5-2020

Evans Syndrome in Pregnancy: A Case Report

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Abstract

Evans syndrome (ES) is a chronic autoimmune disease characterized by autoimmune hemolytic anemia (AIHA) and immune thrombocytopenic purpura (ITP). It is difficult to distinguish ES from other diagnoses more common in pregnancy. Few case reports of Evans syndrome in pregnancy have been published, and guidelines for treatment are not well-defined. We present a case of ES in pregnancy, the clinical course, treatment, and complications postpartum. We also discuss additional considerations for intrapartum and postpartum management for patients with ES.

Introduction

- Evans syndrome is a chronic autoimmune disease characterized by AIHA along with ITP[1]. The clinical features include pallor, weakness, fatigue, jaundice, petechiae, ecchymosis, and epistaxis. The diagnosis is made by a positive direct anti-globulin test (DAT) in the setting of hemolytic anemia.
- The incidence of ITP in pregnancy is 1-5/10,000[2], and Evans syndrome has been diagnosed in 1.8-10% of patients with ITP.
- ES may be associated with other immune disorders such as systemic lupus erythematosus, immunodeficiencies, or autoimmune lymphoproliferative disorders.
- Guidelines for treatment of ES are not well-defined. Steroids and intravenous immunoglobulin (IVIG) are first-line therapies. Second-line therapies include immunosuppressive agents such as rituximab, mofetil mycophenolate, and azathioprine.
- In pregnancy, it is necessary to differentiate between ES and more common disorders such as preeclampsia, disseminated intravascular coagulation (DIC), or syndrome of hemolysis, elevated liver enzymes, and low platelet count (HELLP).

Case Report

- A 23-year-old G2P1001 with no known medical history presented at 38 weeks gestation with spontaneous rupture of membranes, contractions, and blood-tinged vaginal discharge. No prenatal records were available.
- The patient was 8cm dilated on initial cervical exam. Due to patient desire for pain control and in anticipation of expeditious delivery, epidural was placed while pending lab results. Subsequent lab results are shown in Table 1.
- Upon further questioning, patient reported one episode of epistaxis two weeks prior to presentation and a history of chronic easy bruising. She had a previous uncomplicated delivery in 2017. Labs at that time: Hgb 12.5 g/dL and Plt 223K/µL.
- Shortly following admission, patient delivered a healthy male infant by uncomplicated spontaneous vaginal delivery. Quantitative blood loss during delivery was 400 cc. Epidural was subsequently removed while repeat labs were pending. Repeat labs following delivery: Hgb 5.6 g/dL, Plt <10K/µL.
- Peripheral blood smear showed evidence of hemolytic anemia (Figure 1).

Hemoglobin	7.1 g/dL
Hematocrit	22.1%
Mean corpuscular volume	74.7 fl
Mean corpuscular hemoglobin concentration	32.3 g/dL
Red blood cell distribution width	18.1 %
Platelets	<10 K/µL
White blood cell count	9.9 K/µL

Table 1. Initial laboratory values.

- Antibody screen was positive for warm autoantibodies. DAT was positive for anti-IgG and anti-complement antibodies, leading to the diagnosis of Evans syndrome. Preeclampsia, HELLP syndrome, and DIC were excluded on the basis of normal blood pressures and other laboratory testing included in Table 2.

Case Report - continued

Prothrombin time	12.6 sec
Partial thromboplastin time	27 sec
International normalized ratio	0.98
Fibrinogen	388 mg.dL
Liver profile	
Aspartate aminotransferase	16 IU/L
Alanine aminotransferase	7 IU/L
Total bilirubin	0.8 mg/dL
Direct bilirubin	0.1 mg/dL
Alkaline phosphatase	296 IU/L
Lactate dehydrogenase	263 IU/L
Additional labs	
Ferritin	17 ng/mL
D-dimer	2.63 µg/mL FEU
Iron	45 µg/dL
Iron saturation	10%
Folate	12.4 ng/mL
Vitamin B12	136 pg/mL
Total iron binding capacity	448 µg/dL
Haptoglobin	<30.0 mg/dL
Reticulocyte percent	6.0 %
Absolute reticulocyte count	149.4 K/µL

Table 2. Additional laboratory values.

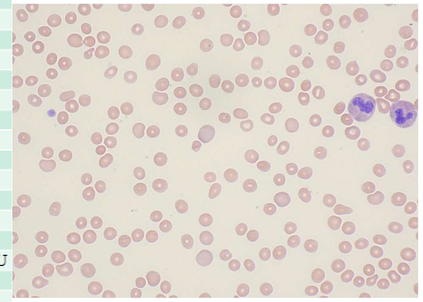

Figure 1. Peripheral blood smear showing microcytic, slightly hypochromic anemia with anisocytosis and polychromasia, thrombocytopenia, and slight leukocytosis. Tear drop cells, reticulocytes, and small spherocytes were present. No overt schistocytes or fragmentation of red blood cells was noted. No overt dysplasia or presence of blasts.

