

Intravenous Immunoglobulin G Therapy in Evans Syndrome

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The combination of coombs positive auto immune hemolytic anaemia and immune thrombocytopenic purpura was first described by Evans in 1951¹. It is rare in childhood, with usually no underlying etiology². The clinical course is chronic and relapsing. Treatment with corticosteroids, immunosuppressive agents and splenectomy is generally unsatisfactory. Successful treatment with high dose intravenous immunoglobulin G was first reported in 1985³ We tried this form of therapy in our patient with chronic AIHA and ITP with good results.

Case Report

An eleven years old boy was admitted to Childrens Hospital with a history of pallor, vomiting and bruises for four days. There was no intake of any drug or infection prior to this illness. He had several episodes of pallor and bruising since the age of five years, requiring hospitalizations and transfusions. Last admission was in Childrens Hospital, four months prior to this episode. He was treated with corticosteroids, blood and platelet transfusions, for three weeks. There was some improvement and he was discharged in stable condition.

Physical examination on admission revealed a pale child in no distress. Temperature was 100.4°F. Pulse 125/min, blood pressure 110/70mm Hg. Weight was 26Kg. He had jaundice, purpura and ecchymosis on the extremities. Liver was palpable 3.5 cms below the right costal margin, spleen 4.0 cms below the left costal margin and there was no lymphadenopathy or ascites.

Laboratory studies revealed a hemoglobin of 4.5 Gms/dl, leukocyte count 10,500/mm with a normal differential count. Reticulocyte count was 40%, Platelet count 45,000/cmm, Total serum bilirubin 4.0 mg/dl, Direct bilirubin 1.0 mg/dl. Liver function tests normal, hepatitis B surface antigen negative and ESR 80 mm 1st hour. Peripheral smear showed hypochromic macrocytic red cells with many target cells. Bone marrow examination showed a hypercellular marrow with erythroid hyperplasia. Hemoglobin electrophoresis was normal. G-6-PD negative and Antinuclear antibodies were not detected. Serum IgG was increased to 30.4 g/l. Serum IgA and IgM were normal. Platelet associated immunoglobulins and anti platelet antibodies could not be determined. Direct Coombs test was positive.

Hematological response to IVIG & Prednisolone in Evans Syndrome

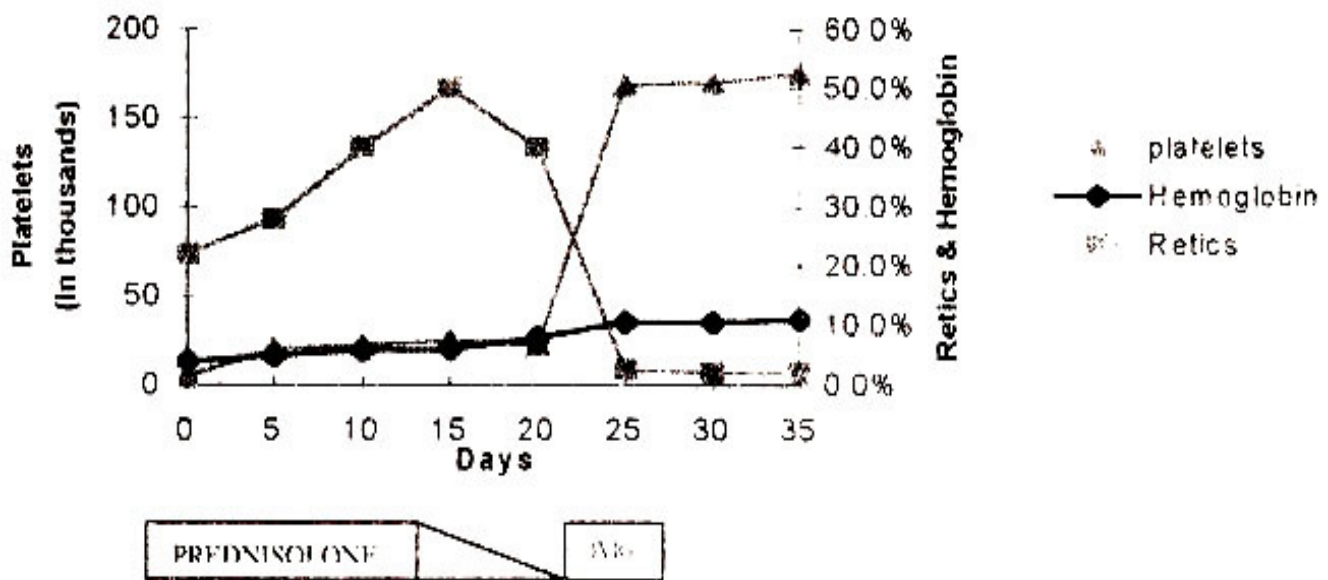


Figure.

He was transfused packed red blood cells and platelets. Oral prednisolone 2.0 mg/kg/d was started. He continued to show reticulocytosis and thrombocytopenia. As there was no response, prednisolone was tapered after fourteen days and discontinued in three weeks. Intravenous Immunoglobulin G was given in a dose of 400 mg/kg/d on day 21st for four days. Platelet count increased and after two days. On day 25 platelet count was 169,000/cmm and Reticulocyte count decreased to 2.5%. He was discharged and followed in the out patient clinic. Five months later, his hemoglobin was 11.2 gms/dl, platelet count 250,000/cmm, and reticulocyte count 1.5%.

Discussion

In 1951 Evans and Co-workers described the association of thrombocytopenia with a Coombs positive hemolytic anemia. This combination was later reported in a number of disorders including systemic lupus erythmatosis^{4,2} dermatomyositis⁵ scleroderma⁴ leukemia² liver cirrhosis, infectious mononucleosis⁶, Castleman's disease⁷, Guillain-Barre syndrome and insulin dependant diabetes mellitus.

In patients with AIHA thrombocytopenia and leucopenia occur relatively frequently^{1,2,8-10} as compared to patients with ITP in which only a few had acute hemolytic anemia². Evans syndrome is characterized by this combination in the absence of an overt cause. Quantitative serum immunoglobulin abnormalities and lymphoid hyperplasia suggest that it may be an immune deficiency disorder¹¹. The presence of granulocytotoxic and lymphocytotoxic antibodies in the sera of these patients also suggest an autoimmune process. Like in ITP, there may be a history of an antecedent febrile illness².

The treatment of children with chronic autoimmune hemolytic anemia has not been very successful. Corticosteroids often result in improvement, but relapses are common and maintenance steroid therapy seems necessary in the majority of effected children⁹. Immunosuppressive agents have also been used, either alone or in combination with corticosteroids². Splenectomy often provides sustained remission in 70% of patients with chronic ITP and 50% of those with chronic AIHA^{9,12}, but it seldom results in

prolonged remission in Evans syndrome². Many recent observations have shown that intravenous immunoglobulin G therapy is useful in the management of acute and chronic ITP¹²⁻¹⁴. As AIHA and ITP are considered to have common pathophysiological mechanisms so treatment of Evans syndrome with intravenous immunoglobulin G seems logical. However the total dose of IgG required to obtain a complete response has been higher than in comparable patients with ITP or autoimmune neutropenia^{14,15}. Although the mechanism of the immunoglobulin effect is not completely known, several possibilities have been considered in ITP. Reticuloendothelial system I-c receptor blockade, decrease in autoantibody synthesis, protection of platelets, have been cited^{2,12,16}. Our report apparently is one of the few successful experiences of intravenous immunoglobulin G in the control of AIHA. Though expensive it has fewer side effects than other modes of treatment. The optimal therapy for Evans syndrome however, still remains undefined^{11,17}.

References

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