



A Case of Evan's Syndrome Presented as Megaloblastic Anaemia and Hypothyroidism

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Received date: June 24, 2019; Accepted date: July 16, 2019; Published date: July 19, 2019

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Abstract

Even though Evan's syndrome is idiopathic it can be associated with many other diseases including Polyglandular Autoimmune Syndromes (PGAS) and Hashimoto's thyroiditis. It is a rare syndrome manifested as autoimmune hemolytic anemia and thrombocytopenia. Since the underlying cause is autoimmune it can be presented as severe hemolytic anemia and many clusters of diseases which share a common pathogenesis. Here we present a case of a 32-year-old female patient with severe hemolytic anemia and found to be Evans syndrome with polyglandular involvement.

Keywords: Autoimmune hemolytic anemia; Immune thrombocytopenia; Hashimoto's thyroiditis; Polyglandular autoimmune syndromes

Introduction

By definition, Evan's syndrome is a clinical syndrome presented as a combination of Autoimmune Hemolytic Anemia (AIHA) and Immune Thrombocytopenia (ITP), occasionally with immune neutropenia, in the absence of unknown underlying etiology [1]. It is diagnosed by excluding other disorders that can act as confounding factors of the syndrome complex. Evans syndrome can be presented as episodes of exacerbations and remissions. Though it is known to be an immune disorder the exact pathophysiology is unknown. But there is both cellular and humoral immune dysfunction in Evan's syndrome [2,3]. The syndrome is associated with significant morbidity and mortality with remissions and exacerbations [1]. Some authors refer it as a dilemma in diagnosing the syndrome and stated on the importance of coomb's test in every patient presenting with autoimmune thrombocytopenia to rule out autoimmune hemolytic anemia and thus excluding this syndrome [4]. The present case emphasizes the importance of presentation of Evans syndrome with a megaloblastic picture which points to evaluate the underlying etiology like pernicious anemia.

Case Report

A 32-year-old female came to OPD with a history of generalized weakness and yellowish discoloration of sclera for one week. On examination vitals: Temp: 98.70f PR: 104bpm BP: 120/60 mmHg RR: 18/min, pallor++, Icterus+, the systemic examination was found to be normal. Lab investigations showed Hb 4.7 gm/dl, Total WBC count 3050 cells/mm³, Neutrophils 46%, Lymphocytes 48%, Eosinophils 02%, Monocytes 04%, Basophils 00%, Platelet count 83,000/mm³ of blood, Red Blood Cell count 1.30 million cells/mm³ of blood, PCV 14.8%, MCV 113.8 fl, MCH 41.5 pg, MCHC 36.5 g/dl. ESR 145 mm/1 hr. Total Bilirubin 3.83 mg/dl, Direct Bilirubin 1.14 mg/dl, Indirect Bilirubin 2.7 mg/dl, SGOT-49 IU/L, SGPT-31 IU/L, ALP-101 IU/L, Total Protein 7.8

g/dl, Albumin 4.7 g/dl, Serum Globulin 3.1 g/dl, A/G ratio 1.5. TSH 6.57 μ IU/ml. Peripheral smear showed macrocytic blood picture with evidence of mild hemolytic anemia with leucopenia and thrombocytopenia. Direct Coomb's test was positive. ANA profile was negative. Urine routine showed no abnormalities.

She was treated with IV Methyl Prednisolone 1 gm OD and patient's hemoglobin, total WBC counts and platelet count improved. The overall impression on hematological examination was hemolytic anemia, megaloblastic anemia with thrombocytopenia. To summarize, the patient had a positive direct Coombs test, evidence of hemolysis in the form of elevated indirect bilirubin.

Discussion

In the above case, it is evident patient had multiglandular involvement. Polyglandular Autoimmune Syndromes (PGAS) are rare immune endocrinopathies characterized by the coexistence of at least two endocrine gland insufficiencies, and associations with non-endocrine immune diseases [5]. In this patient hypothyroidism is evident. Evan's Syndrome can be presented as Hashimoto's thyroiditis with features of hypothyroidism [6]. In our case, blood reports show hypothyroidism with direct Coomb's test positive which confirms an underlying autoimmune mechanism that points to Hashimoto's thyroiditis. A molecular mimicry mechanism may be the initiation of autoimmune events in Hashimoto's thyroiditis along with abnormal antigen-specific induction of T cells due to abnormal Human Leukocyte Antigen (HLA) related genes, mutation of T cells to form abnormal clones, or an immune defect causing reduced induction of T-suppressor cells by specific antigens [7].

Megaloblastic anemia in this patient may point to the autoimmune process against parietal cells of gastric glands that result in pernicious anemia. There are many studies that show an association between pernicious anemia and Polyglandular Autoimmune Syndromes (PGAS) [8].

