Case Report

Perioperative Management of a Patient with Hemophilia C and Allergy to Fresh Frozen Plasma

Sara Kianian, Giacomo Scorsese, Eric Zabirowicz, and Jeremy Poppers

Department of Anesthesiology, Stony Brook University Health Science Center, Stony Brook, NY 11794-8480, USA

Correspondence should be addressed to Giacomo Scorsese; giacomo.scorsese@stonybrookmedicine.edu

Received 24 December 2022; Revised 21 February 2023; Accepted 28 February 2023; Published 29 March 2023

1. Introduction

Hemophilia C is a rare inherited bleeding disorder defined by a deficiency in clotting factor XI (fXI), that occurs in only about 1:1,000,000 people in the general population [1]. Affected individuals are generally asymptomatic, although significant bleeding may occur with trauma or surgery [2]. The utilization of systemic heparinization, sternotomy, extracorporeal circulation, and hypothermia during coronary artery bypass grafting (CABG) procedures results in significant trauma and disrupted hemostatic balance [3, 4]. Factor XI levels can be normalized prior to surgery with either fresh frozen plasma (FFP) or fXI concentrate. However, allergic reactions may occur with FFP administration and the use of fXI concentrate has been associated with thrombosis in patients with concomitant cardiovascular disease [5, 6]. Herein, we present a case of fXI deficiency in a patient who developed a rare allergic reaction to FFP prior to cardiac surgery. Before submission, consent for publication was obtained from the patient. This manuscript adheres to the applicable EQUATOR guidelines.

2. Case Description

A 75-year-old Caucasian male (height 170 cm and weight 82 kg) presented with exertional chest pain and an established history of coronary artery disease for which he had undergone a percutaneous intervention and drug eluting stent placement in the mid-left anterior descending (LAD) artery eight years prior. Other relevant medical history included severe fXI deficiency, otherwise known as hemophilia C, with deep muscle hematoma formation after minor trauma in the past, type 2 diabetes treated with oral antiglycemic medications, and hypertension. Cardiac catheterization revealed severe 3-vessel obstructive coronary artery disease for which revascularization with CABG was recommended.

Preoperative laboratory values were significant for a platelet count of 77,000 (K/μl), an activated partial thromboplastin time (aPTT) of 73.7 seconds (normal range 30–40 seconds), and a severely reduced fXI activity assay at <2% (normal >65%) (Figure 1). Mixing studies failed to demonstrate the presence of an inhibitor. Being that platelet dysfunction as well as heparin induced thrombocytopenia (HIT) are both common phenomena following cardiopulmonary bypass (CPB), the presence of thrombocytopenia prior was of important note. This value would be used to assess the need for platelet transfusions independent of managing his fXI deficiency.

In an attempt to raise the preoperative fXI activity level, the patient received four units of FFP followed by repeated
coagulation studies and FXI activity assay. Soon after initiation of the first unit of FFP, however, the patient developed pruritic urticaria without evidence of angioedema or respiratory compromise. At this time, the transfusion was immediately stopped, and the patient was administered 50 milligrams of intravenous diphenhydramine, 20 milligrams of intravenous famotidine, and 650 milligrams of oral acetaminophen. The patient remained hemodynamically stable, without chest pain, and resolution of his allergic symptoms occurred shortly thereafter. At this point the hematology service was consulted and recommended that further transfusions be pursued at a slower rate of 15 cc per hour, along with pretreatment consisting of 50 milligrams of intravenous diphenhydramine, 20 milligrams of intravenous famotidine, and 650 milligrams of oral acetaminophen. Approximately 8 hours after the first transfusion, the second transfusion was initiated with the given recommendations. Within minutes, the patient again developed a pruritic rash with new onset expressive aphasia. The transfusion was aborted, the patient remained hemodynamically stable without evidence of respiratory compromise, and resolution of these symptoms occurred 30 minutes later.

