

Evans Syndrome: A Case Report

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Abstract: ***Introduction:** Evans syndrome (ES) is a rare and chronic autoimmune disease defined as simultaneous or sequential the presence of direct Coombs-positive autoimmune haemolytic anemia (AIHA) in conjunction with immune-mediated thrombocytopenia. **Case report:** In this case report we are reporting a 25 years old unmarried female with complaints of easy fatigability, shortness of breath and petechial rashes over her trunk which gradually over period of 1 month spread over to other parts of the body associated with gum bleeding and menorrhagia for 15 days. Laboratory evaluations were suggestive of AIHA and ITP. She was treated with PRBC, platelet transfusion and steroids and she was improved. **Discussion:** The typical course of ES is characterized by a heterogeneous chronic disease with clinical variability at onset, spontaneous remissions and exacerbations. Most of the cases of ES presents primarily with severe AIHA and mild thrombocytopenia. Steroids, other immunosuppressive agents and supportive therapy remain the mainstay of treatment. **Conclusion:** Evans syndrome is a rare clinical entity. High degree of clinical suspicion from the beginning is essential for better patient outcome.*

Keywords: Evans syndrome, ITP, AIHA

1. Introduction

Evans syndrome (ES) is an uncommon autoimmune disease that was defined by Robert Evans in 1951 when he studied the relationship between autoimmune hemolytic anemia (AIHA) and immune thrombocytopenic purpura (ITP). Evans syndrome (ES) is a rare and chronic autoimmune disease defined as simultaneous or sequential the presence of direct Coombs-positive autoimmune haemolytic anemia (AIHA) in conjunction with immune-mediated thrombocytopenia^[1]. Some cases significant neutropenia is associated. Abnormalities in both cellular and humoral immunity occurs^[2]. It is a diagnosis of exclusion. So other conditions with similar signs and symptoms have to be ruled out by performing various tests including bone marrow examination. We report a case of a young woman who presented with symptomatic anemia and bleeding tendency and was subsequently diagnosed with Evans Syndrome.

2. Case Report

A 25yrs old unmarried female presented with complaints of easy fatigability, Shortness of breath and petechial rashes over her trunk which gradually over period of 1 month spread over to other parts of the body associated with gum bleeding and menorrhagia for 15 days. There was no history of fever, jaundice, haematuria, hematemesis, melena, arthritis, oral ulcer, photosensitivity, altered sensorium. No history of orthopnea, chest pain, cough, palpitations or pedal edema No history of any drug intake prior to or during course of illness No history of similar illness in family. On examination she had severe pallor and Petechial rashes present all over body but more over lower limbs and sacral area and few areas have non palpable purpuric lesions. Conjunctival hemorrhagic spots were there. Nolympadenopathy, icterus, cyanosis, clubbing or sternal tenderness. no hepatosplenomegaly and examination of other systems revealed no significant abnormalities.

Laboratory investigations revealed severe anemia (Hb-5.9gm%) severe thrombocytopenia (4000 cells/cumm), reticulocytosis (retic count10%), ESR-10 mm/hr with

normal PT and APT. Peripheral smear showed normocytic normochromic anemia, with target cells, raised polychromasia, reduced platelets, rest cell lines normal. (Suggestive of Hemolytic anemia, Thrombocytopenia). Bone marrow aspiration cytology: Hypercellular marrow, accelerated erythropoiesis, rest normal without any evidence of metastasis and leukemia. Direct Coomb's test: Positive (IgG +C3d). Serum LDH: High (1465 U/L). Screening for sickle cell anemia and SLE was negative (ANA negative). Liver function tests and Renal function tests were normal. ICTC, HBsAg, HCV all were negative. Malarial parasite was also not identified. CHEST X-RAY and USG abdomen were normal.

