Case Report

Pregnancy in a woman with congenital F-VII deficiency: a brief review of recent literature and case report

Rima Hajjar a, Inaam Hatoum b, Amina Krounbi b, Rabih Chahine a,b, Rahif Jalloul b, Mohamad K. Ramadan b,*

a American University in Beirut-Medical Center, Department of Obstetrics and Gynecology, Beirut, Lebanon
b Rafik Hariri University Hospital, Beirut, Lebanon

ARTICLE INFO

Article history:
Received 2 June 2021
Accepted 10 July 2021
Available online 15 September 2021

Introduction

Congenital F-VII deficiency is a rare bleeding disorder caused by mutations of the F7-gene located on chromosome 13 long-arm and is believed to be inherited in an autosomal-recessive mode.1 It is encountered in approximately 1:300,000-500,000, whereas, the heterozygous form can reach 1:350 individuals.2 Factor VII-deficiency is also characterized by several phenotypes and patients may be asymptomatic or may suffer from severe bleeding involving the GI system or the CNS.3 The major concern for these patients is bleeding during or after surgery/delivery. Levels of F-VII vary based on the type of mutation. The International Society on Thrombosis and Hemostasis has reclassified FVII deficiency as follows: severe, FVII <10%, risk of spontaneous major bleeding; moderate, FVII 10%–20%, risk of mild spontaneous or triggered bleeding; mild, FVII 20%–50%, mostly asymptomatic disease.4 Nevertheless, despite this classification, FVII activity level does not always correlate with bleeding severity. Patients with similar F-VII activity levels were found to have different bleeding patterns.5 Pregnancy is known to be a hypercoagulable state, where F-VII levels, among other coagulation factors, are typically increased towards the end of pregnancy.6 Bleeding during pregnancy and delivery can be concerning due to increased fetal and maternal morbidity. Whether prophylaxis during labor improves maternal or fetal outcome remains unclear and no guidelines have been made so far. The only existing systematic review included all cases reported between year 1953 and 2011.7 We opted to complement the aforementioned study with analysis of 18 new cases with F-VII deficiency published beyond 2012 along with a new woman managed at our center (a total of 19 cases).

Case presentation

This was a case of a 24-year-old Lebanese lady, G2P0A1, known to have congenital F-VII deficiency. Four years earlier she was diagnosed with F-VII deficiency after consulting a hematologist for easy bruising. Her blood exams were significant for elevated international normalized ratio (INR) of 1.3 and F-VII level of 35% (normal range 60-150%). Two years later, she had one spontaneous abortion at 15 weeks’
gestation that was complicated by hemorrhage, requiring treatment with rFVIIa (1.2 mg) and blood transfusion. Following treatment, F-VII level was found to be 40%. Her family history was significant for a paternal aunt carrier of F-VII deficiency. The patient did not report any history of bleeding following tooth extraction, heavy menstruation, epistaxis, hematuria, rectal bleeding, excessive gingival bleeding or formation of spontaneous or traumatic hematomas.

The woman was referred to our outpatient clinic (OPD) at 35±5 weeks’ gestation. Her antenatal course was uneventful. Blood exam showed an INR of 1.07 and prolonged PTT (control 32s and patient 59s). Obstetric ultrasound done at 37±5 weeks of gestation showed a macrosomic baby with an estimated fetal weight of 3.9 kg (at 95th percentile for gestational age) and normal amniotic fluid index. She presented at 38±1 weeks in labor with regular contractions. Her Bishop score was 6/15. No cervical changes were noted after 5 hours of regular contractions. After multidisciplinary discussions, decision was taken to proceed with primary cesarean delivery, given the presence of fetal macrosomia and the potential for multiple complications including perineal trauma and instrumental delivery. In view of a history of postpartum hemorrhage following previous surgical abortion, prophyaxis with 1.2 mg rFVIIa (20mcg/kg) was given intravenous-drip immediately prior to surgery. Cesarean was done under general anesthesia. Patient was delivered of a live born male infant weighing 3970 grams with optimal Apgar Score. Delivery was complicated by uterine atony with estimated blood loss of 800 cc. Bleeding was controlled with Pitocin IV (20UI), 1gr Tranexamic acid, 3 tablets of Misoprostol (200mcg) rectally. Hemovac-drain was placed intraoperatively. Patient did not require any transfusion of packed red blood cells nor fresh frozen plasma. rFVIIa was continued 1.2 mg intravenous drip every 12 hours for 7 days as recommended by hematology team. The newborn infant was transferred to the normal nursery; the circumcision and the intramuscular injection of vitamin K were deferred. No neonatal hemorrhage was noted. Postpartum course was uncomplicated, hemoglobin dropped from 12.6 to 10.9. Hemovac drain was removed on day 2 post-operatively. The puerperium progressed uneventfully and no adverse events after discontinuing the replacement therapy. The woman and her infant were found to be healthy on routine check-up-visit 6 weeks postpartum.

