Successful pregnancy in a patient with factor V deficiency: Case report and review of the literature

Sanne Vellinga1, Eva Steel1, Inge Vangenechten2, Alain Gadisseur1,2
1Antwerp University Hospital, Hematology; 2Hemostasis Unit Edegem, Belgium

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The clotting factor known as factor V (FV) was first described in 1908 (1), and a deficiency of this factor was first described by Owren as parahaemophilia in 1947 (2). FV is predominantly produced in the liver and to a lesser degree by the megakaryocytes. Circa 80% of FV circulates in the plasma while 20% is stored in platelets. Following α-granule release upon platelet activation, platelet FV can presumably bind immediately to surface receptors optimising prothrombinase complex activity (3). The relationship between plasma FV and platelet FV and their relative significance is to date not fully understood, but FV expression in either platelets or plasma was proven to be sufficient for basal haemostasis in mice (4).

FV deficiency is a rare disease with an incidence of 1.10^{-6} (5, 6, 20–24). It is an autosomal recessively inherited disorder in which the lack of factor V activity impairs clotting. Heterozygous patients show a variable expression with a mild bleeding tendency in 10% of the cases (7), whereas homozygous patients usually present with moderate clinical manifestations of epistaxis, menorrhagia and haemorrhages after trauma (8). There seems to be a poor correlation between plasma factor V levels and clinical phenotype (8), and different opinions exist as to the necessary level of circulating FV for adequate haemostasis. Target FV activity levels during treatment are mainly based on clinical experience (9). Relatively few reports on the subject of factor V deficiency and pregnancy can be found in the medical literature, and these are mainly sporadic case reports (10–18) and three reviews (3, 20, 21).

Case report
A 19-year-old Moroccan woman, born of consanguineous parents, presented with complaints of fatigue, excessive bleeding after dental procedures, frequent nose bleeds, severe menorrhagia and large haematomas of the skin after minor trauma. Laboratory tests showed a microcytic anaemia through iron deficiency with haemoglobin of 8.1 g/dl (nl 12–15 g/dl), an MCV of 61.2 fl (nl 76–96 fl) and ferritin of 5 ng/ml (nl 13.0–150.0 ng/ml). The APTT was clearly prolonged at 110.4 sec (nl 25–39 sec) with a PT of 12% (nl 70–100%). Factor V antigen level was 3% with factor V activity at 1%. All other clotting factors were present in normal amounts. No inhibitor against FV could be found.

Molecular analysis showed the presence of a homozygous factor V (Casablanca) nonsense mutation Q773Ter in exon 13.

The patient was put on oral contraceptives to decrease menstrual blood loss, tranexaminic acid and iron supplements. Both the patient and her husband expressed a strong wish to have children on cultural and religious grounds, and even after full explanation of the possible complications, the couple decided to accept the potential risks this entailed. They were advised to avoid a pregnancy until a haemoglobin level of 12 g/dl was reached, and this came about after 18 months of treatment during which there were only a few minor bleeding episodes. After reaching the target haemoglobin and stopping of the oral contraceptives the patient became pregnant after only three months. The pregnancy itself was uneventful and at 39 weeks an elective Caesarean section was performed because of a breech position. Before surgery the patient was treated prophylactically with fresh frozen plasma (FFP) in a dose of 20 ml/kg, and after surgery a dose of 5 ml/kg every 12 hours was administered for seven days. The desired target level of FV activity was 20–30%. Blood loss was in the normal range, and the woman delivered a healthy baby girl. Postoperative complications consisted of anaemia with haemoglobin of 8.0 mg/dl and pulmonary oedema induced by the large volumes of FFP. The pulmonary oedema together with a concomitant bilateral respiratory infection caused serious respiratory insufficiency. Since the delivery the couple has expressed the wish for more children.

Discussion and review of the literature
Factor V deficiency is a serious problem in obstetrics, because both the pregnancy and the delivery carry a high bleeding risk. There is little literature available on this subject and there are no guidelines available concerning pregnancy (20). Girolami et al. published on a group of 21 successful pregnancies in homozygous women and 15 successful pregnancies in heterozygous women (19). Recently, another case of an uncomplicated pregnancy in a woman with severe FV deficiency without prophylactic therapy was reported (18). Our patient is another example of a successful pregnancy in a homozygous FV deficient patient.

Reported target levels of FV activity vary from a minimal circulating level of 15 U/dl (6) [normal range 71–125 U/dl (8)] to a factor V activity level of > 20% (18, 22). These levels are based both on clinical experience and on the fact that asymptomatic heterozygous individuals show a FV level of 40–60%. In our pa-
tient we tried to maintain a level of 20–30% for seven days and had a favourable outcome without major bleeding.

Pregnancy does not seem to be absolutely contraindicated in homozygous FV deficient patients, provided that adequate substitution therapy with plasma is given prior and post delivery to ensure adequate haemostasis. Since no purified FV concentrate exists, FFP represents the optimal therapy, although the large volumes which need to be infused can cause problems of volume-overload. Of course plasma also carries the theoretical risk of transfusion-transmitted viral infection. Even though it will only be for a limited number of patients, the development of a purified FV concentrate would be an important improvement in the prophylactic treatment and the treatment of bleeding in FV deficiency.

References