Case Report

Medical and Surgical Management of Postpartum Hemorrhage in a Woman with Factor XIII Deficiency

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Received 17 June 2016; Revised 27 July 2016; Accepted 28 July 2016

1. Introduction

Factor XIII (FXIII) is a transglutaminase that circulates in plasma and is activated by thrombin [1]. It plays a key role in the final process of hemostasis in the coagulation pathway by catalyzing the cross-linking of fibrin [1]. This process ensures the strength and stabilization of the clot [2]. The clot also becomes resistant to fibrinolysis with higher concentrations of active FXIII [3]. Inherited FXIII deficiency has an autosomal recessive pattern of inheritance affecting males and females equally, with an estimated incidence of 1:3,000,000–1:5,000,000 [2]. Prevalence is highest in regions where consanguineous marriage is common, including southeastern Iran [4]. Acquired FXIII deficiency is more common and is caused by an autoantibody that binds to FXIII interfering with its main function [2]. Without cryoprecipitate and factor infusion interventions, FXIII deficiency results in delayed wound healing and recurrent spontaneous miscarriages [2, 5]. In addition to this rare coagulopathy, this patient’s case was complicated by her religious beliefs about accepting blood products as a Jehovah’s Witness.

2. Case Presentation

A South American Jehovah’s Witness in her mid-20s with significant past history of two first-trimester spontaneous abortions, hypothyroidism, unilateral renal agenesis, and FXIII deficiency presented to our hospital at 41 weeks’ gestation, with perineal pain and contractions. She started her prenatal care and received prophylactic cryoprecipitate every two weeks to treat her FXIII deficiency abroad, prior to arriving in the United States at 37 weeks’ gestation. Upon admission to the Labor and Delivery Unit, consultation with Maternal Fetal Medicine and Hematology recommended proceeding with a vaginal delivery. She received eight units of prophylactic cryoprecipitate; patient had a successful normal spontaneous vaginal delivery of a live infant with Apgar
of nine at one minute and nine at five minutes. Following
delivery, abrupt hemorrhage occurred soon after evacuation
of the placenta. The hemorrhage was thought to be due
to retained placental elements or uterine trauma, because
the uterus was appropriately contracted following initial
delivery. In this immediate postdelivery period of 20–30
minutes, the patient's blood loss was underappreciated and
was subsequently estimated at 2 L. After lengthy discussion
with the patient and her family, patient consented to receive
blood products in the event of life-saving necessity. A Mas-
tive Transfusion Protocol was initiated; the patient received
approximately 2.5 L of crystalloid while blood products were
prepared. She was transfused eight additional units of cryo-
precipitate, four units of fresh frozen plasma, three units of
packed red blood cells, and one unit of platelets. A continuous
infusion of aminocaproic acid was chosen over intermittent
dosing of tranexamic acid (TXA) to provide a steady more
consistent presence of antifibrinolytic activity; this continued
until FXIII was available several days later.

The patient remained hypotensive and was taken to the
operating room for hemorrhage control; an emer-
gency supracervical hysterectomy was performed. Continued
bleeding was noted from the visceral surfaces and Trauma
Services was consulted intraoperatively for damage control.
The pelvis was packed, drains were placed, and a temporary
closure was performed. The plan was to stabilize the patient
and reverse her coagulopathy. The packing was removed and
delayed closure was performed on postoperative day two.
Patient was subsequently discharged on postoperative day
number six.

3. Discussion

While, in some rare instances, women with FXIII deficiency
are able to successfully deliver live newborns without FXIII
replacement therapy [6], FXIII deficiency is associated with
pregnancy complications including miscarriage, antepartum
hemorrhage, and postpartum hemorrhage [6]. One of these
complications is postpartum hemorrhage, defined as blood
loss exceeding 500 mL in the first 24 hours following vaginal
delivery or blood loss exceeding 1000 mL in the first 24 hours
following caesarean delivery [7]. Postpartum hemorrhage is
the leading cause of maternal mortality [8], responsible for an
estimated 25% of maternal deaths associated with childbirth
[9]. Management of the gravid patient with FXIII deficiency
is focused on prophylaxis with FXIII concentrate, cryopre-
cipitate, or fresh frozen plasma, with FXIII concentrate being
preferred when available [6, 10]. The exact concentration of
FXIII in the blood necessary for optimal pregnancy outcomes
is unknown; however, a systematic review of pregnancy
outcomes in women with FXIII deficiency found that, in
pregnancies reaching viability, a median FXIII concentration
of 12 IU/dL in the blood was maintained during pregnancy
and a median FXIII concentration of 35 IU/dL was main-
tained during labor and delivery [6]. While there is no uni-
versal consensus about the optimal dosing regimen for FXIII
concentrate in pregnancy, administering 250 IU weekly up
until labor and delivery, with a 1000 IU booster dose
has been found to be effective [6]. Due to its approximately
two-week half-life, those receiving prophylactic therapy with
FXIII concentrate should have protective coverage extending
into the postpartum period [6, 10]. In this case, due to the
inability to obtain FXIII prior to delivery, cryoprecipitate was
used instead. Additional crystalloid infusion was recognized
as a potential contributor to dilutional coagulopathy, but,
at the time, hypotension and the required induction of
anesthesia required aggressive volume resuscitation.

