EDİTÖRE MEKTUP/LETTER TO THE EDITOR
J Turgut Ozal Med Cent 2013:20(3):289-290

Journal Of Turgut Ozal Medical Center
www.jtomc.org

Evans Syndrome

Evans Sendromu

İlhami Berber, Mehmet Ali Erkurt, Mustafa Köroğlu, İrfan Kuku, Emin Kaya, Recep Bentli

İnönü Üniversitesi Tıp Fakültesi, Hematoloji Bilim Dalı, Malatya, Türkiye

Dear Editor;

Evans Syndrome (ES) is an autoimmune disease which an individual's antibodies attack their own red blood cells and platelets, sometimes with neutrophils, with a positive direct antiglobulin test in the absence of known underlying etiology (1). The syndrome is characterised by periods of remission and exacerbation, and response to treatment varies even within the same individual. ES is a rare diagnosis and appears to be a disorder of immune regulation, the exact pathophysiology is unknown (2). Clinic presentations may differ according to thrombocytopenia or autoimmune hemolytic anemia either separately or concomitantly. Clinical presentation includes the usual features of thrombocytopenia (mucocutaneous bleeding, petechia, bruising) and/or hemolytic anemia (pallor, lethargy, jaundice, heart failure in severe cases). Examination may reveal lymphadenopathy, hepatomegaly and splenomegaly (2). The most important differential diagnosis is autoimmune lymphoproliferative syndrome (ALPS). Therefore measurement of peripheral blood T-cell subsets by flow cytometry is essential in all cases of Evans syndrome. The presence of double negative (CD4/CD8), CD3+, TCRab+) T cells have been found to be the most sensitive first-line screening test for ALPS (and allow differentiation from cases of Evans syndrome) (3). The diagnosis is made upon blood tests to confirm hemolytic anemia and immune thrombocytopenia, but also an almost positive direct antiglobulin test, may be positive for IgG and/or complement (C3) and absence of any known underlying etiology. Antiplatelet and antigranulocyte antibodies have shown varied results the direct immunofluorescence test.

Raised reticulocyte count, unconjugated hyperbilirubinemia and decreased haptoglobins reveal in sera. Bone marrow investigation may be of use in evaluation for excluding infiltrative processes in patients who present with pancytopenia. The initial treatment is with glucocorticoid corticosteroids or intravenous immunoglobulin (2).

A-50 year old previously healthy female, an ex-smoker admitted with a three weeks history of fatigue and jaundice. There was no relevant past or family history and no history of blood transfusion or exposure to drugs or poisons. On admission physical examination revealed a well orientation. The temperature was 36.7 °C, the pulse 110/min and respirations 44/min. The skin was pale, there was neither abnormal rash nor were there any petechiae. The conjunctiva was pale, scleral icterus was noted. No abnormal enlarged lymph node was palpable on all body. The abdomen was not distended, and the spleen was palpable to 2 cm below the left costal margin. The liver was not palpable. Laboratory values were notable for leukocyte count 7.100/microL, hemoglobin 5.8 g/dL, hematocrit 16%, MCV 114.5 fL, MCH 29.6 pg, MCHC 34.1 gm/dl, RDW (red cell distribution width) 29.5, platelet count 56,000 /microL, prothrombin time 12 sec, the partial thromboplastin time 25.9 sec, lactate dehydrogenase 422 U/L (normal:110-240), total bilirubin 3.3 mg/dl, indirect bilirubin 2.4 mg/dl, IgG direct coombs +3 positive. Peripheral blood smear was respectively 70% neutrophils, 25% lymphocytes, 5% monocytes, 3-4 clustered red blood cells in platelet morphology aniso-poikilocytosis, macrocytosis, normablasts, polychromasia, microsferosit. The reticulocytes were increased (corrected 10%). There was no other evidence of coincidental or precipitating infections. Serology was negative for HIV, hepatitis A, B and C. Anti-nuclear, anti-double stranded DNA antibodies, rheumatoid factor and C-reactive protein were negative. Ultrasonography findings of abdomen were only splenomegaly (length 15.5 cm). We did not analyze flow cytometry for ALPS, because of our patient's clinic (age and no abnormal enlarged lymph node) had not been thought of ALPS. Ruling out other causes of anemia and thrombocytopenia, 2 diagnoses of ES was thought. Methylprednisolone 2 mg/kg/day was initiated. After taking five units erythrocyte suspension, hemoglobin level revealed 11.2 g/dL and peripheral blood smear returned to normal for erythrocyte, but platelet clusters were not seen. In laboratory platelet count was found 9000 /microL. Intravenous immunoglobulin (IVIG) 1 g/kg/day (one day) dose was added to methylprednisolone treatment for thrombocytopenia. After one day from IVIG treatment, the platelet count was detected 76.000/microL and, peripheral blood

smear showed 6-7 clusters. After, there was no decrease in platelet count and hemoglobin level. Patient continued to receive methylprednisolone and was discharged successfully two weeks later from diagnosis. After 3 months from diagnosis methylprednisolone treatment was stopped and IgG direct coombs was detected negative. Patient is still in remission, nine months later from diagnosis.