In our case, direct Coomb's test was positive which is one of the diagnostic features of autoimmune hemolytic anemia. There may be an alteration in T-cell regulation of B cells, with abnormal clones of

immunocytes, or a non-self-antigen formed by a change in antigen structure itself that is followed by the formation of autoantibodies in Autoimmune Haemolytic Anaemia (AIHA) [9].

A rise in serum indirect bilirubin with normal alkaline phosphatase suggests constitutional hemolytic crisis [10]. In Gilbert's disease, autoimmune hemolytic anemia has been reported [11]. We could not evaluate the hepatic conjugating enzyme uridine diphosphate glucuronyltransferase in our case, to exclude Gilbert's disease.

Many mechanisms contribute to autoimmune mechanisms in Idiopathic Thrombocytopenic Purpura (ITP), such as antiplatelet antibodies and B-cell, and T-cell tolerance. But platelet antibodies are only detected in approximately 60% of the patients. This tolerance can be attributed to central tolerance defects during early development and peripheral tolerance defects arising in the setting of immune stimulation [12].

Immune hemolytic anemia coexists with 2% of the patients with ITP (Evan's syndrome) [12]. On the other hand in clinical practice, Evan's syndrome shows a variety of underlying diseases and is classified as primary or secondary [13]. And it is well evident that one patient with one autoimmune disease develops other. This shows a genetic predisposition that underlies both conditions [14].

Since PGAS should be considered in this case the serum electrolytes and glucose levels of the patient was evaluated and found to be normal, thus ruling out adrenal insufficiency. To rule out PGAS organ-specific autoantibody screening tests have to be done. In view of financial constraints, we have not been able to screen for all the organ-specific autoantibodies, but the patient is kept under regular follow-up. Since Evan's syndrome is a diagnosis of exclusion and by definition, other confounding disorders should not be present [15]. But in this patient due to economic constraint, we were unable to complete the investigations.

The first line of treatment includes corticosteroids and in this patient, the improvement was observed after a course of corticosteroids (Figure 1) [16].

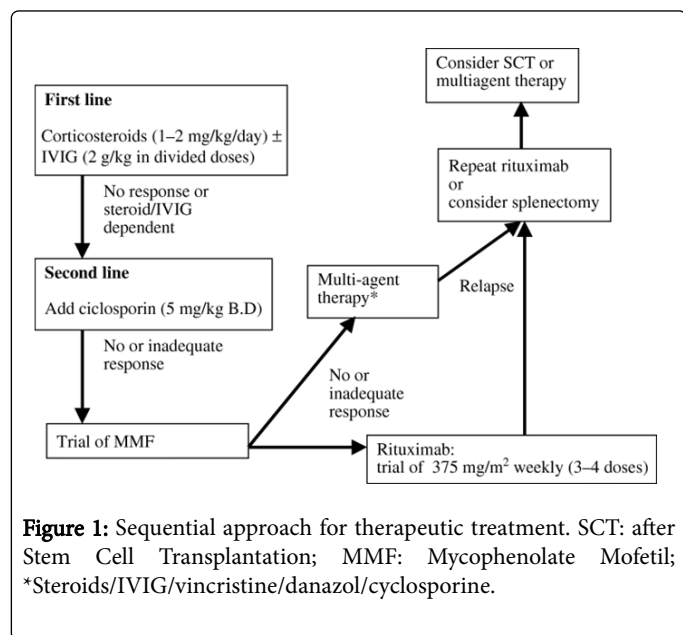


Figure 1: Sequential approach for therapeutic treatment. SCT: after Stem Cell Transplantation; MMF: Mycophenolate Mofetil; *Steroids/IVIG/vincristine/danazol/cyclosporine.

Evan's syndrome is a heterogeneous disorder with significant morbidity and mortality. High incidence of quantitative serum immunoglobulin abnormalities, lymphoid hyperplasia, and associated systemic manifestations suggest that Evan's syndrome may represent a stage of a broader spectrum, generalized immune dysregulation [16]. In a retrospective cohort study, at the time of analysis, after a follow-up, 24% had died and they concluded, Evan's syndrome is a potentially life-threatening condition that may be associated with other underlying autoimmune or lymphoproliferative disorders [17].

Conclusion

To conclude Evan's syndrome should be kept in mind and work up should include detection of various organ-specific antibodies to rule out autoimmune polyendocrine syndromes.

Acknowledgment

The authors would like to thank Dr. MC Vasif Mayan, Assistant Professor Department of Medicine, DM Wayanad Institute of Medical Sciences, Wayanad, Kerala, India, for providing the case details and helping in investigating the case.

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