

Management of Placenta Accreta Complicated by Pulmonary Embolus and Heparin Induced Thrombocytopenia

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Abstract

Background: Placenta accreta threatens both fetal and maternal health in multiple ways.

Case: We present a 39 year-old gravid 5, para 3 with known placenta accreta, whose antenatal course was complicated by development of massive pulmonary embolus and subsequent heparin-induced thrombocytopenia. She underwent successful cesarean hysterectomy at 28 6/7 weeks' gestation, followed by anticoagulation with a direct thrombin inhibitor.

Comment: Once rare, placenta accreta now complicates a significant number of pregnancies each year, jeopardizing both maternal and fetal health. We present a successfully managed case of placenta accreta complicated by pulmonary embolism and heparin-induced thrombocytopenia.

Keywords: Placenta previa; Accrete; Venous thromboembolism; Direct-thrombin inhibitor; PE; HIT; Direct thrombin inhibitor; Lepirudin

Introduction

The incidence of placenta accreta has risen dramatically in recent years. In addition to the neonatal morbidity conferred by iatrogenic preterm delivery, placenta accreta poses multiple maternal risks. Pregnancy itself confers a 4-5 fold elevated risk of VTE as compared with the non-pregnant population; complications that predispose parturients to further immobility increase that risk [1]. Cesarean hysterectomy, massive intra-operative hemorrhage, and large-volume blood transfusion(s) are common intrapartum events in women with placenta accreta. Each substantially increases maternal risk for Venous Thromboembolism (VTE) and subsequent need for systemic anticoagulation [2-4].

Otherwise safe in pregnancy, a major shortcoming of Unfractionated Heparin (UFH) for treatment of acute VTE is the development of Heparin-Induced Thrombocytopenia (HIT). The incidence of HIT among general postoperative surgical patients approaches 5%, whereas in medical patients treated with therapeutic doses of UFH, incidence varies from 0.1-1%. Less than 0.1% of obstetric patients develop HIT. The presence of this complication necessitates use of a Direct Thrombin Inhibitor (DTI) [5,6]. We report the first case in the literature of a patient with known placenta accreta whose antenatal course was complicated by a saddle pulmonary embolus and subsequent development of HIT successfully managed with a DTI.

Case Report

Our patient is an obese (BMI 33.6 cm/kg²) 39 year-old gravida 5 para 1031 with complete placenta previa and accreta diagnosed by ultrasound at 21 weeks gestation. Her surgical history is significant for one prior cesarean delivery and one dilation and curettage. At 21 1/7 weeks gestation, she was admitted to an outside facility following her first episode of vaginal bleeding. During her five-day hospitalization, she remained on modified bed-rest with bilateral pedal Sequential Compression Devices (SCD's) as venous thrombo-embolic prophylaxis. Following discharge, she continued modified bed-rest at home. At 22 6/7 weeks gestation, she was re-admitted for recurrent vaginal bleeding with an estimated blood loss of 200-300 cc. Her thrombo-embolic prophylaxis again was bilateral SCD's and her activity level modified bed rest. At 24 0/7 weeks gestation, she was given a course of

betamethasone steroids for fetal lung maturity. On the twenty seventh day her hospitalization at the outside facility, she experienced sudden onset of shortness of breath and chest pressure, tachycardia to 130 beats per minute and hypoxia with an oxygen saturation of 88% on room air. Her blood pressure dropped from a baseline of 110 systolic to mid 90s systolic. A CT angiogram of the chest demonstrated a massive saddle pulmonary embolus spanning the pulmonary bifurcation and extending into the bronchial segments bilaterally. Her ECG demonstrated right heart strain with classic S1Q3T3 changes, correlating with a rise in her Troponin I to a peak of 1.36 ng/ml and BNP of 383 pg/ml the following day. Echocardiogram demonstrated right heart strain, moderately elevated systolic pressure of 32 mmHg, moderate tricuspid regurgitation with a preserved ejection fraction of 60%. Following placement of a retrievable inferior vena cava filter she was transferred to the intensive care unit and started on intravenous UFH. Her starting platelet count was 181,000 per microliter (µl). The following day she was transferred to our facility for escalation of care at 26 6/7 weeks gestation.

