American Journal of Medical Case Reports, 2023, Vol. 11, No. 4, 81-83
Available online at http://pubs.sciepub.com/ajmcr/11/4/5
Published by Science and Education Publishing
DOI:10.12691/ajmcr-11-4-5

Successful Normal Vaginal Delivery in the Setting of Factor VII Deficiency Diagnosed During Pregnancy: A Case Report and Review of the Literature

Samer Barahmeh[1,2,*], Oadi N. Shrateh[3], Afnan W.M. Jobran[3], Akram karmeh[4], Maysam Hamarsheh[2], Salsabeel Rajab[2]

[1]Assistant Professor, Faculty of Medicine, Al-Quds University, Jerusalem, Palestine
[2]Department of Obstetrics and Gynecology, Al-Istishari Arab Hospital, Ramallah, Palestine
[3]Faculty of medicine, Al-Quds University, Jerusalem, Palestine
[4]Department of Hematology, Al-Istishari Arab Hospital, Ramallah, Palestine
*Corresponding author: samer.barahmeh@iah.ps

Received March 05, 2023; Revised April 10, 2023; Accepted April 19, 2023

Abstract **Introduction:** An uncommon autosomal recessive genetic condition called congenital factor VII deficiency (FVIID) exists. This deficit has a wide range of clinical signs and symptoms. Pregnant women with congenital FVIID face a high risk of bleeding during and after delivery. The most popular kind of replacement therapy for FVIID is recombinant factor VIIa. For pregnant women with congenital FVIID, no standardized diagnosis or treatment strategy has been developed. **Case presentation:** We discuss the clinical background of a woman who was believed to have congenital FVIID when she was pregnant. The pregnant woman received recombinant factor VIIa as a preventative treatment when her cervical opening was complete. She delivered a live baby successfully without any difficulties or complications, including postpartum hemorrhage, neonatal defects, etc. **Discussion and Conclusion:** Pregnant women with hereditary FVIID who are at high risk of bleeding can effectively lower the incidence of postpartum hemorrhage by receiving recombinant factor VIIa as part of their prenatal care.

Keywords: *congenital factor VII deficiency, diagnosis and treatment plan, pregnancy, perinatal management, case report*

Cite This Article: Samer Barahmeh, Oadi N. Shrateh, Afnan W.M. Jobran, Akram karmeh, Maysam Hamarsheh, and Salsabeel Rajab, "Successful Normal Vaginal Delivery in the Setting of Factor VII Deficiency Diagnosed During Pregnancy: A Case Report and Review of the Literature." *American Journal of Medical Case Reports*, vol. 11, no. 4 (2023): 81-83. doi: 10.12691/ajmcr-11-4-5.

1. Introduction

The liver produces and secretes factor VII (FVII), a glycoprotein that is dependent on vitamin K for synthesis. The exogenous coagulation pathway is activated by the protein FVII [1]. A decrease in the amount of FVII or a functional malfunction is the result of congenital factor VII deficiency (FVIID), a rare autosomal recessive hemorrhagic condition caused by a mutation in the F7 gene [2]. The 12.8 kb genome of the F7 gene, which has 9 exons and 8 introns, is found on chromosome 13 (13q34). A total of 283 F7 gene mutations, including 180 missense and nonsense mutations, 39 cutting site mutations, 33 minor alterations inserted or deleted, and single nucleotide polymorphism, were published in the human gene mutation database as of February 2014. The population has a homozygote prevalence of roughly 1:500000 and a heterozygote prevalence of roughly 1:350 [3]. Pure heterozygous patients have an activity of FVII between 20% and 60%, whereas homozygous or compound heterozygous patients typically have less than 10% [4].

The pregnancy and delivery of a patient with congenital FVIID who was admitted to our hospital are described in this report. We talk about the management of the delivery, monitoring, and diagnosis processes. After that, we evaluate the research on pregnancies involving congenital FVIID.

