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Case Report on Management of Combined Factor V and Factor VIII Deficiency during Pregnancy

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Abstract

Combined factor V and factor VIII deficiency (CF5F8D) is a rare autosomal recessive disorder associated with mild to moderate risk of bleeding tendency. These patients have an increased risk of bleeding after surgical procedures. Pregnant women are at increased risk of having a miscarriage, placental abruption, or post partum hemorrhage. Management of these patients requires the replacement of deficient factors. We are reporting a case of management of a 31-year old second gravida female with combined factor V and factor VIII deficiency, who was transfused with fresh frozen plasma before and during labor to prevent bleeding episodes.

Index terms— autosomal recessive, bleeding disorder, post partum hemorrhage, fresh frozen plasma.

1 Introduction

ombined factor V and factor VIII deficiency (CF5F8D) is a rare autosomal recessive disorder requiring both parents to carry the defective gene to transfer the disease. Its prevalence is 1 per 1000000 in the general population. Prevalence is higher in areas where consanguineous marriages are common 1,2 . It is associated with mild to moderate risk of bleeding tendency. Mild bleeding symptoms include easy bruising, epistaxis, gum bleeding, etc. These persons are at high risk of bleeding after surgery, dental extraction, and trauma. Women with combined factor V and factor VIII deficiency are at increased risk of having menorrhagia and post partum hemorrhage. 1 Pregnancy is itself is a risk factor for deranged coagulation, and post partum hemorrhage is an important cause of maternal mortality and morbidity. Hence in obstetrical practice multidisciplinary approach to a patient with bleeding disorders and coagulation factor deficiency is of significant importance. There have been several literatures that document the risk of miscarriage and placental abruption resulting in fetal loss or premature delivery in women with bleeding disorders. There is fewer data available on the optimal management of women with CF5F8D with term pregnancy. The aim of this paper is to report a case of successful pregnancy outcomes in a woman with a combined deficiency of Factor V and Factor VIII.

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2 Case Report

We here report a case of successful pregnancy outcomes in a young woman with combined factor V and factor VIII deficiency. A 31-year old female was admitted to labor room of the obstetrics and gynecological department of Sardar Patel medical college at 38 weeks of gestation for delivery. She had previous one normal vaginal delivery three years back. At the time of admission the patient was hemodynamically stable. At two months of amenorrhea, she consulted a gynecologist. Her routine investigation was done including complete blood count, liver function test, renal function test, blood grouping, and ultrasonography. All blood investigations were normal. She had history of combined factor V and factor VIII deficiency, in view of which her prothrombin time, INR, and APTT was assessed. She had prolonged PT (14.90 sec) and APTT(88.20 sec) patient control ratio being(1.41) and raised INR(1.49). She was also tested for functional factor V and functional factor VIII levels and found to be deficient in both, the levels being less than 3% and 6%, respectively. She was counseled about the maternal and fetal risks and probable pregnancy outcomes. Patient was regular regarding her antenatal visits timely. Opinion from a hematologist was also taken. Regular monitoring of PT and APTT was performed throughout pregnancy. At 38 weeks, she was admitted for delivery after consulting a hematologist. Patient's

routine investigations, including coagulation profile PT, APTT & INR, were performed. Her Hb was-10.8gm% platelet was-155000/mm 3 . The bleeding time was 2.40sec, and the clotting time was 5.10 sec. Her PT(20.50 sec) and APTT(64.00sec) were prolonged, and her INR was 1.47. In view of deranged coagulation parameters, patient was transfused with 150ml/kg of fresh frozen plasma before induction of labor and during labor. After 18 hours of induction, she gave birth to a healthy baby girl of 2.8 kg. Her third stage of labor was actively managed. Her puerperium period was uneventful.

3 III.

4 Discussion

Combined Factor 5 and Factor 8 deficiency was first described by Oeri et al. in 1954. 3 It is a rare autosomal recessive disorder, characterized by concomitantly low levels (usually between 5% and 20%) of the two coagulation factors, Factor V and Factor VIII. 4 Mutations in two genes, lectin mannose-binding protein 1 (LMAN1), and multiple coagulation factor deficiency 2 (MCFD2) are identified as the cause of CF5F8D. These genes encode for proteins involved in the intracellular transport of Factor V and Factor VIII. 5 Its prevalence is 1 per 1000000 in the general population, which is higher in consanguineous marriages. It is associated with a mild to moderate bleeding tendency. CF5F8D patients are characterized by normal platelet count and bleeding time and prolonging both prothrombin time (PT) and partial thromboplastin time tests (PTT). 6 Specific assays of FV and FVIII coagulant activity are necessary to evaluate the residual FV and FVIII coagulant activity.

During pregnancy, the physiological changes in the hemostatic system tend to improve the inherited bleeding disorders. Pregnancy is accompanied by increased concentrations of fibrinogen, FVII, FVIII, FX and, von Willebrand factor, while FII, FV and, FIX are relatively unchanged. 7,8 The active, unbound form of free protein S is decreased during pregnancy and, plasminogen activator inhibitor type 1 (PAI-1) levels are increased. 7 All of these changes lead to the hypercoagulable state of pregnancy, and improve hemostasis in women with rare bleeding disorders. Despite these changes, women with factor deficiencies do not achieve the same factor levels as those women without factor deficiencies. 9,10 And these women remain at high risk of bleeding complications. In view of general recommendations for the management of bleeding disorders in pregnancy, affected women should be managed by an obstetric unit along with a hemophilia center. CF5F8D patients usually do not require regular prophylaxis. Any surgical intervention requires the replacement of factors. The plasma half-life of factors is FV: 36 h; FVIII: 10-14 h. FV concentrates are not available and are not present in cryoprecipitate or prothrombin complex concentrates; replacement of FV can be achieved only through the use of fresh frozen plasma (FFP), preferably with virus-inactivated plasma. For FVIII replacement, many products are available, including FFP, plasma-derived concentrates, or recombinant FVIII (rFVIII). Surgical procedures like vaginal delivery or cesarean delivery should be addressed by administering factor V and factor VIII 30 min before surgery and then every 12 h to maintain FVIII levels above 50 IU dL and FV levels above 25 IU dL until wound healing is established. 11 To women with inherited bleeding disorders, pregnancy and childbirth present a major challenge. All women should be managed by a multidisciplinary team in a center where the expertise, laboratory support, and factor treatment required to provide care to these patients are available at all times. Additional reports are needed for establishing optimal guidelines for hemorrhagic, invasive, and surgical procedures in individuals with combined factors V and VIII deficiency.

5 IV.

6 Conclusion

A combined FV and FVIII deficiency is one of the rarest coagulation factor deficiencies. During pregnancy, this combined deficiency could have adverse consequences by causing uncontrollable bleeding with a risk of maternal death. The management must thus be multidisciplinary and should begin with an early assessment of hemorrhagic risk leading to a written FV and FVIII substitution protocol tailored to each parturient.

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