Rare case of combined factor V and factor X deficiency in pregnancy: presenting as secondary postpartum haemorrhage in first pregnancy and successful outcome in second pregnancy

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Abstract

Isolated factor V and factor X deficiency is a very rare condition affecting 1 in 500,000–1,000,000 persons worldwide. We present a rare first reported case of combined deficiency of factor V and factor X where the patient developed secondary postpartum haemorrhage in first pregnancy, after which she was diagnosed to have this rare disorder and her subsequent pregnancy was then successfully managed.

Keywords

haematology, haemorrhage, high-risk pregnancy

Case report

A 20-year-old gravida 2 para 1 at 40 weeks gestation in a second degree consanguineous marriage attended for routine antenatal registration in a tertiary care centre. Her first pregnancy, two years previously, was managed in the same hospital and she had a normal delivery at term. On that occasion, she had been discharged on day 3 but was re-admitted on the seventh postpartum day with complaints of passage of clots per vagina. She was afebrile, there were no signs of infection in the genital area, and she had moderate pallor. The haemoglobin on re-admission was 5.8 g%.

She was commenced on antibiotics (cefotaxim and metronidazole intravenously) and was transfused with one unit of red cell concentrate (RCC). She continued to have intermittent bleeding per vaginam. Careful inspection revealed an episiotomy haematoma. Her coagulation profile showed normal bleeding time and clotting time, whereas her prothrombin time (PT) was prolonged (17.3 seconds, control 12 seconds) and activated plasma thromboplastin time (aPTT) was 46 seconds (control 29 seconds). She was transfused five units of fresh frozen plasma (FFP) and two units of RCC. She underwent an exploration of the episiotomy with drainage of the haematoma.

Postoperatively she recovered well. On persistent questioning, she revealed a history of sudden and insidious swelling over the scalp after some minor trauma eight years previously which required incision and drainage. It recurred after 24 hours and subsided spontaneously. There was no history of spontaneous bleeding episodes such as epistaxis or haemarthrosis. Her periods had been regular with no menorrhagia. She is a third sibling of a non-consanguineous marriage, and there is no history of any spontaneous bleeding episodes in her parents or siblings.

The patient was referred to a haematologist who performed further investigations which revealed deficiency of factor V (12.6) and factor X (10.1).

In her second pregnancy she had no bleeding complications in the antenatal period and she presented at 40 weeks amenorrhoea with oligohydramnios. A decision was made in consultation with her haematologist to induce labour. Prior to induction, the coagulation profile revealed the expected prolongation of the PT (24.9 seconds), international normalized ratio (INR) 2.08 and aPTT (47.3 seconds). She was transfused four units of FFP on the day of induction, and dinoprostone 0.5 mg one hourly orally was given for cervical ripening. Labour progressed well and she delivered a 2.5 kg girl baby. There was no postpartum haemorrhage (PPH) and the episiotomy was sutured meticulously. She was transfused two units of FFP on days 2, 4, 6

postpartum and was discharged on day 7. The baby did not have any bleeding episode or any bleeding from the umbilical cord stump.

Her husband was counselled to undergo vasectomy as a mode of sterilization. The neonate was referred for genetic counselling but due to non-affordability, the patient refused any further evaluation.

Discussion

Isolated factor V and factor X deficiency is a very rare disorder affecting one in 500,000–1,000,000 persons worldwide.^{1,2} The incidence is higher in developing countries where the rate of consanguineous marriages is high. Combined deficiency of factor V and factor X is very rare and not yet reported. Cases have been reported in the literature in relation to combined deficiency of factor V with factor VIII and combined deficiency of vitamin K dependent factors are also reported.³

Factor V deficiency

Only 150 cases of congenital factor V deficiency (Owren disease or parahaemophilia) have been reported worldwide since 1943.² Its incidence is found to be one in 100,000.² The severity of factor V deficiency varies from easy bruising to fatal haemorrhage. There appears no racial or gender preference. The inheritance of factor V deficiency is autosomal recessive and consanguinity has been observed in families suffering from this disorder. Patients with severe deficiency are either homozygous or compound heterozygous and present within the first six months of life. Heterozygous deficiency is usually asymptomatic and unrecognized. There is mild prolongation in PT and aPTT values. No concentrates of factor V are available commercially; hence FFP infusions are used to correct the deficiency temporarily and should be given daily during a

