Systemic Lupus Erythematosus Presenting as Evans Syndrome.

Robin George Manappallil¹, Gangaprasad Gangadharan², Anju Chacko³, Ani Praveen⁴

¹Consultant, Department of Internal Medicine, ²Consultant, Department of Critical Care Medicine, ³Consultant, Department of Pathology, ⁴Specialist, Department of Pathology, Baby Memorial Hospital, Calicut, Kerala, India

Abstract

Evans Syndrome (ES) is characterized by the sequential or simultaneous development of autoimmune haemolytic anaemia (AIHA), immune thrombocytopenia (ITP) and/or immune neutropenia in the absence of other known aetiologies. It is a rare haematological disorder, and an uncommon presentation of systemic lupus erythematosus (SLE). The patient being reported is a case of secondary ES due to SLE.

Keywords: Evans syndrome, autoimmune haemolytic anaemia, immune thrombocytopenia, systemic lupus erythematosus

Introduction

Evans Syndrome (ES) is an uncommon condition characterized by the sequential or simultaneous development of autoimmune haemolytic anaemia (AIHA), immune thrombocytopenia (ITP) and/or immune neutropenia in the absence of other known aetiologies. The condition was first described by Evan and Duane in the year 1949 [1]. It is seen in 0.8–3.7% of patients presenting with AIHA or ITP [2]. It is a rare presentation of systemic lupus erythematosus (SLE) and may precede it.

Case Report

A 24 year old male, undergoing physical police training, presented with complaints of fatigue and progressive dyspnoea (New York Heart Association Class I to Class III) over a period of 2 weeks. He also noticed yellowish discoloration of eyes. There were no other associated symptoms. He did not have any comorbidity, and was not on any regular medications. He is a non-smoker, with no substance abuse. There was no history of jaundice in the past, and his medical examination prior to joining police training (done 6 months ago) was normal.

On examination, he was conscious, oriented and afebrile. His pulse was 110 beats/minute, blood pressure 100/70 mmHg and systemic examinations were normal. There was no bony tenderness or lymphadenopathy.

His blood investigations showed pancytopenia with hemoglobin 4.3 g/dL, total WBC 2800 cells/cumm (neutrophils 66%, lymphocytes 25%, eosinophils 1%, monocytes 8%) and platelet counts 145,000 cells/cumm. His reticulocyte count was 6.4% and lactate dehydrogenase was 287 U/L (115–221). His peripheral smear showed normocytic normochromic RBC with spherocytes, leucopenia and mild thrombocytopenia, suggestive immune hemolytic anaemia (Figure 1). Liver function test was suggestive of indirect hyperbilirubinemia (total bilirubin 6.9 mg/dL with direct bilirubin 0.3 mg/dL) with normal enzymes. Direct Coombs test was positive. Antinuclear antibody profile was positive for ANA (titer 1:80), anti dsDNA and anti Ro-52. Cyclic citrullinated peptide antibody, lupus anticoagulant and antineutrophil cytoplasmic antibodies (p and c) were negative. Examination of bone marrow aspirate revealed a reactive bone marrow with megakaryocytes and thrombocytopenia. Renal functions, electrolytes, thyroid stimulating hormone, vitamin B12 levels, activated partial thromoplastin and prothrombin time were normal. Peripheral smear for malaria, lepsospirosis serology, Weil Felix and viral markers (HIV, HBsAg and anti HCV) were negative. Blood cultures were sterile. EBV capsid antibody (IgM and IgG) were negative. Urine examination was normal with no hematuria. Ultrasound abdomen, echocardiography and chest X-ray were also normal.

The patient was diagnosed to have ES secondary to SLE. He was given pulse doses of intravenous methyl
prednisolone (20 mg/kg once daily for 3 days) and packed red blood cells transfusion (2 units). His complete blood counts and liver functions were monitored daily. By day 4 of admission, his complete blood counts showed hemoglobin 8.9 g/dL, total WBC 3400 cells/cumm (neutrophils 72%, lymphocytes 16%, monocytes 12%) and platelet counts 140,000 cells/cumm. Total bilirubin decreased to 3.7 mg/dL. He was discharged on day 7 of admission on oral prednisolone (1 mg/kg) and oral hydroxychloroquine (200 mg once daily).

Discussion

ES reflects a state of immune dysregulation. These patients may present with AIHA or ITP either concomitantly or separately. Direct Coombs test is positive. Pancytopenia and neutropenia are seen in 14% and 55% of ES cases, respectively. The second cytopenia may develop months to years after the first immune cytopenia. Clinically, these patients present with features of hemolytic anaemia i.e. pallor, fatigue and jaundice. Heart failure is seen in severe cases. Those with thrombocytopenia may have petechiae, mucocutaneous bleeding and bruising. Lymphadenopathy and hepatosplenomegaly may be chronic or intermittent and in some cases may be present only during episodes of acute exacerbation [3-7]. Steroids with or without intravenous immunoglobulin form the first line of treatment; followed by rituximab, mycophenolate mofetil and cyclosporine. Cyclophosphamide, alemtuzumab, thrombopoietin receptor agonists (romiplostim, eltrombopag) and hematopoietic stem cell transplantation form the third line of treatment. Before the introduction of rituximab, splenectomy was the only option in refractory relapsing patients [8].

SLE is a multigenic autoimmune disease in which the organs and cells are damaged by tissue binding autoantibodies and immune complexes. Females, especially those taking estrogen-containing oral contraceptive pills and hormone replacement, are more prone than males. Exposure to ultraviolet rays, Epstein-Barr virus infection and smoking are some of the risk factors for developing SLE. According to the 2019 European League Against Rheumatism/American College of Rheumatology Classification Criteria for SLE, a score of at least 10 points is required for the diagnosis, and all patients also must also have an ANA titer of at least 1:80 on HEp-2 cells or an equivalent positive test. ES is a rare condition; and can either be primary or secondary in the presence of an underlying disease. It has been observed that secondary ES responds better than primary. Secondary ES can be associated with SLE, and has been reported in 1.7%–2.7% of cases [9,10]. ES presenting as SLE is a rare scenario, and at times can precede the detection of SLE [11].

Our patient presented with ES. He was diagnosed to SLE with a score of 17 according to the 2019 European League Against Rheumatism/American College of Rheumatology Classification Criteria. Hence, his ES was secondary to SLE. He was undergoing physical police training for the past 2 months. Exposure to sunlight (ultraviolet rays) would have been the triggering factor. He responded to steroid therapy and hydroxychloroquine.

Conclusion

ES is a rare condition, characterized by sequential or simultaneous development of AIHA, ITP and/or immune neutropenia in the absence of other known etiologies. SLE presenting as ES is a rare scenario; and ES can precede the detection of SLE. The management is based on distinguishing primary ES from secondary.
Conflict of interest: All authors declare no COI

Ethics: There is no ethical violation as it is based on voluntary anonymous interviews

Funding: No external funding

Guarantor: Dr. Robin George Manappallil will act as guarantor of this article on behalf of all co-authors.

References

1. Evans RS, Duane RT. Acquired hemolytic anemia; the relation of erythrocyte antibody production to activity of the disease; the significance of thrombocytopenia and leukopenia. Blood 1949; 4:1196-1213.


