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Case Report

Factor VII deficiency and pregnancy: A case report and review of literature

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Abstract

Factor VII deficiency is one of the 'rare inherited disorders of coagulation.' Few cases of Factor VII deficiency have been reported during pregnancy, a state which could potentially cause fatal haemorrhage. Here we report a case of a pregnant lady with a history of heavy menorrhagia and multiple first pregnancy failures. Delivery was carried out via Caesarean section due to non-reassuring foetal heart monitoring. Patient was treated with Fresh Frozen Plasma (FFPs) and Factor VII concentrates, however, the patient developed bleeding postoperatively. Literature indicates that whilst Factor VII levels rise during pregnancy in normal women, no increase is seen in homozygous cases, whereas there is a moderate rise in heterozygous individuals. History of heavy menorrhagia, multiple first pregnancy failures and a positive family history for bleeding disorders necessitate investigation and monitoring of Factor VII levels during pregnancy. Factor VII concentrates achieve adequate homeostasis in most cases. Recombinant Factor VIIa, however, is the treatment of choice and does not carry a risk of infection transmission or thrombus formation.

Introduction

Inherited deficiencies of Factor VII are among the 'rare inherited disorders of coagulation.' This bleeding disorder has an estimated prevalence of 1 per 500 000 in its severest form, to one in 350 in the heterozygous state.¹

Few cases have been reported of Factor VII deficiency during pregnancy. Pregnancy has shown to elevate Factor VII levels in normal women whereas no significant increase occurs in homozygous deficiencies.^{2,3}

The serious clinical manifestation of Factor VII deficiency during labour is haemorrhage. This can occur from the site of the placenta, genital lacerations, episiotomies or during Caesarean sections.¹

The generally held view is that for patients with Factor VII deficiency, bleeding diathesis does not become clinically manifest unless the level is <10 IU/dL. This commonly occurs in the severe form of the disease which causes spontaneous bleeding. The range for heterozygous carriers is 20-60 IU/dL, hence, a majority of these cases are incidental discoveries.⁴ However, a poor correlation has been shown between the levels of Factor VII and the risks of bleeding.⁵ As a result,

many heterozygous carriers may begin to bleed even at higher Factor VII levels. These factors make it difficult to identify patients at risk for ante-partum complications and in deciding treatment modalities. The choice of treatment depends on its efficacy, costs, clinical assessment of the patient, risk of infection transmission and developing thrombosis.

Here we report a case of Factor VII deficiency during pregnancy and a review of management of such cases.

Case Report

A 28-year-old Gravide III, Para 0+2 woman at the 39th week of pregnancy, known case of Factor VII deficiency and pregnancy induced hypertension presented to the Emergency Room.

This patient had first presented to this hospital at the age of fifteen with a history of heavy menorrhagia since the onset of menarche (eight months previously). In addition, she had complaints of weight loss, weakness, fatigue and examination revealed extreme pallor. Laboratory reports revealed severe microcytic, hypochromic anaemia (Hb 2.7, Hct 9.2%, RBC 1.78). She was subsequently managed on blood transfusions, platelets, fresh frozen plasma (FFPs), norethisterone, tranexamic acid, NSAIDs and iron supplements. On follow up visits to the clinic, over the next ten years, she was treated under a diagnosis of Dysfunctional Uterine Bleeding followed by Dilatation and Curettage for acute exacerbation of symptoms.

During the previous year, she had two missed abortions that required Dilatation and Evacuation. During her second pregnancy, suspicion of a hereditary bleeding disorder was raised after her sister was diagnosed with Factor VII deficiency. Upon visiting the haematology clinic, coagulation profile showed PT 62, INR 5.28, APTT 21, Factor VII levels at 2.4 % and a diagnosis with Factor VII deficiency was made.

The third pregnancy was uneventful until the 27th week when she was admitted for two episodes of haematuria. She was managed with 4 units of FFPs and was later discharged when there was no further evidence of bleeding.

