

# A Rare Case of Inherited Factor-II Deficiency Causing Life-Threatening Menorrhagia

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## Abstract

Menorrhagia is a common gynecological symptom. In adolescents, the cause is generally dysfunctional uterine bleeding. Menorrhagia may also be due to undiagnosed coagulation defects, endocrine disorders, gynecological abnormalities of the uterus, or other systemic disorders. Menorrhagia may be the only clinical manifestation of an inherited bleeding disorder. We report a case of inherited hypoprothrombinemia (factor II deficiency), a rare bleeding disorder as the cause of life-threatening menorrhagia. In the absence of a readily identifiable cause, all adolescents with menorrhagia should be examined for bleeding disorders.

**Keywords:** Deficiency of clotting, Factor II deficiency, Menorrhagia

## Introduction

Menorrhagia is a common and major health problem for women. The early recognition of an underlying cause would potentially have a major impact in the diagnosis and treatment of menorrhagia. Recent studies report that the incidence of bleeding disorders as a cause of menorrhagia may be as high as 17-20%<sup>[1]</sup> Inherited factor 2 deficiency (hypoprothrombinemia) is an extremely rare bleeding disorder, with not more than 50 cases of this disorder reported worldwide so far.<sup>[2]</sup> Menorrhagia may be the first and the only clinical manifestation of an inherited bleeding disorder. The first patient described with von Willebrand's disease died of menorrhagia at the age of 13 years of age.<sup>[3]</sup> Despite this, coagulopathies are not usually suspected as etiology of menorrhagia and surgical interventions are done, without getting the patient investigated for coagulopathies or any other systemic disorder known to cause abnormal uterine bleeding like hypothyroidism.<sup>[4]</sup> Careful history taking and clinical suspicion for an underlying bleeding disorder in menorrhagic women will not only help in their early diagnosis but also for better management of antepartum/postpartum hemorrhage in such women. In the absence of a readily identifiable cause, all adolescents with menorrhagia should be examined for bleeding disorders.<sup>[5]</sup>

## Case Report

A 22-year-old woman presented to our emergency department with severe menstrual bleeding since 12 days, with signs of congestive cardiac failure. Her history revealed that she had menorrhagia since menarche and had severe postpartum hemorrhage (PPH) in both her pregnancies requiring blood transfusions. In the last pregnancy, she required an emergency subtotal hysterectomy. The patient continued to have regular menstrual cycles with heavy bleeding even after subtotal hysterectomy. She would bleed for 6 to 7 days every 28-30 days. However, she did not have abnormal bleeding manifestations from any other sites in the body or any family history of bleeding disorder.

On examination, she was conscious, oriented, and very pale. On per speculum examination cervix appeared normal. Uterus was not felt on bimanual examination. Laboratory investigations revealed: Hemoglobin = 3 g/dl%, normal bleeding time, prolonged prothrombin time: test-44.5 s, control-17.2 s, prolonged activated Partial Thromboplastin Time: test-41.4 s, control-28.4 s and normal thyroid function tests and liver function tests. Ultrasound examination revealed the presence of bilateral normal ovaries and a small uterine stump measuring 3 × 3 cm. Other organs were normal. As patient had signs of congestive cardiac failure due to severe anemia, three units of packed cell volume under the cover of diuretics was given and the patient had signs of improvement.

Her history of menorrhagia since menarche and PPH in both her pregnancies and prolonged prothrombin time and activated

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Partial Thromboplastin Time was suggestive of an underlying bleeding disorder as the cause of menorrhagia.

A complete coagulation workup identified her to have deficient prothrombin activity of 26%, with all other coagulation factors and platelet functions to be normal. Coagulation workup was as follows: Platelets: 5,99,000/mm<sup>3</sup>, BT: 3 min, platelet aggregometry: normal response to Ristocetin, ADP, epinephrine, arachidonic acid and collagen. PT: Pt: 18.5 s, normal range: 9.7-13.3 s, APTT: pt: 44.5 s, normal range: 23.8-37.4 s, F II: 26%, F V: 153.6%, F IX: 187%, FX: 73.2%, F VIII: C: 171.6%, Ricof: 122%, Fibrinogen: 364.6 mg%, Lupus Anticoagulant: negative, Clot retraction: Good, Factor XIII activity: Normal.

Hence, bleeding disorder was the cause of life-threatening menorrhagia.

After the diagnosis of factor II deficiency, the patient was put on continuous low dose oral contraceptive pill containing levonorgestrel 100 ug and ethinylloestradiol 20 ug to suspend her menstrual cycle. The patient has been coming for regular follow-up and had no further episodes of bleeding per vagina or from any other sites in the body.

## Discussion

Menorrhagia has been found to be a reliable predictor for bleeding disorders and often a patient's coagulopathy is first diagnosed when they are evaluated for excessive menstrual bleeding.<sup>[6]</sup> Our patient had menorrhagia since menarche and severe PPH. Coagulation workup identified her to have deficient factor II activity.

Factor II deficiency is an extremely rare autosomal recessive disorder affecting 1:2000000 of the general population. Two phenotypes are described: hypoprothrombinemia (type I deficiency) and dysprothrombinemia (type II deficiency). In type I deficiency, prothrombin levels and prothrombin activity are reduced. In type II deficiency, prothrombin activity is reduced, but prothrombin levels are borderline or in the reference range. Both disorders are autosomal recessive. The bleeding tendency is inversely proportional to the level of factor II activity. The lowest level noted is 2% and there are no patients with undetectable prothrombin levels. The diagnosis is suspected when activated partial thromboplastin time and prothrombin time is prolonged and factor II assay is reduced while other vitamin K-dependent factors are normal. Patients with prothrombin activity of <5% have severe symptoms, 5-25% have moderate symptoms and patients with 26-50% have mild symptoms.<sup>[7]</sup> In our patient, factor II activity was 26%. While performing subtotal hysterectomy, some parts of the body of her uterus might have been left behind and hence the patient continued to have menstrual cycles. Patients after subtotal hysterectomy generally do not have menstrual cycles.

Continuous low-dose OCP helps in suspending her menstrual cycles and has very little role in improving prothrombin activity/thrombus formation.<sup>[8]</sup>

Jayandharan, *et al.*, in their study described a similar patient with factor II deficiency with history of puberty menorrhagia, requiring multiple blood transfusions and PPH requiring an emergency hysterectomy with blood transfusion.<sup>[9]</sup>

Bleeding disorders as the cause of menorrhagia was seen in 19.16% of cases in a study done by Tarsi *et al.*<sup>[10]</sup>

## Conclusion

Menorrhagia may be the only manifestation of a bleeding disorder. In the absence of a readily identifiable cause, all adolescents with menorrhagia should be examined for bleeding disorders.

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