



Recurrent bleeding after posthemorrhoidectomy caused by factor V deficiency: a case report and review of the literature

Jun Seong Chung, Han Deok Kwak, Jae Kyun Ju

Department of Surgery, Chonnam National University Medical School, Gwangju, Korea

Congenital factor V (FV) deficiency is a rare hemorrhagic disorder that can cause excessive bleeding during and after surgery in the affected patient. This report is the case of a patient who had FV deficiency with recurrent posthemorrhoidectomy bleeding treated with the hemostatic procedure and fresh frozen plasma (FFP) transfusions. A 45-year-old male patient had previously undergone hemorrhoidectomy for multiple hemorrhoids at a local hospital. Hemorrhoidectomy was successful; however, he was transferred to our hospital for evaluation of the origin of the recurrent posthemorrhoidectomy bleeding and underwent a hemostatic procedure. This bleeding was treated with coagulation using electrocautery, multiple sutures, and FFP transfusion (1,600 mL/day) for 7 consecutive days. The patient's plasma FV activity was 23%. Early detection of clotting factor deficiency in patients with hemorrhagic events after surgical treatments may prevent unnecessary procedures such as reoperations and minimize the cost of replacement therapy such as large-volume FFP transfusion.

Keywords: Factor V deficiency; Blood transfusion; Gastrointestinal hemorrhage; Hemorrhoidectomy; Postoperative hemorrhage

INTRODUCTION

Activated human coagulation factor V (FV) is an essential non-enzymatic cofactor of the prothrombinase complex, which accelerates the activation of prothrombin to thrombin [1]. Congenital FV deficiency is a rare autosomal recessive coagulation disorder caused by a homozygotic or heterozygotic mutation of the FV gene. The prevalence of FV deficiency in the general population is approximately 1 in 1,000,000 individuals. Symptomatic FV-deficient patients have less FV activity than asymptomatic FV-deficient patients [2, 3]. FV deficiency is a rare bleeding disorder with variable bleeding manifestations that do not necessarily correlate

with the FV activity level [4]. However, posttraumatic, surgical, and delivery bleeding are common in severe FV deficiency cases. The treatment of bleeding episodes is generally based on factor replacement through fresh frozen plasma (FFP) transfusions with adjunctive pharmacological therapy [5]. Here, we have described a case of a patient with FV deficiency and recurrent posthemorrhoidectomy bleeding who was treated with a hemostatic procedure and FFP transfusions.

CASE REPORT

This study protocol was reviewed and approved by the Institutional Review Board (IRB) of Chonnam National University Hospital (CNUH-2020-075). Written informed consent was waived by IRB.

A 45-year-old male patient was admitted to a hospital for the surgical treatment of multiple hemorrhoids. This patient was a nonsmoker. He does not have any medical, personal, and family history such as a genetic disorder. Hemorrhoidectomy was performed under regional anesthesia. The surgeon identified the hemorrhoids located at the 3 o'clock and 9 o'clock positions, pulled them through the anus, and removed the hemorrhoid tissues us-

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Correspondence to: Jae Kyun Ju, M.D.
Department of Surgery, Chonnam National University Medical School,
160 Baekseo-ro, Dong-gu, Gwangju 61469, Korea
Tel: +82-62-220-6456, Fax: +82-62-227-1635
E-mail: jkju@jnu.ac.kr
ORCID: <https://orcid.org/0000-0003-1605-3310>

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ing a scalpel and electrocautery. The hemorrhoidectomy sites were sutured. However, severe hematochezia occurred at the hemorrhoidectomy sites. The preoperative coagulation profile test showed a mild prolonged prothrombin time (PT) of 16.1 seconds (normal range, 9.8–13.0 seconds) and prolonged activated partial

thromboplastin time (aPTT) of 49.7 seconds (normal range, 26.5–41.0 seconds) at local hospital. On postoperative day 4 after the first operation, the coagulation profile test showed further increase in PT (16.3 seconds), aPTT (50.4 seconds), and bleeding time (5 minutes; normal range, ≤ 3 minutes). He underwent suture hemostasis 3 times for bleeding control over 5 days. Subsequently, he was transferred to our hospital for evaluation of the origin of the recurrent posthemorrhoidectomy bleeding and underwent a hemostatic procedure. Vitamin K and tranexamic acid were administered intravenously at admission. Two days after admission, he presented with massive hematochezia at the previous hemorrhoidectomy sites, which was treated with coagulation using electrocautery, multiple sutures, and FFP transfusion (1,600 mL/day) for 7 consecutive days. Four days after admission, the hematochezia persisted and he experienced cold sweat and dizziness. His hemoglobin level decreased from 10.7 to 7.6 g/dL. He was intensively transfused with packed red blood cells (1,440 mL/day). After 2 weeks of the hemorrhagic event, he did not experience any major bleeding. His laboratory findings and hospital course are summarized in Table 1 and Fig. 1. This analysis revealed FV deficiency (plasma FV activity, 23%).

