

A Unique Case of Post-Biopsy Bleeding in a Jehovah's Witness with a Rare Inherited Undetermined Coagulopathy

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INTRODUCTION

Gastrointestinal (GI) bleeding is a common cause of hospitalization in patients with coagulopathy.^{1,2} In patients with common coagulopathies such as von Willebrand Factor disease, hemophilia A, and hemophilia B, the management of bleeding with recombinant factors and hemostatic agents are well studied and outlined in the literature.^{1,3,4} However, in patients with rare bleeding disorders where incidence is as low as 1-2 per million, there is not a clear consensus on management of bleeding and especially in those patients who decline blood products for religious reasons.³⁻¹⁰ Management of GI bleeding is important for these patients as untreated bleeding can result in hemodynamic instability, and treatment with replacement blood and hemostatic agents can cause volume overload and the associated cardiac and renal sequelae.³⁻⁴

Patients with rare bleeding disorders require integrative management between primary care providers, surgeons, and hematologists for best management and prevention of bleeding events requiring hospitalization.^{3,5-9} Patients also must understand their disorder, even if it is undefined, so that they may alert providers accordingly and modify their lifestyle to minimize bleeding risk. Simple interventions such as electronic health record (EHR) chart alerts and medical bracelets may improve outcomes for these patients.

In this case, a patient who was a Jehovah's Witness presented with an undefined chronic coagulopathy and two weeks of hematochezia following prostate biopsy.

CASE REPORT

A 67-year-old male who was a Jehovah's Witness presented to a local emergency department with a two-week history of hematochezia, dizziness, and fatigue following a prostate biopsy. On arrival, he was hemodynamically stable with anemia (hemoglobin (Hgb) 5.5 gm/dL) and supratherapeutic INR (2.7). Baseline Hgb measured 13 gm/dL. The patient was given oral vitamin K and transferred to our hospital for further management. Because of the patient's status as a Jehovah's Witness, he declined blood products and instead received epoetin alfa, intravenous iron, vitamin B12, ascorbic acid, and folic acid for support. The patient had no evidence of liver disease. Ultrasound of the abdomen obtained showed no ascites, biliary dilatation, or other liver abnormalities. On physical exam, the only abnormality was significant pallor.

During the interview, the patient mentioned having a bleeding disorder. However, he could not define it further and denied any active treatment for his disorder including perioperative management. Prior to proceeding with flexible sigmoidoscopy, the patient's hematology history was reviewed via a phone call with a hematology clinic nurse

and revealed an undetermined chronic coagulopathy with an INR that responds to vitamin K. Also, he noted a first degree relative with a Factor V deficiency.

Flexible sigmoidoscopy revealed an adherent clot at the anal verge consistent with prostate biopsy, as well as maroon colored blood in the rectum. A clip was placed successfully without complications. Over the next several days, the anemia improved to 6.5 gm/dL. The INR decreased to 2.3 and required vitamin K; however, there were no further episodes of lower gastrointestinal bleeding. Several days after flexible sigmoidoscopy, there were new visual field deficits. Magnetic resonance imaging (MRI) brain showed no acute intracranial abnormalities, and the deficit was attributed to patient's history of macular degeneration. There were no further neurologic or bleeding events. The patient was discharged. He was advised to continue epoetin alfa, B12, and folic acid as an outpatient and to follow-up with hematology for management of supratherapeutic INR. On discharge INR was 1.1. One week following discharge from the hospital, there was further improvement in the anemia (Hgb 7.8 gm/dL) and INR increased to 1.8.

On review of the patient's coagulation history, the patient had a history of supratherapeutic INR (1.7) discovered in 2018 when hospitalized with an ischemic cerebral vascular accident. A workup at that time revealed a prolonged partial thromboplastin time (PTT; 48.2 seconds), low levels of factor II (34%), factor VII (21%), and factor IX (40%). Factor VIII level of 137% was noted with suggestion of possible inhibitor present. Workup demonstrated normal liver studies, vitamin K, and vitamin D3. A prothrombin time (PT) and PTT mixing study demonstrated correction of the PT/PTT, indicating a factor deficiency or weak inhibitor.