- Patient was transfused with two units of red blood cells and one pack of platelets. She was treated with oral dexamethasone 40mg daily for four days, with subsequent rise in Plt to 55K/µL (Figure 2). She was discharged on postpartum day (PPD) 4 on oral prednisone 60 mg daily with weekly outpatient lab follow-up.
- On outpatient follow up, platelet count decreased. She received a second course of dexamethasone with initial response, however subsequent drop in platelets was again observed. She then received a third course of dexamethasone along with IVIG. Given the poor response to steroids, rituximab therapy was initiated.
- On PPD #34, patient presented with chest pain and shortness of breath. CT scan revealed an acute pulmonary embolism and ground glass opacities (Figure 3).
- Patient reported exposure to contacts with known novel coronavirus (COVID-19) infection. COVID-19 PCR testing was then performed and was positive. As platelet count remained stable above 200K/µL, rituximab was held for several weeks in the setting of active COVID-19 infection.

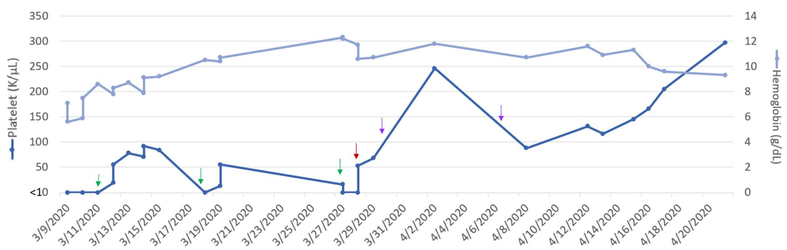

Figure 2. Platelet and hemoglobin values over time. Times of therapy administered are noted by arrows.

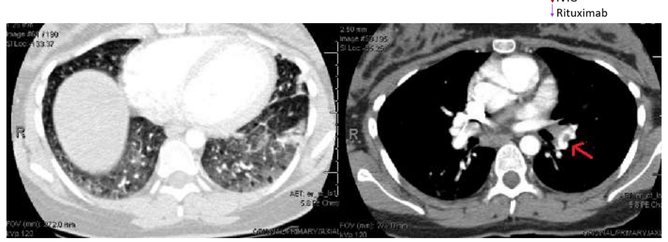

Figure 3. CT chest demonstrating diffuse ground glass opacities (left) throughout both lungs, which can be seen with COVID-19 pneumonia. Acute pulmonary emboli (right) identified in segmental branches of lingula and left inferior lobar pulmonary artery extending into segmental branches of left lower lobe, with filling defect noted by red arrow.

Discussion

- Evans syndrome is an autoimmune disorder with autoantibodies against red blood cells and platelets leading to the development of AIHA and ITP. The prevalence of ES in pregnancy is not well documented, with data available for 14 cases. These were complicated by preeclampsia (5), postpartum hemorrhage (3), placental abruption (1), and stillbirth (2). Treatments included steroids only (5), addition of IVIG (5), eventual splenectomy (5), and plasma exchange (1).
- Many of these cases demonstrated persistent relapsing ITP, with hemoglobin stabilizing early in presentation
- In this case, epidural was placed prior to obtaining laboratory results. This is acceptable by the 2015 Practice Guidelines for Obstetric Anesthesia published by the American Society of Anesthesiologists[8], which states routine evaluation of platelet count is not necessary in healthy parturients.
- Immunosuppressive medications increase the risk of respiratory infections. In this patient, steroids and rituximab may have contributed to development of COVID-19 related pneumonia.
- Cytokine activity in pregnancy may lead to increased autoimmunization against RBCs[7], leading to higher rates of AIHA. Thus, pre-existing COVID-19 infection may have served as an inflammatory trigger for new onset of Evans syndrome in this patient.
- Warm AIHA is associated with a 15-33%[9] risk of venous thromboembolism (VTE). VTEs are associated with IVIG, with added risk conferred to pregnancy and the postpartum period. The use of prophylactic anticoagulation after discharge and systematic screening for VTE for patients with ES is an area that may benefit from further studies.

Conclusion

- Evans syndrome is a rare autoimmune disorder characterized by combined AIHA and ITP that must be differentiated from more common disorders in pregnancy.
- Intrapartum management of patients with ES requires cautious use of regional anesthesia to balance patient desire for pain control with bleeding concerns. A collaborative multidisciplinary approach including consultation with anesthesia is needed to develop an institutional protocol for pre-anesthesia evaluation.
- The relationship of respiratory infections to ES as potential triggers or as adverse risks from treatment should be further delineated.
- Treatments for ES may exacerbate VTE risk. Further investigation is necessary to determine need for prophylactic anticoagulation and VTE screening.

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