



Evan's Syndrome Successfully Treated with Rituximab

Holguin S*

Department of Internal Medicine, Atlantic Health System, USA

Abstract

Evan's syndrome is a rare entity which presents with autoimmune hemolytic anemia and immune thrombocytopenia in the absence of an underlying etiology. In this particular case, the patient initially presented with hemolytic anemia and developed thrombocytopenia later in the hospital course. There was no evidence of autoimmune conditions or malignancies. The patient failed to respond to steroids and intravenous immunoglobulin, therefore he was subsequently treated with Rituximab. Hemoglobin and platelet count stabilized and the patient has been off treatment since then.

Keywords: Immune thrombocytopenia; Intravenous immunoglobulin; Lactate dehydrogenase

Introduction

Autoimmune Hemolytic Anemia (AIHA) combined with the presence of Immune Thrombocytopenia (ITP) and/or neutropenia (up to 5% of cases) in the absence of underlying etiology is referred to as Evans syndrome [1,2]. It's diagnosed in only 0.8% to 3.7% of all patients who present with ITP and/or AIHA at onset [2]. This syndrome has been described in all ages and all ethnic groups. Evans syndrome is a chronic disorder that might present with several exacerbations and periods of remission [3].

Case Presentation

This case presents a 69-year-old Caucasian male with past medical history of hypertension and hypothyroidism who presented with hematuria. In the ED, he was afebrile, normotensive and with a regular heart rate. However, in physical exam he was noticed to be icteric. Laboratories showed a White Blood Cell (WBC) of 13.3/nL, hemoglobin 10.5 g/dL (13.6 g/dL the day prior) and platelets 226/nL. Creatinine 1.1 mg/dL, total bilirubin 12.5 mg/dL, only 0.9 mg/dL being conjugated. AST 100 U/L, ALT 58 U/L. Coagulation studies within normal limit. Urinalysis showed large blood, protein greater than 300, red blood cells 4 to 10/hpf. CT abdomen was significant for hepatomegaly and fatty liver infiltration. Patient was asymptomatic except for the hematuria. The next day, hemoglobin dropped to 7.7 mg/dL and later to 5.6 mg/dL; while WBC went up to 19.1/nL. He received 2 units of red blood cells and was started on empiric antibiotics. Further work up revealed a Lactate Dehydrogenase (LDH) of 1522 U/L, haptoglobin <8 mg/dL and direct Coombs test was positive. The patient was started on methylprednisolone 60 mg IV every 6 hours. Despite these measures, the hemoglobin nadir to 3.8 g/dL while LDH continued to increase and lactic acid went up to 16.1 mmol/L. The same day a drop in the platelets was noticed from 160/nL to 68/nL. Peripheral smear revealed rare schistocytes and megakaryocytes.

Patient needed to be intubated for respiratory distress in the setting of severe metabolic acidosis. Methylprednisolone was increased to 1000 mg daily for 3 days. At this point, since there was no clinical improvement and the patient started to become agitated despite sedation, it was decided to give him Intravenous Immunoglobulin (IVIG) 0.5 mg/kg. ADAMTS13 activity was 61 (within normal limits), and other serologies looking for autoimmune diseases such as ANA, ANCA, anticardiolipins were negative. HIV, parvovirus and hepatitis antibodies were also negative.

Unfortunately, the creatinine peaked to 4.2 mg/dL, and the patient needed to be started on renal replacement therapy. The acute kidney injury was likely related to hypoperfusion in the setting of hemolytic anemia. Due to decrease renal function, only one dose of IVIG was given and then the patient received rituximab 375 mg/m². On day 9th of admission, due to refractory anemia and thrombocytopenia despite previous treatment, he was started on plasmapheresis and continued on IV methylprednisolone.

The patient was successfully extubated on day 14th. After subsequent doses of rituximab, hemoglobin and platelet count stabilized. Nonetheless, his hospital course was complicated with

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*Correspondence:

Holguin S, Department of Internal Medicine, Atlantic Health System, USA, E-mail: silera.hb@hotmail.com

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digital ischemia of the three first digits of the left hand and right foot. This was thought to be one of the uncommon side effects from IV immunoglobulin versus an episode of hypoperfusion in the setting of acute hemolytic anemia. He ended up having amputation of the second and third finger on the hand. Steroids continued to being taper down and the patient was discharged on hemodialysis three times per week. Until this date, his hemoglobin and platelet count have been within normal limits and he's been off steroids.

Discussion

Evan's syndrome presents with laboratory evidence of hemolytic anemia (decreased haptoglobin and increased LDH, reticulocytes and indirect bilirubin) plus thrombocytopenia, in some occasions demonstrating megakaryocytes in the peripheral smear. The hemolytic anemia and immune thrombocytopenia may happen simultaneously or sequentially, like in this patient. The differential diagnoses of the syndrome are AIHA and ITP related to underlying diseases such as malignancies, most commonly lymphoproliferative disorders, and autoimmune conditions (systemic lupus erythematosus, mixed connective tissue disease, scleroderma, among others) or thrombotic microangiopathies such as hemolytic uremic syndrome and thrombotic thrombocytopenic purpura [4]. In this case, imaging and further laboratories were unrevealing for an underlying diagnosis. The pathogenesis involves extravascular hemolysis in the reticuloendothelial system initiated by IgG and IgM that increase the red blood cell phagocytosis, although intravascular lysis may also occur. Similarly, the thrombocytopenia is mediated by IgG antiplatelet antibodies.

First line treatment therapy is usually steroids and/or intravenous immunoglobulin. Second line therapy includes immunosuppressive therapy such as cyclophosphamide, cyclosporine, mycophenolate or rituximab. Danazol has also been used for refractory disease [4]. Splenectomy may also be considered to treat ITP and stem cell transplantation has been associated with long-term cure [3]. This patient failed to response to steroids and IVIG, but platelet count and hemoglobin began to stabilize after first dose of rituximab.

It's important to remember that Evan's syndrome is a diagnosis of exclusion, and most of the time both cytopenias present as a result of an underlying disease. Once the diagnosis is established, appropriate treatment might be difficult to achieve due to disease severity and unpredictable response, therefore is essential to recognize this entity on time and knowing the different medications available to treat it.

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