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Case Report of Evans Syndrome (AIHA and ITP with Immune Neutropenia: Autoimmune Pancytopenia)

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Abstract
Evans Syndrome is a very rare autoimmune disorder in which the immune system destroys the body's red blood cells, white blood cells, and/or platelets. The exact cause of this condition is unknown. It can be primary (no underlying cause identified) or secondary (associated with underlying disease). (1) Secondary causes can include SLE, MCTD, autoimmune lymphoproliferative syndrome, Sjogren, Non-Hodgkin lymphoma, CLL, antiphospholipid syndrome, HIV, and hepatitis C. Evans syndrome was first described in 1951 by R.S. Evans and is characterized by AIHA (autoimmune hemolytic anemia) and ITP (immune thrombocytopenic purpura) with or without neutropenia (leukopenia). In the U.S., this disease is estimated to affect fewer than 5000 individuals. Incidence increased from 0.97 (in 1980) to 1.84 (in 2016) per million years. Prevalence increased from 3.30 (in 1980) to 21.30 (in 2016) per million years. Common symptoms include autoimmune hemolytic anemia, autoimmune thrombocytopenia, autoimmune neutropenia, and petechiae. First-line treatment includes steroids and IVIG. Second-line treatment includes Rituximab. For refractory cases, treatments may include cyclosporine, MMF, cyclophosphamide, azathioprine, and HSCT. (2)

Keywords: Evans Syndrome, AIHA, ITP, Autoimmune Neutropenia, Autoimmune Pancytopenia

1. Introduction

Evans Syndrome is a rare and complex autoimmune disorder characterized by the combination of autoimmune hemolytic anemia (AIHA) and immune thrombocytopenic purpura (ITP), often accompanied by autoimmune neutropenia. This condition, first described in 1951, presents significant diagnostic and therapeutic challenges due to its rarity and the variability in clinical presentation.

2. Case History

Patient is a 30-year-old married woman and resident of Bahadurgarh (Haryana). She reported no history of chronic comorbidity or family history of hemolytic diseases.

Presentation: The patient presented to Safdarjung on 11 March 2021 with complaints of continuous fever and chills. Before presentation, the patient experienced malaise, fatigue, extreme generalized body weakness, and dizziness for 15 days, petechial rash for 10 days, and yellowish discoloration of sclera, bleeding per vaginal, and red-colored urine for 7 days. Bowel and bladder movements were normal.

Prior Treatment: History of blood transfusions for 2 weeks in the previous hospital.

Examination: The patient's vital signs were as follows: blood pressure (BP) was 116/74 mmHg, pulse rate (PR) was 88 beats per minute (bpm), random blood sugar (RBS) was 116 mg/dL, and oxygen saturation (SpO2) was 96% on room air (RA). Clinical examination revealed the presence of pallor, icterus, and petechial rash on both extremities. The per abdomen examination indicated moderate splenomegaly and hepatomegaly with a liver span of 15 cm. Respiratory, cardiovascular (CVS), and central nervous system (CNS) examinations were all within normal limits.

Diagnosis: On presentation, the patient's CBC showed Hb at 1.8 g/dL (reference range: 12-16 g/dL for females), TLC at 2700 (reference range: 4000-11000 /µL), and MPC at 800/mm3 (reference range: 150000-450000 /µL). On discharge, the CBC results improved to Hb at 6.2 g/dL, TLC at 6800, and MPC at 60000/mm3. The bone marrow biopsy indicated erythroid hyperplasia and increased megakaryocytes. The liver function tests (LFT) showed AST at 70 IU/mL (reference range: 10-40 IU/L), ALT at 104 IU/mL (reference range: 7-56 IU/L), ALP at 112 IU/mL (reference range: 44-147 IU/L), and Bilirubin (indirect) at 5.2/3.9 mg/dL (reference range: 0.1-1.2 mg/dL), with INR at 1.18 (reference range: 0.8-1.1). A blood smear revealed normocytic and normochromic macrocytic RBCs with reticulocytosis (retic count: 3.4%), with no atypical cells or hemoparasites seen.