At this admission, the patient presented to the Emergency Room with labour pains. On examination she was not in active labour and foetal heart monitoring revealed a non-reassuring trace, therefore, an emergency caesarean section was planned. Pre-operatively she was infused a single

dose of Factor VII concentrate and 3 units of FFPs 8 hourly, prophylactically. Caesarean Section was performed later that night during which she was given an additional 6 units of FFP and 4 units of cryoprecipitate. A healthy baby boy was delivered weighing 2.9 Kg with an APGAR score of 9 at five minutes. The estimated blood loss during the procedure was 800ml. Red rubber and Redivac drainage tubes were placed intra-operatively and collected 90cc and 10 cc of blood, respectively, 6 hours post-operatively. Post-operative coagulation profile revealed PT 9.4, INR 0.9, APTT 32.3 while her Hb had dropped from 14.9 to 13.2. She was continued on 3units of FFPs 8 hourly, Tranexamic acid 500mg intravenously and antibiotics. She was given TED stockings and regular physiotherapy sessions and closely monitored for any signs of DVT (Deep Venous Thrombosis). Vitaly the patient remained stable during the post-operative period and did not develop fever.

On the 3rd post-op day, the Redivac drain showed an increase of 15cc with a concomitant drop of haemoglobin to 10.6, hence, FFP infusion was increased to every 6 hours. By the 5th post-op day, there was no evidence of further bleed, sutures and drains were removed and FFPs were tapered to 3 units BID. The patient was eventually discharged on the 8th post-operative day on oral tranexamic acid 250 mg 6 hourly for four days and oral antibiotics.

Discussion

The management of Factor VII deficiency during pregnancy involves a balancing act of achieving adequate haemostasis to control excessive ante-partum haemorrhage and to prevent a state of hypercoagulability that will lead to thrombus formation. The normal physiological rise of Factor VII during pregnancy is impaired in cases with homozygous deficiencies, however, a recent case-series revealed that women with mild-moderate disease show an increase in Factor VII levels from a mean baseline of 33 IU/dL to 73 IU/dL at term.³ Majority of women in the case series that were not given any prophylactic treatment and delivered at full term without significant postpartum haemorrhage. Patients with mild-moderate disease on the other hand may be managed expectantly. This study, however, is limited by sample size and results have not been hitherto replicated. Furthermore, early pregnancy losses are likely to occur as any expected rise occurs late during the third trimester. Cases with severe disease, therefore, require prophylactic therapy as part of management.

FFPs may be utilized for management due to easy availability and less thrombogenic potential over prothrombin complexes and other concentrates.⁶ However, fatal thrombosis has been described in cases with congenital Factor VII deficiencies, hence, evidence of hypercoagulability needs to be closely monitored.⁷ Factor VII concentrates

instead are more effective in preventing ante-partum haemorrhage and carry a low risk of viral infection transmission and pulmonary oedema.⁸

More recently, recombinant Factor VIIa (rFVIIa) has become the treatment of choice. The advantage of using recombinant Factor VIIa results from its specific action at the site of vessel injury leading to a low thrombogenic risk. This has been demonstrated using thromboelastographic monitoring to study efficacy of rFVIIa in Factor VII deficiency during pregnancy which effectively reduces risk of bleeding without placing coagulation in prothrombotic range.⁹ There are no clear guidelines for the use of rFVIIa in obstetric cases with deficiencies of Factor VII. Due to its short half-life (approx 2.7h), appropriate dosage was a problem in the few reported cases that utilized rFVIIa. Continuous infusion of rFVIIa has been recommended instead of a single dose in a case report of a Factor VII deficient patient that underwent a caesarean delivery.¹⁰

Conclusion

Our patient was most likely a case of heterozygous Factor VII deficiency. She had a family history of bleeding disorders and a past history of heavy menorrhagia and first trimester pregnancy failures. These features were also the most consistent findings in the reported literature, hence, warrant investigations for an inherited bleeding disorder if present within a patient's history. A combination of prophylactic Factor VII concentrates as well as FFPs had to be utilized to control post-operative haemorrhage for our patient. This demonstrates the ineffectiveness of Factor VII concentrates when compared to recombinant Factor VIIa, however, the former remains the treatment of choice in developing countries where cost and availability of products need to be considered. Alternatively, evidence suggests that heterozygous cases may be managed expectantly. Continuous infusion of recombinant Factor VIIa is the treatment of choice in homozygous cases.

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