2. Case Presentation

Our patient is a 31-year-old primigravida married female patient in her 36th week of gestation. She is a known case of hemophilia type A with a history of severe and recurrent episodes of epistaxis since the age of 3, heavy menstrual periods, significant bleeding following minimal trauma, and a history of one hospitalization after a dental extraction procedure at the age of 16, despite receiving the replacement therapy for hemophilia. The patient has a regular antenatal follow-up without any

remarkable or significant events during the pregnancy. She had a blood and fresh frozen plasma (FFP) transfusion several times in the past. Past surgical of the patient is free. The patient reported no personal and/or family history of cancer; any acute, repeat, or discontinued medications; any allergies; or any genetic or psychosocial issues. The patient came to our attention as a referral from another peripheral outpatient clinic, and upon the first encounter, the clinical appearance and physical assessment of the patient revealed a hemodynamically stable pregnant woman. She started fresh frozen plasma treatment in the 5th month of the pregnancy. After a multidisciplinary and detailed discussion with the hematology team, we decided to deliver the fetus vaginally. Accordingly, a thorough laboratory evaluation process has been performed, including hemoglobin (Hb) of 13.2 g/dl, prothrombin time (PT) of 77 seconds, and an international normalized ratio (INR) of 5.97. The fetal ultrasound was normal, and the fetal cardiotocography (CTG) was reactive without decelerations. The patient ordered a mixing study and, incidentally, was found to have factor VII deficiency with 2% level and normal levels of other clotting factors. The patient initiated recombinant factor VII replacement therapy in preparation of delivery. At the 38th week of gestation, the patient was given 3 units of FFP and 4.5 mg of NOVO 7, and then she underwent a normal vaginal delivery, which yielded a normal live infant with a birth weight of 3 kg and an Apgar score of 9/10. The patient did not experience any postpartum complications, including hemorrhage. Laboratory testing was repeated after delivery and was normal. She was followed up for 6 months, and she adhered to and tolerated the provided pieces of advice without any reported complications or adverse events.

3. Discussion

FVIID is categorized as follows by the International Society of Thrombosis and Hemostasis: significant: FVII 10%, with the possibility of spontaneous bleeding; Mild: FVII 20%-50%, majority of them asymptomatic; moderate: FVII 10%-20%, with the possibility of mild spontaneous or trigger bleeding [5]. FVII activity among severe patients was assessed as being less than 5% by the Seven Therapy Evaluation Registry [6]. Individuals with FVIID are typically asymptomatic, although invasive surgery may result in bleeding. Individuals with FVII activity less than 2% or below the normal level frequently experience severe bleeding [5].

When compared to general cases, FVIID's clinical symptoms are very distinct. Moderate patients only experience little bleeding or post-traumatic bleeding, including menorrhagia, gingival bleeding, epistaxis, ecchymosis of the skin and mucous membranes, and prolonged post-traumatic bleeding. In contrast, patients with FVIID experience severe symptoms in 4.4% to 8.0% of cases [7], which can result in life-threatening bleeding from the joints, the intracranial space, or the gastrointestinal tract. Menorrhagia is the most prevalent bleeding symptom, affecting 46% of female patients with factor VII deficiency, according to analytical data from the cooperation registry of the international registry of factor VII deficiency and seven treatment evaluation registries [8]. Bleeding during placental detachment, genital tract laceration, vulvar incision, or cesarean section are the severe clinical manifestations of FVIID in pregnant women during delivery [9].

Only a few examples of congenital FVIID during pregnancy have been documented as of yet. Four pregnant women with congenital FVIID were reported by Kulkarni et al [10] to have delivered at full term and had increased mean FVII activity from 33 IU/dL to 73 IU/dL. These women also received prophylactic doses of recombinant FVIIa (rFVIIa) at delivery. One of these women gave birth vaginally, while the other three underwent cesarean sections. One of the expecting mothers lost a lot of blood (1400 mL) during the cesarean section but didn't need a blood transfusion. Three pregnant women who underwent cesarean sections lost on average 800 mL of blood. A 22-year-old primipara with congenital FVIID and 1% FVII activity was admitted by Eskandari et al. [11] and received rFVIIa at 50 g/kg at the cervix's full opening and 35 g/kg four hours later. There were no complications with the bleeding. During the 30 minutes following each injection, FVII activity increased by more than 900%. As a result, the authors felt that they employed too much rFVIIa.

