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Pregnancies with factor V deficiency: a case report and review of the literature

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Summary

Case report: A 30-year-old Japanese nulliparous woman visited for pregnancy at 33 weeks with a massive ovarian tumor located in the pouch of Douglas. By preoperative screening, her prothrombin time (PT) and activated partial thromboplastin time (APTT) were prolonged, and her FV activity was significantly decreased to 4.8%. After prophylactic FFP 20 ml/kg was administered and her FV factor was 19.3%, cesarean delivery was performed, and her perioperative course was uneventful. One year later, she underwent a dilatation and evacuation because of a missed abortion, although prophylactic FFP was not administered. During a third pregnancy, after prophylactic FFP 20 ml/kg was administered and FV activity increased to 21.1%, elective cesarean delivery was performed, and her postoperative course was uneventful. *Conclusion:* For surgical therapy or delivery, the goal of therapy is to maintain FV activity above 20%. It is particularly useful to administer prophylactic FFP.

Key words: Pregnancy; Congenital factor V deficiency; Prophylactic fresh frozen plasma (FFP); Autosomal recessive disorder.

Introduction

Factor V (FV) deficiency is a rare autosomal recessive disorder that is accompanied by a high hemorrhagic risk during delivery and post-partum. Factor V deficiency was first reported as parahemophilia in 1947 [1]. No precise epidemiologic data exist for congenital FV deficiency, but its prevalence has been estimated to be one in one million persons, and no clear ethnic predisposition is apparent.

The authors report the case of a woman diagnosed with congenital FV deficiency during preoperative screening for a planned cesarean delivery; prophylactic fresh frozen plasma (FFP) was administered before surgery, and this approach avoided hemorrhagic complications.

Case Report

A 30-year-old Japanese nulliparous woman visited the present perinatal center at 33 weeks of gestation after having undergone routine prenatal care elsewhere. She did not have a history of severe menorrhagia or excessive bleeding after dental procedures or trauma. At 18 years, she was diagnosed with an ovarian tumor and underwent laparotomy under general anesthesia. The intraoperative and postoperative course was unremarkable. Her pregnancy was uneventful except for an ovarian tumor, which was diagnosed as a ten-cm mature teratoma located in the pouch of Douglas. Cesarean delivery was planned because of this massive ovarian tumor.

On preoperative screening, her prothrombin time (PT) and activated partial thromboplastin time (APTT) were prolonged, and her FV activity was significantly decreased to 4.8%. She was diagnosed with FV deficiency. Her parents were not consanguineous. At 37 weeks and four days, prophylactic FFP 12 ml/kg was administered, and her plasma FV activity increased from 4.0% to 14.1% of normal plasma clotting activity. At 38 weeks and two days gestation, prophylactic FFP 20 ml/kg was administered, and her FV factor was 19.3% of normal plasma clotting activity. At 38 weeks and three days gestation, cesarean delivery was performed with a total blood loss of approximately 600 ml. After surgery, FFP 12 ml/kg was administered. Her postoperative course was uneventful.

The FV activity of her father and mother were 55% and 79% of normal plasma clotting activity, respectively. Citrate-anticoagulated blood samples were collected from the proband and her parents. Genomic DNA was isolated from whole blood, and the PCR products were analyzed by direct DNA sequencing. The proband was revealed to have a T67C homozygous missense mutation leading to Phe190Ser, and her parents were determined to be heterozygous carriers of this mutation.

After one year, the patient presented again to the present perinatal center with irregular vaginal bleeding for three weeks and was diagnosed with a missed abortion. She underwent a dilatation and evacuation to prevent massive unexpected bleeding. The total blood loss was 50 ml, although prophylactic FFP was not administered, and her FV factor was 3.6% of normal plasma clotting activity.

During a third pregnancy, she presented to the department at 24 weeks of gestation. Her pregnancy course was uneventful, and her FV was 3.5-5.0 % of normal plasma clotting activity during pregnancy. Prophylactic FFP 20 ml/kg was administered, and FV activity increased from 5.2% to 21.1% of normal plasma clotting activity. Planned elective repeat cesarean delivery was performed. After surgery, FFP four ml/kg was administered, and the postoperative course was uneventful. Prior to surgical procedures or deliv-

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ery, administration of prophylactic FFP is useful, and the goal of therapy is to maintain FV activity above 20%.