His coagulopathy was thought to be due to a supplement the patient was taking causing a possible vitamin K deficiency. The patient received 10 mg vitamin K by mouth daily for three days. His INR decreased to 1.2. Following this hospitalization, the patient declined hematology referral and vitamin K therapy. In 2020, the patient developed an intramuscular hematoma following a fall and he again declined hematology referral and vitamin K therapy after extensive encouragement from his primary care provider. In 2022, the patient was hospitalized with COVID-19 and had a prolonged hospitalization due to supratherapeutic INR of 4.6.

DISCUSSION

Rare bleeding disorders are named aptly due to their low incidence in the general population (1-2 per 1 million persons). Because of their rare nature, there is not standardized information in the literature on how to manage these disorders.^{3,5-10} In patients with undefined bleeding disorders, management is not clear. Therefore, extensive hematologic workup and integrative management between multiple specialties is necessary. Bleeding is a common complication of these rare bleeding disorders and is of special concern in patients undergoing procedures.³ These patients require perioperative management to prevent complications and should have a plan in place to manage bleeding even in

undefined disorders.

Although rare bleeding disorders are not common, hemophilia treatment centers have registries, and the treatments patients typically respond to have been studied.^{3,5} In rare disorders, such as factor II, V, VII, dysfibrinogenemia, and afibrinogenemia, patients have seen hemostatic response to fresh frozen plasma, activated prothrombin complex concentrate/prothrombin complex concentrate, epsilon-aminocaproic acid, and recombinant factor VII.^{3,5,6} However, patients who identify as Jehovah's Witnesses tend to deny blood products including packed red blood cells, plasma, fresh frozen plasma, and cryoprecipitate. The use of recombinant factors is typically acceptable in Jehovah's Witness patients; however, the use of activated prothrombin complex concentrate/prothrombin complex concentrate is accepted variably.⁷ Therefore, there is even fewer hemostatic options in patients with rare bleeding disorders who are Jehovah's Witnesses.

For management of GI bleeding, current recommendations are to proceed with endoscopic hemostasis in patients with an INR of 1.5-2.5 with the use of reversal agents before or with endoscopy.² However, in patients with INR greater than 2.5, reversal agents should be utilized prior to endoscopic management.^{1,2,9} There also has been investigation into the use of perioperative tranexamic acid plus or minus desmopressin for minimizing bleeding risk with some mild supporting evidence, however, further research is needed to know if this is a significant treatment.^{1,2,9}

Because there is not a clear outline on how to manage patients with rare bleeding disorders, coordinated and extensive management needs to be undertaken by providers. Patients must demonstrate personal responsibility to inform medical personnel of a serious bleeding disorder even if it is undefined. These patients must be managed by hematologists to receive a full hemostatic workup, including identification of any factor inhibitors or acquired antibody mediated coagulopathies. Rare bleeding disorder patients should have routine lab monitoring and management to ensure sufficient factor concentrations.^{3,4,6} If a hematology center is not sufficient for management, patients may be referred to hemophilia treatment centers.⁶

In aging patients, even greater care is required as these patients are at risk for thromboembolic complications and related pathologic change of vessels with age despite chronically anticoagulated blood.³ A cross sectional analysis of cardiovascular disease in hemophilia patients demonstrated a reduced risk of cardiovascular disease in patients with hemophilia, however, more studies need to be done to confirm this risk reduction.¹¹ Patients with chronic bleeding disorders and cardiovascular disease need close management with cardiologists as well to balance bleeding disorder with thromboembolic risk.³ There is also additional concern with volume overload in patients requiring frequent transfusions and reversal agents.

CONCLUSIONS

In patients with rare bleeding disorders, coordinated management is important to prevent significant bleeding events requiring hospitaliza-

tion.⁸⁻⁹ Although management and monitoring are not defined clearly in patients with undetermined coagulopathies, and especially those who are Jehovah's Witnesses, close follow-up and perioperative hemostatic management plans need to be in place to prevent complications. Patients also must be aware of the serious nature of their disease in events of spontaneous or provoked bleeding and must inform healthcare personnel of this issue for proper management.

Potential interventions may include EHR alerts on all patient charts with rare bleeding disorders with details of the disorder and effective hemostatic agents. Medical bracelets also may be another necessary intervention in cases where access to an EHR is not available. Although these simple interventions are likely to improve care for these patients, further genetic analysis of rare bleeding disorders and development of non-blood based hemostatic agents need to be investigated to address these concerns and provide the highest level of care in this small patient population.

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