

An Integrated Approach to von Willebrand Disease and Surgical Myocardial Revascularization

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Abstract

Keywords

- ▶ bleeding disorders
- ▶ coronary artery disease
- ▶ off-pump bypass surgery

Cardiac surgery in patients with preexisting bleeding disorders can be a challenge. Cardiopulmonary bypass can lead to bleeding disorders, above all in patients with coagulopathy. We report the case of a 42-year-old woman, with type I von Willebrand disease, who underwent off-pump coronary artery bypass grafting. Beating heart surgery associated with an adequate replacement of von Willebrand factor and factor VIII levels were chosen to prevent bleeding disorders. Her postoperative course was uneventful and she was discharged home after 5 postoperative days.

Background

von Willebrand disease (VWD) is an autosomal dominant bleeding diathesis. It is an inherited bleeding disorder that is caused by a deficiency or dysfunction of von Willebrand factor (VWF).¹ Coagulation changes resulting from the surgical procedure associated with the platelet dysfunction caused by the VWD require the elaboration of a strategy to prevent excessive bleeding during and after cardiac surgery. Contact of blood with foreign surfaces of extracorporeal circulation results in altered coagulation integrity and increased risk of bleeding.² Patients with preexisting bleeding disorders are particularly vulnerable. Performing off-pump coronary artery bypass grafting (OPCABG), all cardiopulmonary bypass' negative aspects, including coagulation disorders, can be prevented.³ We report the successful outcome of a 42-year-old woman with type 1 VWD who required coronary artery bypass grafting (CABG). As a strategy for the control of the coagulopathy, OPCABG was performed and a concentrate of factor VIII and VWF (VIII/VWF concentrate) was infused.

Case Presentation

A 42-year-old woman with type 1 VWD was admitted because of recurrent chest pain and activity-limiting angina

unresponsive to clinical treatment. She was obese and with a medical history of non-Hodgkin lymphoma, successfully treated with chemotherapy, diabetes, and hypothyroidism. She reported previous episodes of gingival bleeding and epistaxis. Treadmill stress test was positive for myocardial ischemia. Severe two-vessels, coronary disease was revealed by coronary angiography—80% of stenosis in the circumflex ostial and right coronary artery calcified and proximal occluded—so the patient was scheduled for surgical myocardial revascularization. An endovascular procedure has been excluded in this patient because of the high bleeding risk linked to the postprocedure dual antiplatelet therapy. Because of the coagulation deficiency, the patient required special perioperative care. The main concern, in fact, was the risk of significant bleeding. The patient's coagulation parameters were below the normal range (▶ **Table 1**). Decreased VWF levels due to VWD cause a concomitant lowering of the blood VIIIIF level. Therefore, an adequate replacement of VWF and VIIIIF level is necessary to prevent bleeding and to control the coagulopathy. A replacement protocol with VIIIIF/VWF concentrate was prescribed by the hematologist. The day before surgery, 50 IU/kg of VIIIIF/VWF was infused intravenously (IV). During the surgery, a bolus of 1,000 IU IV was given. Therefore, to prevent coagulation disorders and excessive bleeding linked to cardiopulmonary bypass, we decided to perform OPCABG.

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Table 1 Pre- and postoperative coagulation parameters

Coagulation profile	Preoperative	Postoperative	Discharge
Hb (12–16 g/dL)	12.8	10.4	11.2
Plt (130–400 × 10 ³ /μL)	229	212	273
aPTT (24–35 s)	38	26	35
INR	1.2	0.98	2.1
VWF Ag (61–158 IU/dL)	40	121	–
VWF:RCo (58–175 IU/dL)	39	–	–
FVIII (70–130%)	101	123	–
RCo:Ag ratio	0.97	–	–
PFA coll/EPI (94–165 s)	194	–	–
PFA coll/ADP (71–118 s)	131	–	–

Abbreviations: aPTT, activated partial thromboplastin time; FVIII, factor VIII; Hb, hemoglobin; INR, international normalized ratio; PFA coll/ADP, PFA-100 assay with collagen/adenosine diphosphate; PFA coll/EPI, PFA-100 assay with collagen/epinephrine; Plt, platelet count; RCo:Ag ratio, ratio von Willebrand factor activity (ristocetin cofactor) to von Willebrand factor antigen; VWF Ag, von Willebrand Factor antigen; VWF:RCo, von Willebrand factor activity (ristocetin cofactor).

Therefore, the patient received just 150 IU/kg of heparin IV. Two saphenous vein grafts were performed: the first to an obtuse marginal branch and the other to the right posterior descending artery. After the OPCABG procedure, a complete reversal of heparin was performed with protamine sulfate. No adverse cardiac or hematological events occurred during the surgery. The patient was extubated in the cardiac intensive care unit 5 hours after surgery, with a total blood loss volume after surgery of ~300 mL. The patient did not require any blood product transfusion. The patient's stay in the intensive care unit was less than 24 hours. The patient was intolerant to antiplatelet. Despite the use of antiplatelet agents is recommended to maintain graft patency, the patient could not take them for a strong intolerance. Although it does not have the same efficacy compared with antiplatelet, some studies^{4–6} showed that warfarin could keep long-term graft patency. So warfarin was given on the 3rd postoperative day. No bleeding complication linked to anticoagulant therapy was observed. The patient was discharged on the 5th postoperative day. After 4 weeks at a follow-up visit, the patient was asymptomatic and with no bleeding events reported.