Discussion

The authors present the case of a woman diagnosed with congenital FV deficiency during preoperative screening for cesarean delivery. The FV activity level has a limited correlation with the severity of bleeding, but overall, patients with lower levels are more likely to have bleeding episodes than those with higher levels. Patients who come to medical attention are typically symptomatic homozygotes or compound heterozygotes with FV activity levels less than 5% [2].

Information on pregnancy outcome and management in women with FV deficiency is scarce. A study of 15 pregnancies in 11 heterozygous women and three pregnancies in two homozygous women was reported; prophylactic FFP and/or whole blood transfusion were performed, and the fetal outcome was good in all cases.. In another study of 17 cases of women heterozygous for FV, pregnancy and delivery were not accompanied by any bleeding complications [3]. Symptoms of factor V deficiency in 35 Iranian patients were reported [4]. The most frequent symptom was bleeding in the oral cavity (57% of all cases). Postoperative and postpartum bleeding together affected 43% (15/35) of the patients [5]. Yousei *et al.* reported successful delivery in five women with homozygous severe factor V deficiency [6]; four of the patients had a history of abortion and postpartum bleeding attributable to a coagulation factor deficiency in their families. Because, in each case, the factor V activity was 1.5% of normal activity, prophylactic FFP and/or whole blood transfusion were administered, and each of the pregnant women had a successful pregnancy and delivery without any significant bleeding complications during or after gestation [4].

Shinozawa *et al.* reported different symptom in three unrelated Japanese patients with FV deficiency [6]. While patient 1 had severe bleeding symptoms (plasma FV activity, < 1%; FV antigen, 9%), patient 2 had moderate bleeding symptoms (plasma FV activity, < 1%; FV antigen, 4%), and patient 3 had very mild symptoms (plasma FV activity, 1%; FV antigen, 5%). A study of recombinant protein expression revealed that the FV coagulant-specific activities in conditioned media for patient 3 and patient 1 and 2 mutants were reduced to approximately 40% and 28% of wild-type FV, respectively. The amounts of patient 3 protein and messenger RNA in the platelets were similar to those of healthy subjects; however, the amount of patient 1 and 2 protein was decreased. Their data suggest that the severity of the bleeding tendency in patients with FV deficiency is correlated not only with plasma FV activity, but also with the amount of FV protein in the platelets [6]. The very mild symptoms of the patient in the present case (plasma FV activity < 5%) suggests a normal amount of FV protein in the platelets.

To date, FFP is the primary therapeutic agent for patients with FV deficiency because no FV-specific concentrate is available. Most patients are only treated for symptoms such as menorrhagia or massive bleeding after trauma or before an invasive procedure. Especially for a surgical procedure, the administration of prophylactic FFP is recommended. For acute hemorrhage or surgical therapy, the goal of therapy is to maintain FV activity above 20%. The half-life of FV is 12-36 hours. The recommended starting dosage is 15 to 20 ml/kg, to be repeated daily to keep FV at hemostatic levels when prolonged treatment is needed. In some instances, this schedule can cause volume overload [5]. For the patient in the present case, the starting dosage was 12 to 20 ml/kg; however, this was not repeated daily, because she had a history of laparotomy under general anesthesia without massive bleeding and an unremarkable postoperative course at age 18.

In conclusion, the authors presented the case of a woman diagnosed with congenital FV deficiency during preoperative screening for a planned cesarean delivery. Women with FV deficiency, especially those with low FV levels, appear to be at increased risk of postpartum bleeding. Therefore, careful management during delivery and the immediate postpartum period is necessary. For acute hemorrhage or surgical therapy, the goal of therapy is to maintain FV activity above 20%. It is particularly useful to administer prophylactic FFP before surgery or delivery. A further study is necessary to research why different symptoms occur in patients with low FV activity.

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