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Case Report

Postpartum Hemorrhage in a Patient with Factor XII Deficiency: A Case Report

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Abstract

Factor XII, (Hageman factor) is a serine protease zymogen that, when activated, initiates the intrinsic pathway of blood coagulation. Patients with Factor XII deficiency do not have excessive bleeding tendency despite prolongation of the activated partial thromboplastin time (APTT) in their serum. Postpartum Hemorrhage (PPH) is a potentially fatal obstetric complication, and its presence in the setting of a prolonged APTT can be worrisome to the treating obstetrician. Here, we report a case of PPH with prolonged APTT due to underlying factor XII deficiency who was successfully managed conservatively. The findings of this case report show that FXII deficient patients presenting with PPH can effectively be managed conservatively in the same way as other individuals with normal FXII levels.

Keywords: Factor XII deficiency, Hageman factor deficiency, Postpartum hemorrhage, Thrombosis

Key Messages: This study highlights that FXII deficiency in pregnant women is not associated with excessive bleeding and patients with this condition having post-partum hemorrhage can be managed conservatively similar to normal individuals.

Introduction

Factor XII (Hageman factor) is known to be implied in triggering blood coagulation. Factor XII deficiency is a known rare autosomal recessive trait that presents with increased activated partial thromboplastin time (APTT) without increased bleeding tendency [1].

Postpartum hemorrhage (PPH) is the most common cause of maternal mortality in the developing world [2,3].

There has been a controversy regarding the effects of FXII deficiency on the course of pregnancy. Mild PPH have been reported in pregnant women with factor XII deficiency [4,5]. Hereby, we present another case of a patient with FXII deficiency, who developed PPH.

Case History

A 22-year-old lady, primigravida at 38 weeks of pregnancy, was referred to our hospital (King Khalid University Hospital, Riyadh, and KSA**)** because of prolonged APTT. The course of pregnancy was uneventful. She had not experienced any abnormal bleeding episodes or symptoms of thrombosis. She was not on any medication and had never received anticoagulation. There is no known family history of bleeding or thrombotic tendencies.

The general physical examination was normal, her body built was within average, and the vital signs were within normal limits. There were no signs of jaundice, pallor, cyanosis, or bruise marks. On abdominal examination, the fundal height was corresponding to gestational age with cephalic presentation. Fetal heart beat tracing was reassuring with no signs of premature uterine contractions.

Laboratory results were as follows: Hemoglobin levels=11.3 gm/dl, platelet count = 398x10/L, LFTs, urea and electrolytes were normal. Coagulation profile showed PT = 15.7 (Normal reference= 11.5-16.5), APTT <120/sec (Normal reference= 26-39) and TT= 16.5 (Normal reference= 14-21). Mixing studies showed complete correction of APTT, suggesting factor deficiency. Factor assay showed extremely low

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Laboratory test	Result	Normal range	Laboratory test	Result	Normal range
PT	15.7	11.5-16.5 sec	Factor XII assay	3%	70-145%
PTT	<120	26-39 sec	Factor VIII assay	118%	50-200%
TT	16.5	14-21 sec	VWD ANTIGEN	294%	50-260%
Fibrinogen assay	5.42	2-4 g/L	Protein-C assay	140	70-140%
FIX assay	200%	50-150%	Protein-S assay	78	65-140%
FXI assay	200%	75-155%	Anti- Thrombin III	96	80- 120%
Ristocetin activity	113%	(40-260)	Platelet count	398	150-400 x10/L

PT: Prothrombin time
PTT: Partial thromboplastin time
TT: Thrombin time
VWD : Von Willebrand disease

Table 1. Maternal coagulation parameters in labour

Factor FXII activity (3%, reference value 70-145%) with elevated levels of coagulation factors (XI, IX, vWF Ag & fibrinogen). Protein C, protein S, antithrombin III, lupus anticoagulant and anticardiolipin antibodies levels were unremarkable (Table 1).