Urine routine microscopy indicated pus cells at 5-7 (reference range: 0-5 /hpf), RBCs at 1-2 (reference range: 0-4 /hpf), protein at 3+ (reference range: Negative), and 24-hour urine protein at 49.3 mg/24 hours (reference range: <150 mg/24 hours), which is within normal limits. Additional tests showed CD55/CD59 as negative (reference range: Negative), DCT as positive (reference range: Negative), and ICT as positive (reference range: Negative). The patient's blood group was B Neg Rh E antigen. The ANA test was 1:320-positive (reference range: Negative), and the ENA test indicated borderline nRNP/sm levels (reference range: Negative). Serum haptoglobin was decreased at 0.1 g/L (reference range: 0.3-2.0 g/L). Vitamin B12 and folic acid (FA) levels were normal at 185 pg/mL (reference range: 200-900 pg/mL) and 9.14 ng/mL (reference range: 2.7-17.0 ng/mL), respectively. Karyotyping results were normal (reference range: Normal).

Treatment Administered: The patient's medication regimen included several intravenous (IV) and oral treatments. The patient received Inj Magnex at a dose of 1.5 gm IV twice daily (BD), Inj Amikacin 500 mg IV once daily (OD), Inj Pantop 40 mg IV once daily, and Inj Emset 4 mg IV as needed (SOS). During the hospital stay, eight units of B negative but least incompatible blood were transfused, along with six units of platelet-rich plasma. Additionally, the patient was administered Inj Eldervit, one ampoule daily for three days, and Inj Methylprednisolone at a dose of 1 gm per day for three days. The treatment also included oral Tab Prednisone, starting at 60 mg once daily and gradually tapered to 10 mg once daily over 6-8 months. The patient improved with pulse MPS.