The patient was maintained on intravenous heparin due to the drug's pharmacodynamic predictability and ability to be rapidly reversed, if needed. Her aPTT remained therapeutic between 65-100 s throughout her hospital course. On hospital day number 11 at our facility, she experienced a painless 20 cc quantified vaginal bleed. Repeat platelet count was 127,000 per µl. At this time, she was given a rescue course of betamethasone steroids. On hospital day number 13 the patient developed gross hematuria. Her platelet count was 86,000 per µl. Given the greater than 50% decline from her original platelet count, she was given a presumptive diagnosis of HIT and her intravenous heparin drip discontinued. A confirmatory serotonin release assay was ordered and returned positive several weeks later.

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The following day at 28 6/7 weeks gestation, the patient reported new onset low-back pain with continued frank hematuria. External tocodynamometry demonstrated regular uterine contractions. Given the concern for preterm labor in the setting of suspected placenta percreta with frank hematuria and risk for significant hemorrhage, she underwent cesarean hysterectomy. Total quantified blood loss was 4,500 cc for which she was transfused five units of packed red blood cells, five units of fresh frozen plasma, and two units of platelets. She gave birth to a female infant with Apgars 8 and 9, weighing 992 g. Twenty four hours post-operatively; the patient was started on the DTI, Lepirudin at 2.4 mg/hr and continued on this until day of discharge. Her post-operative course was uncomplicated. Coumadin was initiated on post-operative day number four and she was discharged home on post-operative day number nine, hospital day number twenty four, in stable condition once a therapeutic INR was achieved. Her platelet count on day of discharge was 316,000 per μ l. The infant was discharged home on day of life number 50. The neonatal course was complicated by respiratory distress syndrome and stage 1 retinopathy of prematurity.

Comment

The current incidence of placenta accreta is approximately 1 in 533 and mirrors the rising number of cesarean deliveries performed in the U.S. The risk of placenta accreta is approximately 8-fold higher in women with two prior cesarean deliveries, but 51-fold higher in those with two prior cesarean deliveries and a placenta previa [7]. One of the greatest risks posed by placenta accreta is that of peripartum hemorrhage. Blood loss averaging 3,000-5,000 cc may necessitate transfusion of multiple and various blood products [7]. Although our patient's VTE predated her delivery, it is well known that cesarean delivery, obstetric hemorrhage and transfusion of blood products all substantially increase the risk for VTE during the intrapartum and postpartum states [2,3]. Other than her obesity, pregnant state, and recurrent episodes of antepartum bleeding resulting in prolonged immobility, our patient did not have any personal or family history of VTE events and therefore was not considered to be at significantly high risk for development of VTE. Whether additional thromboprophylaxis in the form of low dose heparin or low molecular weight heparin may have prevented development of her VTE is unclear. Current recommendations suggest that intermittent pneumatic compression devices are sufficient thromboprophylaxis in pregnant women at low risk for VTE [8].

Pulmonary embolism remains the leading cause of maternal death in the developed world with an incidence of 1 to 1.5 per 100,000 deliveries in Western countries. Following her diagnosis of VTE, our patient was initially managed on intravenous UFH. A major risk of initiating heparin is the development of HIT. Heparin exposure leads to the formation of immune complexes which result in platelet activation, thrombin formation and ultimately formation of venous and arterial thromboses. Risk factors for the development of HIT include both type and duration of heparin exposure, with UFH conferring the greatest risk. The characteristic onset of thrombocytopenia, defined as a platelet count of less than 150,000 per μ l, typically occurs 5-10 days post exposure but can occur as late as three weeks. Although functional antigen assays, such as the Serotonin-Release Assay (SRA) are both sensitive and specific for a diagnosis of HIT, clinical gestalt should ultimately guide decision making. Once a diagnosis of HIT is suspected, anticoagulation with a direct thrombin inhibitor should be initiated [6].

DTIs are both safe and effective in the pregnant and postpartum state for treatment of VTE in women who develop HIT. Furthermore, there appears to be little difference in efficacy, bleeding and clinical outcomes amongst the various DTIs [5,9,10]. Lepirudin was chosen in this case based on its pharmacokinetic predictability, safety profile in the setting of HIT, ease of monitoring and physician preference.

This clinical scenario, while uncommon, illustrates the comorbidities that providers may soon be challenged with as a result of the rising number of cesarean deliveries performed in the U.S. A keen awareness of the complications which may develop, and a basic knowledge of their management with understanding of the appropriate timing for transfer to a higher level of care is essential in caring for women with placenta accreta. We have shown that these obstetric complications can be managed successfully under the care of subspecialists in tertiary care centers.

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