The patient had induction of labor for postdate pregnancy at 41 weeks gestation using prostaglandin E2 vaginal tablets. She progressed rapidly and had a precipitous labour in 90 minutes with occipito-posterior position. This was complicated with PPH with blood loss of approximately one liter. She received two units of packed red blood cells. Postpartum haemorrhage caused by Atony was treated medically by the administration of Prostaglandin F2-alpha 0.25 mg intramuscularly. She delivered a 3.1 kg healthy boy infant with good Apgar score; there was neither bleeding from the cord stump nor bruise marks on his body. Post-delivery, the patient had a smooth and uneventful recovery with normal lochial discharge. She was given Enoxaparin for thromboprophylaxis and discharged in good condition.

At six weeks' follow up, she was clinically well with no history of heavy vaginal bleeding during puerperium. She opted to take oral contraceptive pills (OCP) after discussing the available contraceptive options with her doctor. At three months' follow up, OCP's were well tolerated with no thromboembolic episode or any other complication. The infant did not show any bleeding tendency as revealed by the laboratory coagulation assay results up till the age of three and a half months.

Discussion

Factor XII (FXII, Hageman factor) is a plasma serine protease zymogen that is converted to activated Factor XII (FXIIa) following contact to negatively charged surfaces. FXIIa is known to be implied in triggering blood coagulation and fibrinolysis [1].

PPH is the most common cause of maternal mortality in the developing world. According to WHO statistics, approximately one fourth of maternal deaths are due to PPH [2,3].

Common etiologies of PPH include uterine atony, trauma to genital tract, chorioamnionitis, retained products and coagulation disorders. PPH is an obstetrical emergency that requires prompt management to resuscitate the patient and prevent complications such as shock and disseminated intravascular coagulation [3].

Although catastrophic bleeding and blood loss associated with pregnancy and delivery is fairly rare, hemorrhage after delivery is still one of the leading causes of maternal morbidity and mortality [3]. A series of procoagulant changes occur during normal pregnancy, which help to prevent excessive bleeding at the time of delivery. The concentrations of most coagulation factors rise significantly during pregnancy [6].

FXII (Hageman factor) is a serine protease that activates surface-activated blood coagulation tests including APTT. When exposed to negatively charged surfaces, FXII is auto-activated into the activated enzyme FXIIa which initiates the coagulation cascade known as the intrinsic coagulation pathway by activating Factor XI (FXI) [1]. However, FXI in vivo can be activated in the absence of FXIIa, hence explaining the absence of bleeding tendency in FXII deficient patients. Several studies discussed pathways of FXI activation in the absence of FXIIa; they concluded that FXI dependent coagulation can be initiated by tissue factor and α-thrombin [7].

Since coagulation factor XII first discovery in 1955, its deficiency was connected with thrombosis instead of bleeding. The story originated after the report that John Hageman, the index patient with this defect, had died of pulmonary embolism [8]. However, it is often forgotten that this event occurred after a traumatic pelvic fracture with consequent prolonged immobilization. Hence, several reports have highlighted the correlation between FXII deficiency and thrombosis [9]; however, a causal relationship is still questioned [10,11].

Nevertheless, it is known that FXII deficiency does not lead to increased bleeding tendency despite an increase in APTT [1,7,12]. There is evidence that FXII deficient patients can withstand even major surgical procedures without bleeding or thrombotic complications [12].

The clinical implications of FXII deficiency in pregnancy are controversial. There is a general consensus that FXII deficiency usually does not manifest in a hemorrhagic diathesis and only exceptionally has a mild bleeding tendency been reported [5,13-15]. Girolami, et al., reported that occasional mild bleeding that was recorded in pregnancy with FXII deficiency was due to an associated cause as thrombocytopenia or decrease uterine contraction. Both deep venous thrombosis and mild PPH have been found in other small series of pregnant women with factor XII deficiency [5].

In our case, courses of gestation were perfectly normal despite of FXII activities <3%. However, the patient developed atonic PPH.

In conclusion, our study highlights that FXII deficiency is not associated with excessive bleeding and that patients with this condition having PPH can be managed conservatively similar to normal individuals.

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