

Factor V Deficiency and Mechanical Valve Replacement: Challenges in Perioperative Hemostasis and Anticoagulation

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ABSTRACT

Factor V deficiency is a rare autosomal recessive bleeding disorder marked by impaired thrombin generation and variable bleeding risk. Perioperative management becomes particularly challenging in high-risk surgeries, such as aortic valve replacement, due to the absence of targeted replacement therapies and the limited efficacy of fresh frozen plasma (FFP) in restoring factor V levels. We report the case of a 30-year-old woman with congenital factor V deficiency (baseline activity 18%) who underwent successful mechanical aortic valve replacement and mitral valve repair for infective endocarditis. She received preoperative FFP aiming for a factor V level >20%. Her perioperative management included careful monitoring with a total of 23 units of FFP administered. Despite persistently low postoperative F levels (<20%), she experienced minimal bleeding complications, limited to transient anemia and one episode of gross hematuria requiring platelet transfusion. Outpatient follow-up revealed heterozygosity for both factor V Leiden and a prekallikrein variant, potentially explaining her relatively mild bleeding phenotype. This case highlights the disconnect that may exist between laboratory values and clinical bleeding risk, emphasizing the need for individualized perioperative planning and cautious anticoagulation management.

KEYWORDS: Factor V deficiency; Factor V levels; Bleeding risk; fresh frozen plasma; aortic valve replacement; perioperative management

INTRODUCTION

Factor V is mainly produced by hepatocytes and stored in platelet alpha granules, where it plays an essential role in facilitating localized thrombin production during hemostasis. It plays a key role in hemostasis and coagulation by combining with activated factor X to form the prothrombinase complex, which converts prothrombin into thrombin.¹ Factor V deficiency is an exceptionally rare autosomal recessive bleeding disorder, affecting roughly one in a million individuals (homozygous form).² It results in prolonged prothrombin time (PT) and activated partial thromboplastin time (aPTT) on laboratory testing.³ Patients with activity levels

above 10% are often asymptomatic, levels between 1% and 10% may be associated with mild to moderate bleeding, and levels below 1% are classified as severe (or parahemophilia) with risk of spontaneous hemorrhage.¹ Interestingly, several reports have documented cases in which patients with even severe factor V deficiency did not exhibit significant bleeding.^{4,5} Laboratory values do not always reflect a patient's actual bleeding risk. In surgical contexts, especially those involving high-risk procedures like mechanical valve replacement, management becomes particularly challenging. Balancing the risk of bleeding against the need for effective anticoagulation demands meticulous perioperative planning, individualized treatment strategies, and close interdisciplinary coordination.

CASE PRESENTATION

We present the case of a 30-year-old woman with a self-reported remote history of congenital factor V deficiency and recent cesarean delivery four months ago, who developed worsening heart failure secondary to *Enterococcus faecalis* infective endocarditis (IE) involving the aortic valve (AV). A few months postpartum, she was hospitalized with sepsis and was found to have *Enterococcus* bacteremia. Transesophageal echocardiography (TEE) confirmed AV involvement. She was treated with intravenous (IV) vancomycin and cefepime. Despite appropriate therapy, she re-presented with acute decompensated heart failure and pulmonary edema, prompting further evaluation and management. Of note, the patient reported that her mother told her she was diagnosed with factor V deficiency in childhood, although no prior formal hematologic records are available to confirm this. Interestingly, despite this reported diagnosis, she has no clinically significant bleeding history, including menorrhagia, epistaxis, excessive bleeding with dental procedures, or postpartum hemorrhage.

Repeat imaging revealed severe aortic regurgitation (AR) and moderate mitral regurgitation (MR). Cardiothoracic surgery recommended mechanical AV replacement and mitral valve (MV) repair. Due to her history of factor V deficiency, her bleeding risk was assessed. Her International Society on Thrombosis and Hemostasis (ISTH)-Bleeding Assessment Tool (BAT) score was 0, which suggests no evidence of an increased bleeding tendency based on history. Laboratory

results showed: PT 15.9 seconds (ref 10.2–12.9), INR 1.4 (ref 0.9–1.1), aPTT 38.6 seconds (ref 25.1–36.5), mild anemia with Hb of 10g/dl along with normal fibrinogen and platelet count, and isolated factor V activity of 18.2% (ref 50–180); other coagulation factor levels were normal. Moreover, renal and liver function tests were within normal limits too. Despite abnormal labs, her unremarkable bleeding history suggested low perioperative hemorrhage risk. Accordingly, the patient and team proceeded with mechanical AV replacement for superior durability, accepting lifelong warfarin anticoagulation.