The patient was given packed red cells and platelet transfusions along with oral prednisolone (2mg/kg/day) and her condition improved clinically and hematologically within 2 weeks. He was advised to continue for 2 weeks and tapered off over a period of 2 weeks. Though the she went for remission and she was advised to be under follow up as a relapsing course is expected.

3. Discussion

Evans syndrome (ES) is defined as the simultaneous or sequential association of autoimmune hemolytic anemia (AIHA) and immune thrombocytopenic purpura (ITP).^[1] The typical course of ES is characterized by an heterogeneous chronic disease with clinical variability at onset, spontaneous remissions and exacerbations.^[1, 2] Most of the cases of ES presents primarily with severe AIHA and mild thrombocytopenia. Clinical phenotype includes symptoms of hemolysis (fever, pallor, jaundice, lethargy) and thrombocytopenia (petechiae, bruising and mucocutaneous bleeding). Physical examination may reveal lymphadenopathy, hepatomegaly and/or splenomegaly. Its worldwide frequency is unknown; however, research of Evans syndrome in AIHA is available in some cohorts that report an incidence of about 37%–73% in this setting.^[3, 4] A higher rate in female gender has been reported in 60%–70% of ES patients.^[2, 5, 6]

The etiology is unknown and immune dysregulation may be involved in the pathogenesis of the disease. More recently, the spectrum of the disease has broadened, especially in children, and there is increasing evidence to suggest that it may be associated with other diseases or conditions such as systemic lupus erythematosus (SLE),^[7] lymphoproliferative disorders.^[8,9]

Several authors have proposed different disease pathways, summarized by the presence of immune dysregulation with antibodies against erythrocytes, platelets and/or granulocytes and decreased CD4: CD8 ratio. Deficiency of CTLA-4 (CD152) an inhibitory transmembrane receptor at the surface of regulatory T-cells and LRBA (intracellular protein that binds to CTLA-4 cytoplasmic fraction in regulatory T-cells and inhibits its degradation) and Deficiency of TPP2 (tripeptidyl peptidase 2) a molecule associated with cell ageing and B-cell function. Also decreased CD4: CD8 ratio is seen.^[10,11]

Laboratory features requires a complete blood count and direct examination of peripheral blood; anemia, thrombocytopenia, reticulocytosis, poikilocytosis, mainly due to the presence of spherocytes. Increased indirect bilirubin and lactate dehydrogenase and a positive direct anti-human globulin test (DAT) test confirming ongoing immune hemolysis^[3, 12, 13, 14] are to be expected. Neutropenia may be present in 55% of the cases.^[15] Total serum immunoglobulin levels IgG, IgM levels may be decreased. Autoimmune diseases and lymphoproliferative diseases that may be underlying in many cases needs to be excluded.

Steroids remain the first-line of management and despite a good initial response (as high as 80% in most series), sustained response rates are lower, relapses are frequent. Prednisone at 1–2 mg/kg/day^[16, 17] must be administered in all cases, and in patients with severe clinical manifestations, an initial dose of 4–6 mg/kg/day within the first 72 hours is recommended^[16, 17]. Second-line agents like immunosuppressive drugs, especially cyclosporin or mycophenolate mofetil, vincristine, danazol or a combination of these agents. 7-10 have been used with varying degrees of success and need to be considered early.^[18] Splenectomy can be done in cases of resistance to second line treatment^[19] More recently a small number of patients have been treated with rituximab, which induces remission in the majority although such responses are often sustained for <12 months.^[20] SCT (stem cell transplantation) is the only curative option for Evans Syndrome. Studies suggest allogeneic HSCT may be superior to autologous HSCT^[21] but both carry risks of severe morbidity and of transplant-related mortality. Umbilical cord blood can be used for transplant after conditioning with busulfan, thiopeta, etoposide and ant thymocyte globulin.^[22]

4. Conclusion

Evans syndrome is a rare clinical entity. The exact etiopathogenesis is unknown. High degree of clinical suspicion from the beginning is essential for better patient outcomes.

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