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Evans syndrome: A rare presentation

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Abstract
Evan's syndrome was 1st reported by Evans in 1951 and is defined as the consequent or subsequent occurrence of idiopathic thrombocytopenia (ITP) and autoimmune hemolytic anemia (AIHA). It is reported to occur most commonly in adolescents and rarely in adults. Pathogenesis suggests a defect in humoral and cell-mediated immunity. Its definitive management with corticosteroids or intravenous immunoglobulin (IVIG) has proved to be curative. Here we present a case of a 17-year-old female patient complaining of easy fatigability, abdominal pain, generalized weakness, ecchymosis, per rectal bleeding, and bruising being diagnosed by decreased hemoglobin, reticulocytosis, and increased immature platelet fraction, increased serum lactate dehydrogenase and positive Direct Coomb's test. She was treated with prednisone and rituximab.

Keywords: syndrome, ITP, AIHA, IVIG

Introduction
Evan's syndrome is a rare disease with an annual incidence rate of 1.8 per million population per year and an annual prevalence of 21.3 per million population per year [1]. Evan's syndrome primarily presents in adolescents[1]. It presents as either a primary case (idiopathic) or secondary case (with associated conditions like systemic lupus erythematosus (SLE), common variable immunodeficiency (CVID), or chronic lymphocytic leukemia (CLL) [2, 3]. Pathogenesis suggests a defect in cell-mediated and humoral immunity [3, 4]. Typical symptoms of anemia and thrombocytopenia may be presented [4]. Definitive treatment is available with steroids [4]. Rituximab or splenectomy is helpful in refractory cases [4]. The median survival rate in Evan's is approximated to be 7.2 years (primary Evans-10.9 years and secondary Evans-1.7 years) [8].

Case presentation
A 17-year-old female patient presented with complaints of easy fatigability, abdominal pain, generalized weakness, ecchymosis and bruising since 4 months, melena, vomiting, and giddiness since 10 days. There was no complain of fever, cough, menorrhagia, or convulsion. The patient had a history of pica in early childhood. The patient did not have any history of deep vein thrombosis, blood transfusion, or any major illness in the past.
On general examination the patients vitals are normal. Pallor was present and all other general examination findings were unremarkable. Bruising was seen over the body.
On laboratory investigations, platelet count was found to be decreased significantly, which suggested idiopathic thrombocytopenic purpura (ITP). Also, hemoglobin was found to be reduced associated with reticulocytosis and increased serum lactate dehydrogenase and the direct IgG antiglobulin test was found to be positive (Direct Coomb's test positive). Serum immature platelet fraction was 37.5%. This suggested presence of autoimmune hemolytic anemia (AIHA). The anti-nuclear antibody test was found to be negative and the thyroid function test was normal. Bone marrow biopsy showed increased megaloblatosis and reticulocytosis.
The comparison of before and after 11 days lab values are as follows:

Table 1

	Before	After 11 days	Reference Value
Platelet	10000	129000	150000-410000/cmm
Hemoglobin	6.6	11.5	M:13-18 g/dl F:11.5-16g/dl
RBC Count	2.59	4.42	M:4.6-6.0 mill/cmm F:4.2-5.7 mill/cmm
WBC Count	6200	13400	4000-11000/cmm
Differential count			
Neutrophils	92	82	40-75%
Lymphocytes	7	16	20-45%
Monocytes	1	2	0-10%
Eosinophils	0	0	0-4%
% Basophils	0	0	0-1%

The patient was started on Prednisolone given at a dose of 1mg/kg/day. Rituximab was used at the dose of 100mg/week for 4 weeks. The patient was transfused 300ml of single donor plasma on 3rd day. Patient's platelet count, hemoglobin, and all other lab parameters improved on subsequent follow-up. She was asked to continue steroids for 1 month over which the dose was tapered down and platelet count and hemoglobin concentration were monitored. The patient lives completely well after three years of treatment.

Discussion

Evan's syndrome is a consequence of immune thrombocytopenia (ITP) and autoimmune hemolytic anemia (AIHA) and rarely neutropenia [2]. It represents 0.3-7% of AIHA and 2-2.7% of ITP. It is a rare disease having an annual incidence of 1.8 per million population per year[1]. It is an autoimmune disease having defective cell-mediated and humoral immunity [3, 4]. Recent theories suggest the pathophysiology of Evan's syndrome includes low CD4/CD8 ratio, deficiency of LRBA, and tripeptidyl peptidase 2 (TPP2) gene [4]. The patients present with typical symptoms of fatigue, pallor, dyspnea, tachycardia, and fever. Jaundice, hematuria, and hepatosplenomegaly may also occur [3, 4]. Evan's patients may present with petechiae, bruising, and mucocutaneous bleeds as a consequence of thrombocytopenia [3, 4]. AIHA can be confirmed by hemoglobin<-2SD (7/8 gm %) with reticulocytosis, elevated lactate dehydrogenase, and positive IgG antiglobulin test [5]. ITP was confirmed by exclusion of thrombotic thrombocytopenic purpura, hemolytic uremic syndrome, disseminated intravascular coagulation, paroxysmal nocturnal hemoglobinuria, myelodysplastic syndrome, lymphoproliferative syndrome, infection (HIV, Hepatitis C) and drug-induced thrombocytopenia and platelet count was found to be <100*10^9/L. Bone marrow biopsy showed megaloblastosis and increased immature platelet fraction. Definitive treatment included corticosteroids or intravenous immunoglobulin (IVIG) [4, 6]. Rituximab in low doses is increasingly being used these days and was also used in treating this patient. Immunosuppressive drugs can be used as a last resort in cases refractory to rituximab or spleenectomy [6, 7]. The most common causes of death in Evans syndrome were due to bleeding, infections, and hematological cancer (2.9% chances of developing chronic lymphocytic leukemia [6, 8, 9].

Conclusion

Evans syndrome, a rare presentation, occurring most commonly in children and adolescents, has a concomitant association between ITP and AIHA. Annual incidence and prevalence of the condition has increased to 1.8 and 21.3 per million population per year respectively. A definitive diagnosis can be made by ruling out other conditions. Proper treatment should be started early in order to decrease fatality. The primary treatment option is prednisone and rituximab is being used recently at low doses.

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