PERIOPERATIVE MANAGEMENT

Preoperative planning included transfusing fresh frozen plasma (FFP) at 15–20 mL/kg to target factor V activity of 20% [6]. For her 90 kg weight, this corresponded to ~1350 mL of FFP. Thus, she received a total of four units of FFP (1275 mL) before surgery. Platelet transfusion was considered due to the platelet-associated factor V pool, but was reserved for active bleeding. Postoperatively, the patient was immediately started on a heparin infusion along with warfarin in the setting of a mechanical AV; the initial INR goal was set at 2.5–3.5 due to prolonged INR at baseline, which was later reduced to 2.0–3.0 prior to discharge. Daily factor V trough levels were monitored; levels remained between 12–19%, with most values consistently above 15%, prompting FFP supplementation as needed. She ultimately received

a total of 23 units of FFP perioperatively, corresponding to a cumulative volume of 7,225 mL.

Despite no intraoperative bleeding, the patient developed postoperative anemia, with hemoglobin decreasing from ~8 g/dL immediately after surgery to a nadir of 6.8 g/dL by postoperative day 4, when she received her first unit of blood. She also had one episode of frank hematuria on post-operative day 7, for which she received one unit of platelets. There was no evidence of valve-induced hemolysis in her blood work or peripheral smear. **Figure 1** and **Table 1** elucidate detailed perioperative factor V activity levels and corresponding transfusion and laboratory data.

Figure 1. Factor V Activity Timeline

The vertical axis shows plasma factor V activity (%), while the horizontal axis denotes hospital day, including surgery and postoperative days (POD 1–11).

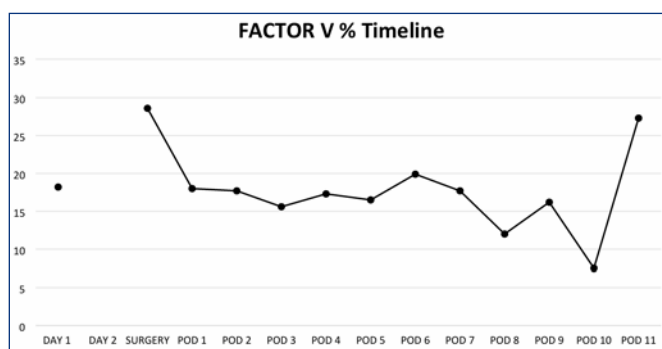


Table 1. Postoperative Hematologic Parameters, Transfusions, and Anticoagulation in a Patient With Factor V Deficiency Undergoing Mechanical Aortic Valve Replacement

	Day 1	Day 2	Surgery	Pod 1	Pod 2	Pod 3	Pod 4	Pod 5	Pod 6	Pod 7	Pod 8	Pod 9	Pod 10	Pod 11
Factor V (%)	18.2		28.6	18	17.7	15.6	17.3	16.5	19.9	17.7	12	16.2	7.5	27.3
FFP Transfused (units)		3	1	2	3	3	3	3	1		2	1	1	
PLT Transfusion (units)											1			
PRBC (units)									1	1	1			
Hb (g/dL)	10.3	10.1	8.3	7.9	8.2	7.2	6.8	6.3	6.2	6.8	6.7	7.3	7.7	8
HCT (%)	34	34	27	26	28	25	23	22	22	23	27	24	25	26
PLT ($\times 10^3/\mu\text{L}$)	416	406	267	241	278	244	237	240	277	257	256	276	302	329
INR	1.4		1.5	1.6	1.7	1.9	2.1	2.2	2.1	2.3	2.4	2.3	2.1	1.9
PT (sec)	15.9		17.5	18.1	20	21.7	24.2	24.9	24.4	26.4	27.5	26.4	24.8	21.8
aPTT (sec)	38.6		35.2	39.8	41.1	57.9	46.9	86.7	80.8	80.4	92.3	98.4	116.2	
Heparin Infusion			Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Enoxaparin (mg, subq)			40											
Warfarin (mg)			3	3	4	4	4	4	5	4	5	5	6	6
Aspirin (mg)			81	81	81	81	81	81	81	81	81	81	81	81

FFP: fresh frozen plasma; PLT: platelet; PRBC: packed red blood cell; Hb: hemoglobin; HTC: hematocrit; INR: international normalized ratio; PT: prothrombin time; PTT: partial thromboplastin time; POD: post-operative day; subq: subcutaneous

OUTPATIENT FOLLOW-UP

Following her hospitalization, the patient was seen in the hematology clinic for further evaluation of her factor V deficiency. Genetic testing confirmed two factor V mutations: one classified as likely pathogenic and the other as a variant of uncertain significance (VUS). Interestingly, she was also heterozygous for factor V Leiden and carried a heterozygous prekallikrein variant, both of which may confer a prothrombotic predisposition. No inhibitors were detected.