A 30-year-old woman with mild FVII insufficiency (FVII activity was 5%) and HIV infection gave birth via cesarean section after receiving continuous infusions of rFVIIa to keep the plasma FVII level at almost 100%, according to Jiménez-Yuste et al.'s report from 2012 [12]. There were no consequences from the bleeding. According to Ariffin et al.'s report [13], a couple with severe congenital FVIID lost their first two newborns to significant intracranial hemorrhage. The two dead children's samples were not collected, but the level of FVII activity matched that of conjugal complex heterozygotes with genetic damage. When the mother became pregnant again three years later, a villus sample was collected at 10 weeks of gestation to rule out severe coagulation (FVIID). Using exon polymerase chain reaction amplification and villus sequence analysis, it was discovered that the fetus only had the heterozygous FVIID genotype that was inherited from the father. A male baby who underwent an elective c-section at term and had a good clinical outcome both at the time of delivery and a year afterwards. An intravenous dose of 20 g/kg rFVIIa was administered to a 35-year-old woman with coagulation FVIID at the time of the cervix's full opening at 40 weeks' gestation, and the same quantity was administered again 4 hours later. Initial FVII activity for the woman was 18% (normal range: 60%–150%). The delivery by vaginal method went off without a hitch, and neither the expectant mother nor the baby experienced any issues with bleeding. The degree of FVII activity and the likelihood of bleeding were shown to have rather weak relationships. The risk of bleeding in patients with FVIID cannot be predicted by the FVII genotype, coagulation test, or bleeding history [14]. As a result, it is challenging to forecast the risk of bleeding and choose the appropriate treatment in practical practice.

Congenital FVIID cases have not been successfully treated with vitamin K supplements, according to research [1]. The infusion of fresh frozen plasma, prothrombin

complex concentrate, activated prothrombin complex concentrate, plasma-derived FVII concentrate, rFVIIa, etc. is a key component of the treatment strategy for pregnant women with congenital FVIID. With a low risk of thrombosis (0.4%), rFVIIa can be coupled with tissue factor to control bleeding at specific sites [14]. rFVIIa is currently the chosen alternative therapy [8].

However, at this time, there is still debate about the use of rFVIIa prophylaxis as a treatment during the delivery of congenital FVIID in pregnant women. Retrospective analysis by Kulkarni et al [10] of 62 women and 94 neonates with FVIID revealed that cesarean section patients are 2.9 times more likely to get preventive interventions than vaginal birth patients. Just 10% of postpartum hemorrhages during labor with preventative measures and 13% of cases during labor without preventive measures, according to studies. Prior to pregnancy, the median FVII activity in the serum of pregnant women in the two groups was 5.5%. The authors proposed that rFVIIa should only be utilized in unavoidable situations, believing that taking preventive action was unnecessary [4]. According to Kolucki et al. [15], keeping FVII activity above 15%–25% can produce an adequate hemostasis impact for the majority of surgical procedures. According to Hasoon and Rivers [4], cesarean sections require a technique of prevention, whereas vaginal deliveries do not need to be prevented using rFVIIa unless there is evidence of postpartum bleeding.

Each delivery method, bleeding propensity, FVII activity in late pregnancy, FVII genotype, bleeding history of the patient and family members, coagulation-related indicators, pregnancy status, and patient age should all be taken into account when deciding whether to use an alternative delivery method [16]. rFVIIa is not required as a prophylactic strategy but can be utilized for surgical intervention or bleeding management.

4. Conclusion

Congenital factor VII deficiency can have a wide range of clinical symptoms, from a mildly asymptomatic instance to a deadly hemorrhage. Obstetricians and gynecologists face significant hurdles in estimating the risk of bleeding during and after childbirth in pregnant women with congenital factor VII deficiency. Here, we describe a case of a pregnant woman with congenital factor VII deficiency and talk about how to handle this condition during pregnancy and delivery.

As with tables and equations, figures should be set in one column if possible unless two-column display is essential. The resolution of graphics and image should be adequate to reveal the important detail in the figure.