Our patient's condition was further complicated when she
experienced disseminated intravascular coagulation (DIC).
DIC can be categorized into either overt or nonovert based on
the criteria set out by the International Society of Thrombosis
and Hemostasis (ISTH) [11, 12]. The scoring takes into
account platelet count, prothrombin time, the amounts of fib-
rinogen, and D-dimer (Table 1) [12]. Overt DIC, or the stage at
which a patient becomes decompensated, is considered with
a score greater than or equal to five [12]. A study conducted by
Song et al. [13] set out to investigate the correlation between
FXIII and DIC. Their study population consisted of patients
with DIC from conditions ranging from malignancies to
infections. After measuring FXIII levels, the team discovered
that plasma levels were significantly decreased in overt DIC
patients compared to nonovert DIC patients. DIC scores were
inversely correlated to FXIII activity [13]. It can therefore be
deduced that those with lower FXIII activity, such as our
patient, may be more likely to reach the decompensating stage
of DIC and thereby suffer more severe hemorrhage.

When medical management fails to reverse coagulopathy,
surgical management must be considered as a life-saving
procedure. Intraoperatively, the patient had lost 3 L of blood,
an intraoperative consult to Trauma Services was obtained
to perform damage control surgery (DCS). DCS is a surgical
strategy frequently used by trauma surgeons to control
surgical bleeding in patients with multiple visceral and/or
vascular injuries. Damage control is often life-saving in
critical surgical patients; a review by Shapiro et al. concluded
that up to 60% of patients survive with this approach [14].
DCS is practiced in a three-stage approach [14]. The first stage
is the initial laparotomy that aims to quickly stop hemorrhage
by packing, suturing, ligation, or balloon tamponade [14, 15].
Balloon tamponade and B-Lynch suture compression were

|                | Value | Points |
|----------------|-------|--------|
| Platelet count (μL) | <100000 | 1 point |
|                 | <50000 | 2 points |
| Prolongation of PT (s) | >3 but <6 | 1 point |
|                 | ≥6     | 2 points |
| Fibrinogen (mg/dL)   | 100    | 1 point |
|                 | 0.5–1  | 1 point |
|                 | 1–3    | 2 points |
|                 | ≥3     | 3 points |

Table 1: International Society of Thrombosis and Hemostasis (ISTH) criteria for overt versus nonovert DIC. A score greater than or equal to 5 is compatible with overt DIC whereas a score less than 5 is suggestive for nonovert DIC.
considered as temporizing maneuvers; ultimately, however, expeditious exploration and hysterectomy were chosen over potentially time-consuming attempts at uterine salvage. The main goals of DCS are to avoid a downward spiral of the “lethal triad” (hypothenmia, metabolic acidosis, and refractory coagulopathy) and to limit operative time so the patient can be transferred to the surgical Intensive Care Unit (ICU), which is stage II of DCS, for physiologic stabilization [14, 16, 17]. Once the patient is stabilized in the ICU, including optimization of hemodynamic status, reversal of coagulopathy, and fluid resuscitation, the patient is brought back to the operating room for stage III of the DCS strategy, which includes removal of the packing, definite repair of injuries, and definitive abdominal closure [14, 17]. In our case, the major element of the damage control surgery included pelvic packing to stop the massive hemorrhage.

A variety of techniques exist for pelvic packing, with the most common one being insertion of absorptive materials, such as gauze rolls, into the abdomen and pelvis for tamponade of the bleeding and to provide sufficient pressure to achieve hemostasis. However, there is a delicate balance between packing the abdomen too tight, which may result in compartment syndrome, and not packing tight enough, which can lead to continued hemorrhage after packing is placed. Complications from overly forceful packing can include neuropathies, compression of the inferior vena cava (IVC), and renal failure secondary to IVC compression. As a result of an intentionally retained foreign body, febrile morbidity and sepsis are also concerns [18].

Jehovah’s Witnesses decision to abstain from blood or blood fractions is a personal choice based on individual religious beliefs. Administration of blood products against the wishes of a patient is a potentially criminal act that could be subject to prosecution [19]. These forbidden blood products include red cells, white cells, platelets, and plasma. Blood fractions, including cryoprecipitate and individual clotting factors, are acceptable to some Jehovah’s Witnesses, including the patient in this case [19]. In the past, our patient had previously accepted prenatal infusion of cryoprecipitate. In the postpartum state, she initially refused transfusion of other blood products but eventually consented to receive red blood cells, plasma, and platelets due to the severity of her condition with postpartum hemorrhage and DIC requiring an emergent supracervical hysterectomy and DCS. She also consented to receive recombinant FXIII in the postpartum state. Ideally, a patient’s final decision about blood products would be made prior to any complications so the treatment team can plan accordingly; however, we recognize that emergent situations similar to this case may occur.

This case also highlights the unique patient population treated at our hospital in South Florida, in which a large percentage of our patients are international patients from either Latin America or the Caribbean. While several international and national registries have been established for rare bleeding disorders [20, 21] the true incidence of rare bleeding disorders such as Factor XIII in Latin American populations may be underestimated due to the fact that international registries draw heavily from data gathered from Europe, North America, and Iran [21].

Competing Interests

The authors declare that they have no conflict of interests.

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