Moreover, coagulation studies were obtained to assess the effect of warfarin therapy in the context of underlying factor V deficiency. Vitamin K-dependent factors were variably suppressed: factor II at 48.2% (normal 60–180%), factor VII at 38.3% (65–170%), and factor X at 27.7% (75–150%), while factor IX remained relatively preserved at 73.1% (65–150%). Her INR was elevated at 2.0, consistent with therapeutic anticoagulation. Factor V activity remained low at 21.4%, similar to her prior levels.

These findings highlight the importance of measuring individual factor levels when interpreting INR in patients with baseline coagulation abnormalities, particularly rare bleeding disorders, to avoid misinterpretation of anticoagulation efficacy.

DISCUSSION

Factor V deficiency is a rare bleeding disorder characterized by low levels of factor V. Unlike other coagulation factor deficiencies, there are no concentrated factor V products available. Its rarity combined with the lack of targeted replacement therapies makes management particularly challenging, especially in high-risk surgical settings such as cardiothoracic procedures. Thus, clinicians rely on supportive transfusion strategies, primarily FFP, for management of factor V deficiency.² Additionally, platelets store factor V within their alpha granules, representing a potential supplemental source. However, the role of platelet-derived factor V in major surgeries, such as the one described in this case report, is not well established. Further research is needed to determine whether this could serve as a reliable alternative when plasma alone is inadequate or contraindicated. Recombinant activated factor VII (rFVIIa) has been reported as a bypassing agent in exceptional cases where standard therapy with FFP is contraindicated or has failed, promoting thrombin generation independently of factor V by directly activating factor X; however, its routine use is limited, and evidence is largely anecdotal.^{7,8}

A unique aspect of this case is the requirement for long-term anticoagulation following mechanical valve replacement. Patients with congenital bleeding problems are typically barred from having a mechanical prosthesis due to their increased bleeding risk. With meticulous perioperative management, including FFP supplementation to achieve a factor V activity level of 20%, she successfully tolerated

both major cardiac surgery and therapeutic anticoagulation with heparin and warfarin, experiencing only a single episode of frank hematuria. Daily postoperative monitoring showed factor V activity consistently above 15%, aligning with European Network on Rare Bleeding Disorders (EN-RBD) registry data suggesting patients with activity >10% are often asymptomatic and may not experience spontaneous bleeding.⁹ Thus, our case contributes to a growing body of evidence suggesting that with careful management, warfarin therapy is not contraindicated in patients with factor V deficiency.

Our case also underscores an essential principle that laboratory values alone do not always correlate with clinical bleeding risk. The discrepancy between factor activity and clinical phenotype has been documented previously and supports a patient-specific approach to perioperative planning and anticoagulation.¹⁰ It is unclear whether her relatively mild phenotype was due to her factor V level being slightly above the minimum hemostatic threshold (>15%) or by concurrent pro-thrombotic mutations, such as heterozygous factor V Leiden and prekallikrein variants, that mitigated her bleeding risk.

It is important to note that anticoagulation management in individuals with rare bleeding disorders is inherently complex. Warfarin inhibits vitamin K-dependent factors (II, VII, IX, X), though the degree of suppression is not always uniform. In this patient, all these factors, except IX, were reduced to ≤30% after she was started on warfarin, suggesting therapeutic anticoagulation despite an already prolonged baseline INR. These findings underscore the importance of monitoring individual factor levels, rather than relying solely on INR, to guide safe anticoagulation in patients with baseline coagulation abnormalities.

In conclusion, this case illustrates the complexities involved in managing rare bleeding disorders during high-risk cardiothoracic surgery. Despite persistently low postoperative factor V levels, the patient tolerated mechanical aortic valve replacement and long-term anticoagulation without significant bleeding events. Her clinical stability, even in the face of subtherapeutic factor V activity, emphasizes the importance of individualized management guided by bleeding history and clinical presentation rather than laboratory values alone. The case also reinforces the need for tailored transfusion and anticoagulation strategies and highlights the ongoing need for targeted factor V therapies to improve outcomes in this challenging patient population.

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