Discussion and conclusions

This patient was a 24 year-old lady whose last F-VII activity level before delivery was 40% (mild F-VII deficiency), yet, given a history of hemorrhage following previous abortion at 15 weeks’ gestation that responded to rFVIIa replacement therapy and blood transfusion, we elected to proceed with primary cesarean rFVIIa prophylaxis in current pregnancy. She received 1.2 milligrams intravenous drip immediately prior to her operation followed by similar doses every 12 hours for 7 days as recommended by the hematology team. This dose seemed to be sufficient in this case as no intrapartum bleeding was observed. The operative delivery was uneventful in spite of the development of transient uterine atony that was successfully managed with massaging and uterotonics. The uterine bleeding immediately accompanied uterine atony. This happened even after receiving rFVIIa 30 minutes before delivery which has certainly raised F-VII activity to levels > 40%. No bleeding was observed from surgical sites. Usually, when F-VII activity level is below 10 IU/4L, clinically apparent bleeding diathesis emerges and it is generally agreed that supplementation with rFVIIa in these patients is a reasonable approach before surgery/delivery and this is usually administered 30-60 min prior to surgery. Nevertheless, for unclear reasons, individuals with milder forms can also manifest bleeding especially in association with surgery/delivery rendering correlation between F-VII activity levels and bleeding tendency very poor. Replacement for patients with higher F-VII activity levels, however, remains controversial. Management and delivery of women with milder F-VII deficiency is mostly approached on a case-by-case basis. Beneficial effect of replacement before delivery to all patients with milder F-VII deficiency is mostly observed in severe cases as a component of a syndrome. We also excluded articles and abstracts that did not discuss intrapartum management of Factor VII deficiency. Only English and French articles were considered.

Identified, were ten relevant articles reporting on 10 cases, another one reporting 5 cases with 6 pregnancies and last one describing two cases. A new case managed at our center was added to this series (totaled 19 cases). A summary of prominent features was displayed in Table 1.

One woman carried twin gestation while remaining women had singleton pregnancies. All women gave birth at full-term except one case who was delivered by cesarean section at 29 weeks’ gestation due to placental...
Table 1 – Recent similar cases reported to the literature with relevant clinical findings.