Test for genes associated with FV deficiency was not performed because this patient was lost to follow up. The patient had a mother and 3 sisters who reported no bleeding tendency. However, he had a history of intraoperative bleeding during strabismus surgery in his childhood. The patient was relatively young, and he had no medical history of liver disease, autoimmune disease, vital threatened surgery, certain medications, or malignant cancer.

Table 1. Laboratory findings including coagulation parameters in this patient

| Parameter | Result | Reference range |
|----------------------------------|----------|-----------------|
| PT (sec) | 14.9 | 9.8–13.0 |
| aPTT (sec) | 49.0 | 26.5–41.0 |
| PT mixing test | 11.6 | |
| Incubated PT mixing test | 13.1 | |
| aPTT mixing test | 36.9 | |
| Incubated aPTT mixing test | 41.5 | |
| Factor II activity (%) | 75.0 | 65–125 |
| Factor V activity (%) | 23.0 | 60–140 |
| Factor VIII activity (%) | 54.1 | 50–150 |
| Factor X activity (%) | 63.0 | 70–120 |
| Factor V Leiden mutation | Negative | |
| Fibrinogen assay (mg/dL) | 182 | 180–350 |
| Platelets ($10^3/\text{mm}^3$) | 462 | 130–450 |
| Protein C activity (%) | 72.4 | 72–160 |
| Protein S activity (%) | 72.8 | 60–150 |
| Antithrombin III test (mg/dL) | 20.5 | 19–31 |

PT, prothrombin time; aPTT, activated partial thromboplastin time.

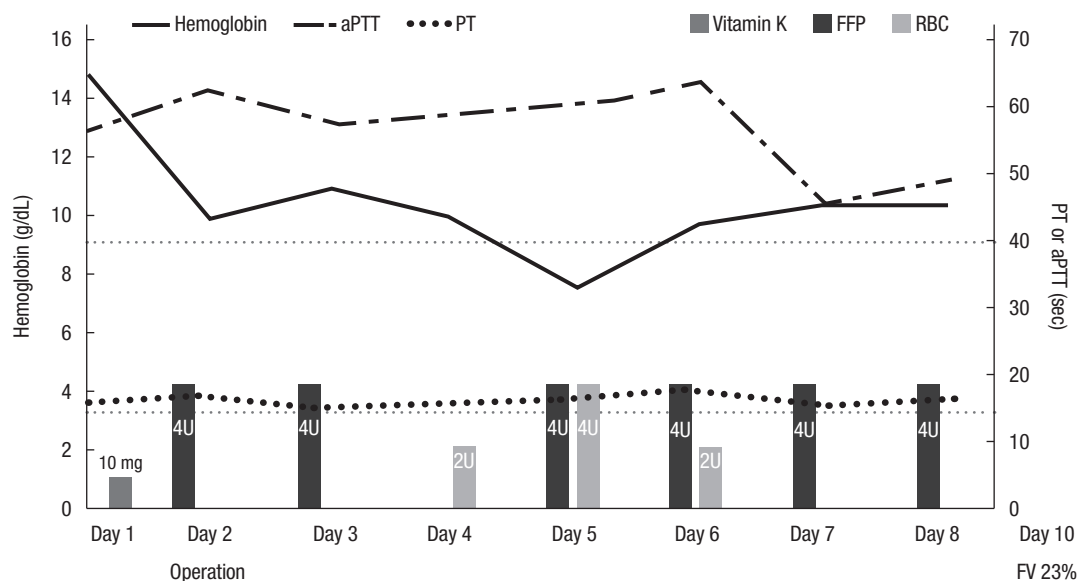


Fig. 1. Hospital course of the patient according to the transfusion. PT, prothrombin time; aPTT, activated partial thromboplastin time; FV, factor V; FFP, fresh frozen plasma; RBC, red blood cell.