ES appears to be a disorder of immune regulation. The exact pathophysiology is unknown, but evidences support abnormalities in both cellular and humoral immunity in Evans syndrome. Wang et al. found decreased percentages of T4 (T-helper) cells, increased percentages of T8 (T-suppressor) cells and a markedly decreased T4/T8 ratio compared with normal controls and patients with chronic ITP (4). Karakantza et al. found a decreased CD4/CD8 ratio in a 12-year-old boy with ES and reduced CD4/CD8 ratio persisted postsplenectomy. They also found increased interleukin-10 and interferon-γ which caused activation of autoreactive, antibody-producing (5). In our patient, we could not show the autoantibodies and CD4/CD8 ratio.

Hematopoietic cell-specific autoantibodies in patients with ES are specific to their target cells and, as shown by absorption and elution, do not cross-react. Antiplatelet and antigranulocyte antibodies have shown varied results and mostly only on the patients' own cells as demonstrated by the direct immunofluorescence test. In only a few patients were autoantibodies demonstrable in the patients' sera (6,7). In our case, autoantibodies of red cells responded methylprednisolone but platelet autoantibodies did not.

Corticosteroids remain the essential of treatment for control of the acute, symptomatic cytopenias with good initial results despite the lack of controlled trials demonstrating their effectiveness. The dose of prednisolone used has generally varied from 1 mg/kg/day to 4 mg/kg/day (7). After an addition of IVIG 1g/kg/day dose to methylprednisolone treatment, a platelet count of 76.000/microL was detected. Intravenous immunoglobulin are used in those cases where steroids are ineffective or unacceptably high doses are required to remain in remission, or due to toxicity results, the most commonly used first-line therapy is IVIG (2). IVIG may regulate the immune response by reacting with a number of membrane receptors on T cells, B cells, and monocytes that are pertinent to autoreactivity and induction of tolerance to self (8).

As a conclusion we think that, in ES different autoantibodies effect in different ways, so these autoantibodies may respond to different treatments.

KAYNAKLAR

1. Evans RS, Takahashi K, Duane RT, Payne R, Liu C. Primary thrombocytopenic purpura and acquired hemolytic anemia. Arch Int Med 1951;87:48–65.
2. Norton A, Roberts I. Management of Evans syndrome. British J Hematol 2006;132: 125–37.
3. Teachey DT, Manno CS, Axsom KM, Andrews T, Choi JK, Greenbaum BH et al. Unmasking Evans syndrome: T-cell phenotype and apoptotic response reveal autoimmune lymphoproliferative syndrome (ALPS). Blood 2005;15;105:2443-8.
4. Wang W, Herrod H, Pui C, Presbury G, Wilimas J. Immunoregulatory abnormalities in Evans syndrome. Am J Hematol 1983;15:381–90.
5. Karakantza M, Moukaki A, Theodoropoulou M, Bussel J.B, Maniatis A. Th1 and Th2 cytokines in a patient with Evans' syndrome and profound lymphopenia. British J Hematol 2000;110:968–70.
6. Pegels JG, Helmerhorst FM, Van Leeuwen EF, De Plasvan Dalen C, Engelfriet CP, Von DB. The Evans' syndrome: characterisation of the responsible autoantibodies. British J Hematol 1982;51:445–50.
7. Pui C, Wilimas J, Wang, W. Evans syndrome in childhood. J Pediatr 1980;97:754–8.
8. Bayry J, Thirion M, Misra N, Thorenoor N, Delignat S, Lacroix-Desmazes S et al. Mechanisms of action of intravenous immunoglobulin in autoimmune and inflammatory diseases. Neurol Sci 2003;24:217–21.

Received/Başvuru: 24.11.2012, Accepted/Kabul: 07.01.2013

Correspondence/İletişim

İlhami BERBER
İnönü Üniversitesi Tıp Fakültesi, İç Hastalıkları Anabilim Dalı, Hematoloji Bilim Dalı, MALATYA/TÜRKİYE
E-mail: drilhamiberber@hotmail.com

For citing/Atıf için:

Berber I, Erkurt MA, Koroğlu M, Kuku I, Kaya E, Bentli R. Evans syndrome. J Turgut Ozal Med Cent 2013;20(3):289-290 DOI: 10.7247/jtomc.20.3.23