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bleeding episode. A factor V level between 10% and 20% of normal is sufficient to prevent bleeding, even after surgery. With proper treatment, these patients have a good prognosis.^{2,3}

Factor X deficiency

Clotting factor X or Stuart-Prower factor is a vitamin K dependent serine protease that serves as the first enzyme in the final common pathway of coagulation. Factor X deficiency can be inherited or acquired, and is one of the rarest factor deficiencies worldwide.¹ Homozygous factor X deficiency has an incidence of one in 500,000 whereas the heterozygous form is more common: one in 500–2000.¹ Inherited factor X is an autosomal recessive condition with the heterozygote remaining asymptomatic. Pedigree analysis of these patients often reveals consanguinity. Factor X deficiency may arise from decreased synthesis of the protein which is called Type I deficiency, or because of the production of a dysfunctional molecule which is called Type II deficiency.⁴ Complete absence of factor X is incompatible with life. Only 50 cases of factor X have been reported worldwide.⁴ These patients can present at any age although the more severe cases present in infancy. Both the PT and aPTT are prolonged while the bleeding time is normal. Assay of factor X reveals reduced values.^{5,6}

Combined factor deficiency

Combined deficiency disorders like factor V and VIII, deficiency of vitamin K dependent factors, factor XI and XIII, factor V and VII are very rare and account for 3–5% of all inherited coagulation disorders.³ Due to their rarity, the information about pregnancy complications and management is derived from case reports. There is a reported incidence of one in 1,000,000 for combined factor V and VIII deficiency.²

Management

The mode of delivery should be governed by the obstetric condition of the patient. There is no contraindication for vaginal delivery in cases of coagulation factor deficiency. The delivery needs to be managed in a tertiary care centre, with ready availability of blood components.

Since commercial preparations of factor V and Factor X are not available, FFP forms the main line of treatment. Any active bleeding episode is managed by infusion of FFP in a loading dose of 10–20 mL/kg followed by maintenance dose of 3–6 mL/kg every 16–24 hours to be given for 3–10 days.^{7,8} The half-life of FFP is 24–36 hours and it should be carefully administered avoiding any fluid overload.

Alternatively, prothombin complex concentrates can be administered in factor X deficiency. They contain factors II, VII, IX, X and Protein C. The dosage of PPC is 50–125 U/kg. Not more than 2–3 doses should be administered in the first 36–48 hours because of an increased risk of thrombosis.^{7,8}

Additional medications like tranexamic acid and amino caproic acid may be used for additional benefit as they are fibrinolysis inhibitors.

Out of pregnancy, the combined oral contraceptive pill may be a useful contraceptive as well as reducing the associated meno-metrorrhagia, improving anaemia and decreasing transfusion needs.⁹ Tubal ligation may be carried out with FFP cover. Vasectomy should be the preferred mode of sterilization when the partner is not affected.⁹

Conclusion

From our experience with this rare case of combined factor V and X deficiency, we would recommend the following approaches in pregnancy:

- Expert assessment and consultation prior to delivery involving an obstetrician, haematologist and paediatrician to delineate the

nature of the deficiency and plan the management of pregnancy. Separate factor assays are preferred;

- Predelivery coagulation screen including PT, aPTT and INR;
- Prior to delivery (either vaginal or operative⁸), administer a loading dose of FFP 10–20 mL/kg and continue a maintenance dose of 3–6 mL/kg every 16–24 hours^{7,8} for 3–10 days. The dose needs to be individualized according to the person and situation. The aim is to keep the factor levels above 10–20%;^{7,8}
- The woman must be observed closely for PPH and wound bleeding;
- Although these are very rare conditions, with appropriate management, the prognosis in less severe cases is excellent. Genetic counselling should be offered to all patients and their families.

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Ethical approval

The patient has given written consent to publish this case report.

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