The following day, an interdisciplinary discussion ensued, which included representation from the allergy and immunology, hematology, cardiothoracic surgery, and cardiothoracic anesthesiology teams. The group considered the possibility of an immunoglobulin A (IgA) deficiency and need for IgA deficient donor FFP for subsequent transfusions, but laboratory investigation failed to identify an IgA deficiency. Moreover, the team considered alternative treatment modalities such as platelet transfusion alone and prothrombin complex concentrate (PCC). However, neither were pursued as PCC were deemed suboptimal for aPTT correction alone, and follow-up laboratory analysis revealed a correcting thrombocytopenia, without the need for platelet transfusion. Ultimately, the administration of 200 milligrams of intravenous hydrocortisone, 50 milligrams of intravenous diphenhydramine, 20 milligrams of intravenous famotidine, 650 milligrams of oral acetaminophen, and 10 milligrams of oral montelukast provided optimal pretransfusion therapy, allowing for the administration of 5 units of FFP over a period of ten hours without incident. Follow-up aPTT results were obtained with correction from presentation (70 to 36) and FXI activity increased to 25%, however it never approached normal values of greater than 65% (Figure 1). Ultimately, aPTT was considered more predictive of perioperative hemorrhage as the bleeding phenotype in hemophilia C is not well-correlated with FXI activity alone, but rather the presentation of bleeding events along with coagulation parameters such as aPTT [7]. Subsequently, the patient underwent a successful two-vessel CABG the following day (left internal mammary graft to the LAD and saphenous vein graft to the first obtuse marginal artery). Cross-clamp time was 63 minutes and total time on cardiopulmonary bypass time was 112 minutes. The estimated blood loss during the surgery was determined to be minimal by the surgical team, with a total of 2.6 L of washed fluids yielding 264 milliliters of cell-saver-packed red blood—which was returned to the patient at the conclusion of surgery. Hemoglobin concentrations preoperatively, intraoperatively, and postoperatively were also tracked (Figures 2 and 3). The patient was extubated 3 hours after arrival in the cardiothoracic intensive care unit and subsequently discharged four days thereafter.

3. Discussion

Factor XI is one of many clotting factors required for the propagation of thrombin generation and is one of the critical factors needed to induce the thrombin burst for coagulation [8]. While a necessary factor for clinical assays, such as aPTT and FXI has been described to have a variable role in clinically significant bleeding for patients with FXI deficiency, otherwise known as hemophilia C [9]. Hemophilia C or FXI deficiency is a rare bleeding disorder with an incidence suspected to be only 1:100,000 in the general population [1]. Although rare, this condition requires careful monitoring and management, especially for patients undergoing surgery or otherwise has some provocation of bleeding. Given that the circulating half-life of FXI is known to be between 60 and 80 hours, it is relevant to reassess
the careful use of premedication utilizing diphenhydramine, acetaminophen, and hydrocortisone, as well as slow administration of FFP. This would ultimately allow our team to strike a balance between achieving preoperative hemostasis and mitigating potential adverse events related to this patient’s rare allergic reaction to FFP. Ultimately, extensive collaborative efforts between the cardiothoracic surgery, cardiothoracic anesthesiology, hematology, and allergy and immunology teams resulted in a clear preoperative plan allowing for the normalization of the aPTT and, finally, for the CABG to be performed without complication or excessive bleeding.

### Abbreviations

- fXI: Factor XI
- FFP: Fresh frozen plasma
- CABG: Coronary artery bypass grafting
- LAD: Left anterior descending
- aPTT: Activated partial thromboplastin time
- IgA: Immunoglobulin A
- PCC: Prothrombin complex concentrate.

### Data Availability

The data used to support the findings of this study are included within the article.

### Conflicts of Interest

The authors declare that they have no conflicts of interest.

### Authors’ Contributions

Sara Kianian contributed to the literature search, literature review, manuscript drafting, manuscript editing, and revision of the manuscript. Giacomo Scorsese contributed to the literature review, manuscript drafting, manuscript editing, and revision of the manuscript. Eric Zabirowicz contributed to manuscript drafting, manuscript editing, and revision of the manuscript and also served as a subspecialty advisor and faculty mentor.

### References


