections such as EBV and Mycoplasma pneumoniae, are usually of cold type [1]. In cold AIHA, IgM autoantibodies target i and I-antigens of RBCs, causing hemolysis[2]. Only three published case reports of wAIHA secondary to EBV infection exist to date. The mechanism of EBV-induced AIHA remains unclear. One possibility is the production of antibodies against EBV that cross-react with RBCs membrane antigens, triggering the complement cascade [3,4].

In conclusion, we reported a case of wAIHA secondary to EBV infection. While EBV is commonly associated with cold AIHA, the occurrence of warm antibody 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].

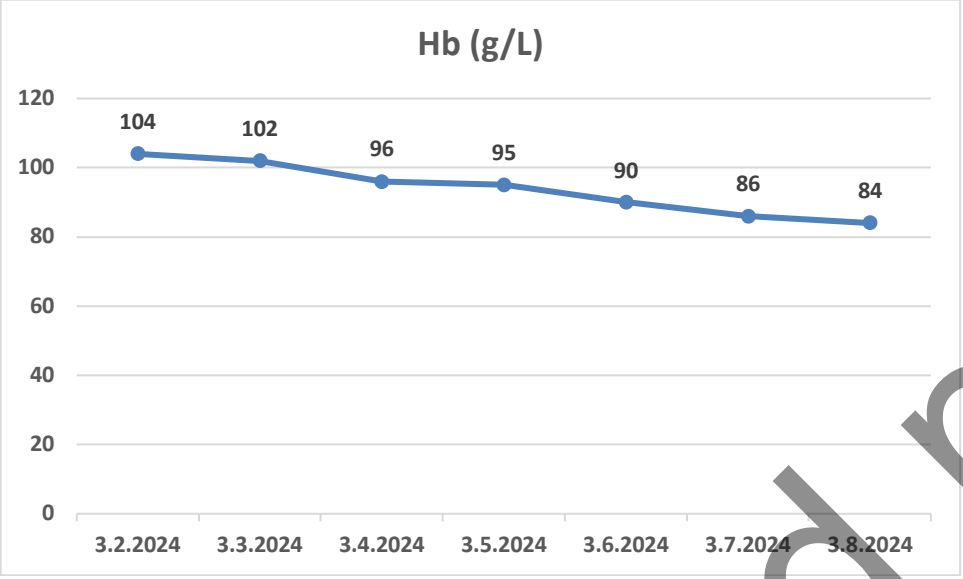

Figure 1. Graph showing gradual fall in Hb prior to treatment with corticosteroids

Keywords: Warm autoimmune haemolytic anemia, Epstein Barr Virus, corticosteroids, IgG autoantibody, Direct anti-globulin test

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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No conflict of interest was declared by the authors.

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