CLINICAL VIGNETTE

Polycythemia vera and Pregnancy

Nimit Sudan, MD

A 34-year-old female presented with pruritic generalized rash, thought to be eczema, and was evaluated by Allergy and Immunology. She denied any fevers, night sweats, or weight loss. She had no history of thrombosis but complained of easy bruising and occasional bleeding with brushing her teeth. CBC revealed leukocytosis of 11.29, absolute neutrophil count 7.51, hemoglobin 16.1, hematocrit 49.5 and platelet count 1,294,000. LDH was elevated at 272. Ferritin was 95. Von Willebrand screen revealed mild decrease in high molecular weight multimers with a von Willebrand factor antigen of 85% and ristocetin cofactor activity of 32%. Bone marrow biopsy revealed hypercellular hematopoiesis, consistent with myeloproliferative disease. Cytogenetics were normal. Molecular studies revealed JAK2 V617F mutation. Skin biopsy was nonspecific, with no evidence of malignancy. On physical exam, a faint generalized, erythematous rash was appreciated. There was no hepatosplenomegaly. She initiated phlebotomy and hydroxyurea 500mg daily, with platelet count goal of <600 and hematocrit <45. Low dose aspirin was not initiated, given mild acquired von Willebrand's disease and bleeding. Hydroxyurea was titrated to 1000mg daily. All of her counts improved to normal reference range with 2 months of treatment. Aspirin 81mg was then initiated with no reported bleeding. The rash and pruritus improved significantly with treatment and resolved with systemic steroids. At age 36, she expressed an interest in pregnancy. Hydroxyurea was discontinued and counts again increased with a peak platelet count of 1,225,000, hematocrit 49.5 and leukocytosis of 11.01. Interferon alpha was considered but the patient declined in fear of side effects. She eventually conceived and her HCT and platelets gradually declined during her pregnancy. Near the end of the third trimester, platelet count improved to 532 and HCT 37.7. WBC was still elevated at 13.5 with nonspecific differential. She had an uneventful normal vaginal delivery without any complications.

Polycythemia vera (PV) is classified under chronic myeloproliferative neoplasms (MPNs) and is characterized by elevated red blood cell mass. PV is reported in all populations and ages, though is relatively rare in young women.[1] The median age of diagnosis is approximately 60 years and only 10% of patients are diagnosed before the age of 40.[2] The incidence is higher in men than women. Incidence in women in the age group 20-34 is estimated to be 0.04/100,000 cases.[3]

PV is suspected in any patients with increased red cell mass or increased hemoglobin/hematocrit without evidence of chronic hypoxemic conditions. Clinical signs and symptoms include increased hematocrit, leukocytosis, thrombocytosis, splenomegaly, pruritus, vasomotor symptoms, thrombosis, bleeding, and rash.[2] In patients with PV and platelet counts >1 million, acquired von Willebrand disease may occur, leading to bleeding. WHO diagnostic criteria for PV includes hemoglobin > 16.0 and hematocrit > 48% in women, presence of JAK2 V617F or exon12 mutation, and subnormal serum erythropoietin level.[4] A bone marrow biopsy can be considered if the evaluation is inconsistent and suspicion remains high.

Patients less than age 60 with no history of thrombosis are considered low risk. All others are considered high risk. Goals of treatment include reducing risk of thrombosis, ameliorate symptoms, prevent bleeding, and reduce risk of evolution to myelofibrosis, acute myeloid leukemia or myelodysplastic syndrome.[5] Preferred treatment for low risk patients include phlebotomy and low dose aspirin.[6] Cytoreductive therapy is considered for patients with uncontrolled symptoms or counts.[5,6]

PV has been reported in only a limited number of cases in pregnancy and poses unique risks of complications and treatment challenges. Pregnant patients with PV are at a high risk of pregnancy-related complications, such as thrombosis, hemorrhage, miscarriage, hypertension, intrauterine growth restriction, preeclampsia and placental abruption.[7] Pregnancy complications have been reported in 27.2% and risk of fetal loss in 18.2% of patients in a case series by *Elli et al*.[8] Other case series have reported higher complication rates. The goal of therapy of PV in pregnant women is to maintain hematocrit levels <45%.[9] The preferred agent for cytoreductive therapy is interferon-α as other agents, such as hydroxyurea or ruxolitinib, have teratogenic potential.[10,11] Low-dose aspirin is also strongly recommended to reduce the risk of thrombosis.[6,11] European LeukemiaNet, British Society of Hematology and NCCN guidelines have recommendations for management of PV and MPNs during pregnancy. For low risk pregnancy, the recommendation is to keep Hct below 45% and use low-dose aspirin. LMWH can be considered after delivery, until 6 weeks postpartum. For high-risk pregnancy, LMWH and IFN should be considered, in addition to aspirin.[9, 12-14]

Many published reports indicate a decline in platelet counts and hematocrit during pregnancy.[15-17] A 43% decline in platelet counts and a 20-30% decline in red call mass have been reported. The mechanisms include dilutional effects and increased sequestration in the splenic and placental circulation.

The counts increase and return to baseline, usually within 2-3 months after delivery.

This patient declined cytoreductive therapy with interferon alpha, despite multiple publications citing poorer pregnancy outcomes compared to normal population. She continued on low dose aspirin. During her pregnancy, her HCT and platelet counts declined. She did not have any recurrence of her rash or pruritus, nor any thrombosis or unexpected bleeding. After delivery, she elected to breast feed for 3 months, prior to reinitiating hydroxyurea therapy due to increasing counts.

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