Conclusions

VWD is an inherited bleeding disorder secondary to a quantitative or a qualitative defect within the VWF. VWF is a multimeric plasma glycoprotein whose main functions are to facilitate platelet adhesion to the damaged vascular endothelium by binding to the platelet membrane, and to function as a VIIIIF carrier and stabilizer in plasma. Either reduced VWF levels or an inadequate functioning of this protein results in an impaired coagulation. There are three main types of VWD. Type 1 (deficiency of VWF), the most common, usually is mild; type 2 (abnormal VWF) is less common; type 3 (complete absence of VWF), and pseudo von Willebrand forms are rare, and the presentation signs

and symptoms are variable.⁷ Hemorrhagic manifestations may vary among individuals. Typically, there is easy bruising and mucosal bleeding, such as epistaxis and menorrhagia in milder forms of VWD.⁸ Moreover, contrary to what one might expect, patients affected by VWD have not been shown to have a decreased incidence of coronary artery disease.⁹ Then, heart surgery is always a dangerous challenge for a patient with VWD. Cardiopulmonary bypass can cause bleeding. In on-pump CABG, hemodilution and anticoagulation lead to coagulation disorders, activation of the hemostatic system, and a multitude of other clinical consequences. Clinically, adverse effects include lowered intravascular colloidal oncotic pressure, release of vasoactive substances into plasma and platelet damage.¹⁰ Cardiopulmonary bypass also causes systemic inflammation response syndrome through the activation of blood constituents. The activation of platelets reduces platelet numbers and this causes increased postoperative bleeding times. Shortly after starting cardiopulmonary bypass, reductions in the plasma concentration of coagulation factors II, V, VII, IX, X, and XIII occur. In a patient with no bleeding disorders, during bypass, the plasma concentration of VWF generally decreases, but usually remains well above levels normally considered adequate for hemostasis.¹⁰ Patients with preexisting bleeding disorders are particularly vulnerable. Performing OPCABG, all cardiopulmonary bypass' negative aspects, including coagulation disorders, can be prevented.³ Few are the reports concerning the management of patients with VWD underwent cardiac surgery. In the early 1970s, Komp et al demonstrated that open heart surgery may be achieved also in patient with bleeding disorders,¹¹ as like as Aris et al that performed aortic valve replacement in a patient with VWD maintaining adequate levels of FVIII during the operation.¹² Patients with VWD undergoing cardiac surgery usually require prophylactic therapy aiming at preventing hemorrhagic complications.

A treatment commonly consisted in the IV infusion of FVIII/VWF concentrate, platelets or desmopressin, according to the coagulation status and the type of disease.^{11,12} In the present case, besides the administration of the FVIII/VWF concentrate, a surgical strategy was adopted to prevent major bleeding: OPCABG. Beating heart techniques have gained widespread diffusion as alternative techniques to conventional on-pump CABG. On-pump CABG, with respect to OPCABG, causes a transient increase in fibrinolysis and a decrease in platelet count.³ Even if anticoagulation is mandatory during OPCABG surgery, it requires less heparinization than on-pump CABG. Moreover, there is no contact with the foreign surface of the extracorporeal circulation circuits, so systemic inflammatory response and bleeding disorders are avoided.² Cardiac surgery in complex patient can obviously be performed only after careful and complete assessment of the patient. An interdisciplinary approach between the hematologist and the cardiac surgeon is mandatory for the control of the coagulation disorder. OPCABG and the administration of VIIIIF/VWF concentrate in the patient with VWD was a successful strategy. It simplified the whole intra- and postoperative management and was effective in the prevention of bleeding and in the control of coagulation disorder. Avoiding bleeding complications, this approach might be used in other patients with the same disease who require surgical myocardial revascularization.

Competing Interests
None declared.

References

- 1 Mannucci PM. Treatment of von Willebrand's disease. *J Intern Med Suppl* 1997;740:129–132
- 2 Paparella D, Yau TM, Young E. Cardiopulmonary bypass induced inflammation: pathophysiology and treatment. An update. *Eur J Cardiothorac Surg* 2002;21(2):232–244
- 3 Chassot PG, van der Linden P, Zaugg M, Mueller XM, Spahn DR. Off-pump coronary artery bypass surgery: physiology and anaesthetic management. *Br J Anaesth* 2004;92(3):400–413 Review
- 4 Pantely GA, Goodnight SH Jr, Rahimtoola SH, et al. Failure of antiplatelet and anticoagulant therapy to improve patency of grafts after coronary-artery bypass: a controlled, randomized study. *N Engl J Med* 1979;301(18):962–966
- 5 Gohlke H, Gohlke-Bärwolf C, Stürzenhofecker P, et al. Improved graft patency with anticoagulant therapy after aortocoronary bypass surgery: a prospective, randomized study. *Circulation* 1981;64(2 Pt 2):II22–II27
- 6 McEnany MT, Salzman EW, Mundth ED, et al. The effect of antithrombotic therapy on patency rates of saphenous vein coronary artery bypass grafts. *J Thorac Cardiovasc Surg* 1982; 83(1):81–89
- 7 Pruthi RK. A practical approach to genetic testing for von Willebrand disease. *Mayo Clin Proc* 2006;81(5):679–691
- 8 Federici AB. Clinical diagnosis of von Willebrand disease. *Haemophilia* 2004;10(Suppl 4):169–176
- 9 Spiel AO, Gilbert JC, Jilma B. von Willebrand factor in cardiovascular disease: focus on acute coronary syndromes. *Circulation* 2008; 117(11):1449–1459
- 10 Woodman RC, