Intraoperative Hemostatic Management of A Patient with type 3 vWD Undergoing CABG

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INTRODUCTION

Von Willebrand factor (vWF) is a multimeric protein produced by platelets and endothelial cells that is stored within granules. This antigen plays a central role in platelet aggregation as well as the stabilization of factor VIII. Von Willebrand disease (vWD) is the most common inherited bleeding disorder, affecting 1-2% of the population.[1]

In most subtypes of vWD, the cornerstone of treatment involves the administration of DDAVP (desmopressin).

In the rare type III subtype, there is a severe quantitative defect of vWF and FVIII which is unresponsive to treatment with desmopressin.

Here we describe the importance of formulating a systematic approach for the intraoperative hemostatic management of a patient with type III vWD undergoing open heart surgery.

CASE DESCRIPTION

A 73-year-old Caucasian male with a history of vWD was found to have significant multi-vessel coronary artery disease. He was referred to cardiothoracic surgery for open revascularization.

Previous testing indicated that the patient had low serum levels of factor VIII, vWF antigen, and von Willebrand ristocetin cofactor activity. The initial impression was that the disease case was of type III subtype. A hematology consult resulted in several recommendations.

One hour prior to surgery, the patient received 4800 units (50 units/kg) of vWF:FVIII concentrate (Humate P, CSL Behring, Kankakee, IL) intravenously.

Induction of anesthesia, invasive line placement, initiation and termination of cardiopulmonary bypass (CPB) were unremarkable. A 5 gram bolus of aminocaproic acid (Amicar) was administered over one hour, followed by 1 gm/hr infusion. Following heparin reversal, 1 unit of cryoprecipitate, followed by 1 unit of platelets and a 28 mcg dose of desmopressin were given.

Coagulation studies including thrombo-elastography (TEG) all fell within normal ranges. Throughout the case, no significant bleeding of any type was observed and the postoperative course was unremarkable. The patient was discharged on postoperative day 8.

DISCUSSION

vWF allows platelet adhesion at sites of injury by binding to subendothelial collagen and platelet GP1b receptors. Depending on either qualitative or quantitative defects of this protein, von Willebrand's disease can be divided into various subtypes.[2] Diagnosis is made via vWD assay, comprised of factor VIII activity, vWF antigen, and ristocetin cofactor activity.[3]

In the case described above, the disease was initially thought to be of subtype III, wherein there is a severe depression of vWF as well as factor VIII. Both intracellular as well as plasma levels of these proteins are markedly low in this setting.

Treatment	Dosage
vWF:FVIII concentrate (Humate P)	4800 units (50 units/kg) IV 1 hour prior to surgery
Epsilon-aminocaproic acid (Amicar)	5 gram bolus followed by 1 gm/hr infusion
Monitoring of hemostasis	Baseline ACT of 106 seconds
Full heparinization for transition to CPB	300 units/kg with a target ACT >400
Protamine sulfate for heparin reversal	350 mg via controlled infusion
Cryoprecipitate	1 unit over 15 minutes
Platelet concentrate	1 unit following cryoprecipitate administration
DDAVP	28 mcg following platelet administration

Table 1: Chronological Dosing Scheme for Hematological Management

First line therapy involves the administration of desmopressin, which induces the exocytotic release of vWF from endothelial cells as well as platelets. In type III vWD, as there is a virtual absence of stored vWF, this treatment is ineffective and contraindicated as it requires functional integrity of the vWF multimer.[4]

In the case described above, desmopressin was given following platelet transfusion in the post bypass stage in order to release vWF from storage sites contained in the transfused platelets. Another crucial component in this case was the administration of vWF:Factor VIII concentrate (Humate P). This product has an approximate vWF:FVIII ratio of 1.0.

It is important to emphasize that this product should be given in conjunction with guidance from an experienced hematologist.[5] Aside from the 50 units/kg given 1 hour prior to incision, the advised regimen in this case included 3000 units to be given 12 hours postoperatively, with repeat dosing of 30-50 units/kg every 12 hours as necessary.

CONCLUSIONS

Though eventually determined to be of an indeterminate subtype, the case here was approached with the consideration that vWF and FVIII were markedly low, consistent with Type III vWF.

Needless to say, arriving at a specific diagnosis of vWD is crucial in formulating a perioperative strategy. The approach in this setting was to optimize vWF and FVIII levels in the preoperative, intraoperative, as well as postoperative periods. The administration of Humate P was central to this plan.

Intraoperatively, administering cryoprecipitate and platelets, followed by DDAVP, likely served to enhance vWF and FVIII in the post bypass period. In the case described here, adequate hemostasis was clinically observed in the intraoperative and postoperative period.

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