References

[1] He J, Zhou W, Lv H, Tao L, Chen X, Wang L. Novel IVS7+ 1G> T mutation of life-threatening congenital factor VII deficiency in neonates: a retrospective study in China. Medicine. 2019 Oct; 98(40).

[2] Lee YJ, Ju DH, Yi SW, Lee SS, Sohn WS. Successful management of maternal factor VII deficiency in a cesarean section. Obstetrics & gynecology science. 2014 Jul 15; 57(4): 314-7.

[3] Hunault, M. and K.A. Bauer. Recombinant factor VIIa for the treatment of congenital factor VII deficiency. in Seminars in thrombosis and hemostasis. 2000. Copyright© 2000 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New ….

[4] Hasoon, J. and J.M. Rivers, A case of heterozygous factor VII deficiency in pregnancy. Journal of Obstetrics and Gynaecology, 2020. 40(7): p. 1025-1026.

[5] Jain S, Donkin J, Frey MJ, Peltier S, Gunawardena S, Cooper DL. Phenotypical variability in congenital FVII deficiency follows the ISTH-SSC severity classification guidelines: a review with illustrative examples from the clinic. Journal of Blood Medicine. 2018 Nov 19: 211-8.

[6] Cramer TJ, Anderson K, Navaz K, Brown JM, Mosnier LO, von Drygalski A. Heterozygous congenital Factor VII deficiency with the 9729del4 mutation, associated with severe spontaneous intracranial bleeding in an adolescent male. Blood Cells, Molecules, and Diseases. 2016 Mar 1; 57: 8-12.

[7] Alam MM, Moiz B, Rehman KA, Jethwani P, Fadoo Z. Congenital factor VII deficiency in children at tertiary health care facility in Pakistan. Clinical and Applied Thrombosis/Hemostasis. 2015 Oct; 21(7): 639-44.

[8] Shapiro, A., The use of prophylaxis in the treatment of rare bleeding disorders. Thrombosis Research, 2020. 196: p. 590-602.

[9] Zaidi, S.M.A., R. Qureshi, and S.N. Adil, Factor VII deficiency and pregnancy: a case report and review of literature. Journal of the Pakistan Medical Association, 2010. 60(2): p. 136.

[10] Kulkarni, A., C. Lee, and R. Kadir, Pregnancy in women with congenital factor VII deficiency. Haemophilia, 2006. 12(4): p. 413-416.

[11] Eskandari, N., N. Feldman, and J.S. Greenspoon, Factor VII deficiency in pregnancy treated with recombinant factor VIIa. Obstetrics & Gynecology, 2002. 99(5): p. 935-937.

[12] Jimenez-Yuste V, Villar A, Morado M, Canales M, Hernandez MC, Sanjurjo MJ, Quintana M, Hernandez-Navarro F. Continuous infusion of recombinant activated factor VII during caesarean section delivery in a patient with congenital factor VII deficiency. Haemophilia: the Official Journal of the World Federation of Hemophilia. 2000 Sep 1; 6(5): 588-90.

[13] Ariffin H, Millar DS, Cooper DN, Chow T, Lin HP. Prenatal exclusion of severe factor VII deficiency. Journal of pediatric hematology/oncology. 2003 May 1; 25(5): 418-20.

[14] Loddo A, Cornacchia S, Cane FL, Barcellona D, Marongiu F, Melis GB, Angioni S, Paoletti AM, Neri M. Prophylaxis of peripartum haemorrhage using recombinant factor VIIa (rfVIIa) in pregnant women with congenital factor VII deficiency: A case report and literature review. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2019 Apr 1; 235: 77-80.

[15] Kolucki FR, Morris GJ, Thomas LC, Scialla S. Factor VII deficiency in pregnancy and delivery: a case report. Haemophilia. 2011 Oct 26; 6(17): e1005-.

[16] Matei A, Dolan S, Andrews J, Rivard GÉ. Management of labour and delivery in a patient with acquired factor VII deficiency with inhibitor: a case report. Journal of Obstetrics and Gynaecology Canada. 2016 Feb 1; 38(2): 160-3.

© The Author(s) 2023. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (http://creativecommons.org/licenses/by/4.0/).