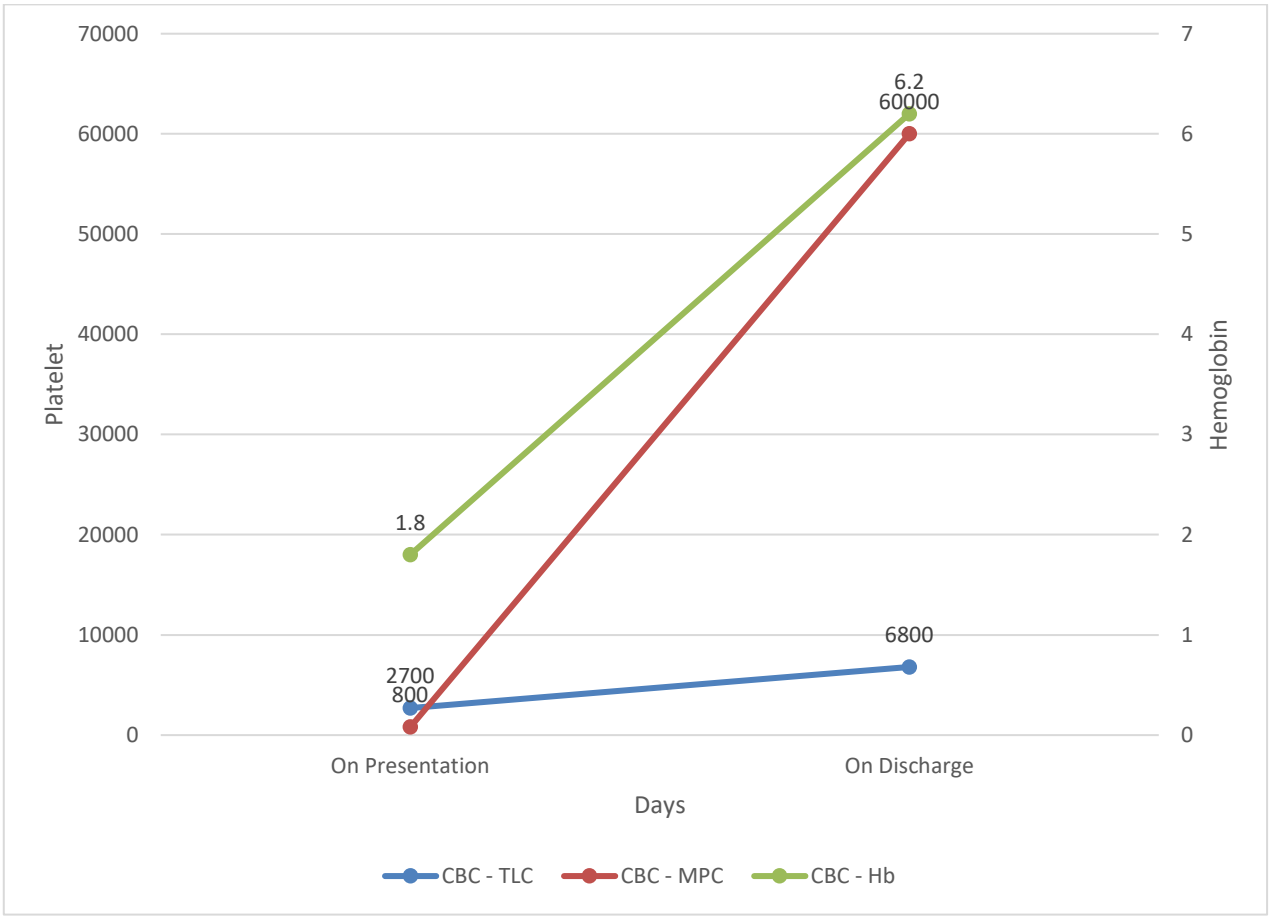

Figure 1 Line diagram showing the hemoglobin, TLC and platelets levels since the patient presentation

3. Discussion

Evans syndrome is an autoimmune disorder characterized by the combination of autoimmune hemolytic anemia (AIHA) and immune thrombocytopenia. (1) Although the worldwide incidence of Evans syndrome (ES) has not been documented in the literature, a French national observational study of 265 patients with AIHA revealed that 37% had ES. Additionally, Pui et al. reported that 73% of a cohort of 15 children with AIHA had ES.(3,4) The pathophysiology of Evans syndrome (ES) is not clearly defined but is most likely related to a generalized dysregulation of the immune system, involving both cellular and humoral immunity. (5,6) The downregulation of T-cell control over autoreactive B-cell clones results in a disrupted Th1/Th2 ratio, leading to increased production of IL-10 and INF-γ and decreased generation of TGF-β. The heightened secretion of INF-γ (a Th1 cytokine) stimulates autoimmune B-cell clones to produce autoantibodies against red cell-specific and platelet-specific antigens. (7) Additionally, ES is observed in the context of autoimmune lymphoproliferative syndrome (ALPS), common variable immunodeficiency (CVID), 22q11.2 deletion syndrome, and IgA deficiency, suggesting that immunodeficiency may be a predisposing factor for this autoimmune phenomenon. (8–10)

A similar case report by Sanam dhakal etal. involved a 50-year-old female referred from Makalu Hospital to the ICU of Birat Medical College and Teaching Hospital with severe symptoms, including bleeding from the mouth and gums, bluish patches, generalized weakness, and blood-mixed stool. Laboratory tests revealed significantly low hemoglobin, RBC count, and platelets, with neutrophilic leukocytosis and a

positive direct Coombs test. Treatment included blood transfusions, antibiotics, Vitamin B12, intravenous steroids, and Rituximab, leading to gradual clinical and hematological improvement. She was discharged on the 14th day with weekly follow-ups, showing a stable condition by the 8th week. This case highlights the complexity of managing severe anemia and thrombocytopenia through comprehensive medical intervention and continuous monitoring. (11)

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