Table 2. Literature review of factor V deficiency in Korean patients

| No. | Sex | Age (yr) | PT (sec) | aPTT (sec) | FV (%) | Severity | Major bleedingsymptoms | Type | Treatment | Survival | Reference |
|-----|-----|----------|----------|------------|--------|----------|---|------|---------------------------------|----------|---------------|
| 1 | M | 9 | 36.0 | 110 | 6 | Moderate | Hemarthroses | I | FFP | Alive | [7] |
| 2 | M | 1 mo | 24.9 | >120 | 4 | Moderate | Purpuric Pigmentation on skin | I | FFP | Alive | [8] |
| 3 | M | 53 | 18.0 | 49.0 | <1 | Severe | CNS bleeding | I | FFP | Alive | [9] |
| 4 | F | 28 | 31.3 | 67.8 | 3 | Moderate | Hemoperitoneum | I | FFP | Alive | [10] |
| 5 | M | 73 | 54.1 | 180 | 2 | Moderate | Postoperative bleeding | A | FFP, steroids+IVIG | Dead | [11] |
| 6 | F | 63 | 73.1 | 190 | 2 | Moderate | Retroperitoneal bleeding (postoperative bleeding) | A | FFP, steroids+ cyclophosphamide | Alive | [12] |
| 7 | F | 17 | 17.4 | 50.9 | 16 | Mild | Postoperative bleeding, persistent menorrhagia | I | FFP | Alive | [13] |
| 8 | M | 24 | 35.7 | 111.7 | 4 | Moderate | No symptoms | I | FFP | Alive | [13] |
| 9 | M | 3 mo | 45.0 | 72.5 | 1 | Moderate | Recurrent epistaxis | I | Local measures | Unknown | [13] |
| 10 | F | 49 | 16.7 | 63.4 | 11 | Mild | Postoperative bleeding | I | FFP | Alive | [13] |
| 11 | M | 45 | 14.9 | 49.0 | 23 | Mild | Postoperative bleeding | I | FFP | Alive | Current study |

PT, prothrombin time; aPTT, activated partial thromboplastin time; FV, factor V; M, male; F, female; I, inherited; FFP, fresh frozen plasma; CNS, central nervous system; A, acquired; IVIG, intravenous immunoglobulins.

DISCUSSION

FV deficiency is a rare bleeding disorder that can be dangerous of variable bleeding tendency irrespective of the FV activity level. The normal range of plasma FV activity is 76% to 126% [6]; however, our patient had an FV activity of 23%. A literature review revealed that only 10 cases of FV deficiency have been reported thus far in Republic of Korea (Table 2) [7-13]. The age of 10 patients ranged from 1 month to 73 years. Male was slightly predominant (male:female = 6:4). The median of PT and aPTT were 31.3 and 110 seconds, respectively. Most of the patients presented with bleeding symptoms (90%) and moderate FV deficiency (70%). FV activity levels ranged from <1% to 16% and all patients were treated mainly with FFP transfusions. A plasma FV activity of 20% to 25% is required for effective replacement, with a threshold of 15% [4, 14]. It is important to control acute hemorrhagic events by attempting to transfuse FFP for the treatment of FV deficiency. Even in case of gastrointestinal bleeding, after initial stabilization, source control is more likely to resolve the bleeding than exclusive hemorrhagic management. Likewise, suture hemostasis and FFP transfusion were also performed in this case to diminish the frequency and severity of the hemorrhagic episode. Although our patient did not have severe FV-deficiency state, he experienced recurrent and intractable posthemorrhoidectomy bleeding. Our study suggests that the bleeding phenotype can be severe in a FV-deficient patient, even in the presence of low plasma FV levels.

Because the prevalence of FV deficiency is very rare, it is difficult to perform coagulation factor assays in all patients before surgery. However, we would like to suggest situations where addi-

tional coagulation factor assays should be performed.

In general, all surgical patients undergo blood tests including PT and aPTT as routine preoperative test. When prolongation of PT or aPTT is observed and there is no specific finding in medical history, such as liver disease, anticoagulation therapy, genetic hemostatic disorder, other medications, performing the coagulation factor assay will be necessary to prevent serious bleeding or abnormal bleeding after surgery and to promptly treat it properly.

Accurate history taking of the patient's medication, surgery, and family history must precede the implementation. In addition, if abnormal findings are observed in the coagulation factor assay, if possible, a genetic test can be performed to distinguish whether it is an acquired or inherited disease, for appropriate treatment.

FV deficiency in Republic of Korea might be ignored because of a lack of understanding; however, there could be more cases of minor unexplained bleeding episodes. Therefore, early detection of clotting factor deficiency in the patient who presented with hemorrhagic events after surgical treatments may prevent unnecessary procedures such as reoperations and minimize the cost of replacement therapy such as large-volume FFP transfusions.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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ORCID

Jun Seong Chung, <https://orcid.org/0000-0002-9164-8317>

Han Deok Kwak, <https://orcid.org/0000-0002-0716-6914>

Jae Kyun Ju, <https://orcid.org/0000-0003-1605-3310>

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