<table>
<thead>
<tr>
<th>Author/year</th>
<th>Case No</th>
<th>Predelivery F-VII level</th>
<th>Family History</th>
<th>Bleeding phenotype</th>
<th>Prophylaxis rFVIIa</th>
<th>Dose</th>
<th>Delivery Route</th>
<th>PP-HGE / Uterine Atony / birth-canal laceration (EBL in ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harkouk (2012)&lt;sup&gt;13&lt;/sup&gt;</td>
<td>1</td>
<td>94%</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td></td>
<td>NVD</td>
<td>NONE, vaginal laceration (EBL=800ml)</td>
</tr>
<tr>
<td>Hansen (2012)&lt;sup&gt;23&lt;/sup&gt;</td>
<td>1</td>
<td>1%</td>
<td>NA</td>
<td>Yes</td>
<td>No</td>
<td></td>
<td>NVD</td>
<td>NONE</td>
</tr>
<tr>
<td>Hansen (2012)&lt;sup&gt;23&lt;/sup&gt;</td>
<td>2</td>
<td>1%</td>
<td>NA</td>
<td>Yes</td>
<td>No</td>
<td></td>
<td>NVD</td>
<td>NONE</td>
</tr>
<tr>
<td>Yazicioglu (2013)&lt;sup&gt;15&lt;/sup&gt;</td>
<td>1</td>
<td>35%</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td></td>
<td>CD</td>
<td>Placental abruption (EBL=900ml)</td>
</tr>
<tr>
<td>Laiteslart (2014)&lt;sup&gt;16&lt;/sup&gt;</td>
<td>1</td>
<td>2%</td>
<td>Neg</td>
<td>No</td>
<td>Yes</td>
<td>30iu/kg</td>
<td>NVD</td>
<td>NONE 3&lt;sup&gt;rd&lt;/sup&gt; degree perineal laceration (EBL=NA)</td>
</tr>
<tr>
<td>Lee (2014)&lt;sup&gt;17&lt;/sup&gt;</td>
<td>1</td>
<td>7%</td>
<td>Neg</td>
<td>Yes</td>
<td>No</td>
<td></td>
<td>CD</td>
<td>NONE</td>
</tr>
<tr>
<td>Das (2014)&lt;sup&gt;18&lt;/sup&gt;</td>
<td>1</td>
<td>2%</td>
<td>NA</td>
<td>Yes</td>
<td>Yes</td>
<td>1mg</td>
<td>NVD</td>
<td>NONE (EBL=250ml)</td>
</tr>
<tr>
<td>Chen (2016)&lt;sup&gt;19&lt;/sup&gt;</td>
<td>1</td>
<td>11.8%</td>
<td>NA</td>
<td>Yes</td>
<td>NO</td>
<td></td>
<td>CD</td>
<td>NONE (EBL=400ml)</td>
</tr>
<tr>
<td>Pfrepper (2017)&lt;sup&gt;20&lt;/sup&gt;</td>
<td>1</td>
<td>1% Homozygous</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td></td>
<td>NVD</td>
<td>NONE (antenatal retroplacental hematoma) treated antenatally with rFVIIa</td>
</tr>
<tr>
<td>Loddo (2019)&lt;sup&gt;21&lt;/sup&gt;</td>
<td>1</td>
<td>18%</td>
<td>Neg</td>
<td>Yes</td>
<td>Yes</td>
<td>20ug/kg</td>
<td>NVD</td>
<td>NONE</td>
</tr>
<tr>
<td>Lee (2020)&lt;sup&gt;22&lt;/sup&gt;</td>
<td>1</td>
<td>1%</td>
<td>Yes</td>
<td>YES</td>
<td>Yes</td>
<td>15ug/kg</td>
<td>NVD</td>
<td>2&lt;sup&gt;nd&lt;/sup&gt; degree perineal laceration (EBL=800)</td>
</tr>
<tr>
<td>Lee (2020)&lt;sup&gt;22&lt;/sup&gt;</td>
<td>2</td>
<td>16%</td>
<td>Neg</td>
<td>YES</td>
<td>No</td>
<td></td>
<td>CD</td>
<td>Uterine atony (EBL=1000ml)</td>
</tr>
<tr>
<td>Lee (2020)&lt;sup&gt;22&lt;/sup&gt;</td>
<td>3</td>
<td>16%</td>
<td>Neg</td>
<td>YES</td>
<td>Yes</td>
<td>15ug/kg</td>
<td>CD</td>
<td>Uterine atony (EBL=800ml)</td>
</tr>
<tr>
<td>Lee (2020)&lt;sup&gt;22&lt;/sup&gt;</td>
<td>4</td>
<td>68%</td>
<td>Neg</td>
<td>YES</td>
<td>No</td>
<td></td>
<td>CD</td>
<td>2&lt;sup&gt;nd&lt;/sup&gt; degree perineal laceration (EBL=500ml)</td>
</tr>
<tr>
<td>Lee (2020)&lt;sup&gt;22&lt;/sup&gt;</td>
<td>4</td>
<td>64%</td>
<td>Neg</td>
<td>No</td>
<td>No</td>
<td></td>
<td>NVD</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; degree perineal laceration (EBL=600ml)</td>
</tr>
<tr>
<td>Lee (2020)&lt;sup&gt;22&lt;/sup&gt;</td>
<td>5</td>
<td>38%</td>
<td>Neg</td>
<td>No</td>
<td>No</td>
<td></td>
<td>CD</td>
<td>NONE</td>
</tr>
<tr>
<td>Hasoon (2020)&lt;sup&gt;21&lt;/sup&gt;</td>
<td>1</td>
<td>24%</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td></td>
<td>NVD</td>
<td>Uterine atony &amp; Perineal laceration (EBL=650ml)</td>
</tr>
<tr>
<td>Balluet (2020)&lt;sup&gt;22&lt;/sup&gt;</td>
<td>1</td>
<td>5%</td>
<td>Neg</td>
<td>No</td>
<td>No</td>
<td></td>
<td>NVD</td>
<td>NONE</td>
</tr>
<tr>
<td>Current case (2021)</td>
<td>1</td>
<td>40%</td>
<td>Yes</td>
<td>YES</td>
<td>YES</td>
<td>20iu/kg</td>
<td>CD</td>
<td>Uterine atony (EBL=800ml)</td>
</tr>
</tbody>
</table>

EBL: estimated blood loss; Nl: normal; Cs: C-section; NVD: normal vaginal delivery; PPH: post-partum hemorrhage; NA: not available.
Patients

This association was not observed in this group, where FVII level did not influence the decision to administer prophylaxis nor it influenced the route of delivery. In the above mentioned review, postpartum hemorrhage complicated 54% of women who did not received prophylaxis with rFVIIa as opposed to only 22% of women who received prophylaxis. In their review, Kreuziger et al reported that women with FVII-deficiency who underwent cesarean section were 3 times more likely to receive prophylaxis with rFVIIa. However, the authors concluded that rFVIIa prophylaxis should not be mandatory as it did not decrease the risk of postpartum hemorrhage. This association was not observed in this group, where FVII level did not influence the decision to administer prophylaxis nor it influenced the route of delivery. 

Conflicts of interest

The authors declare no conflicts of interest.

References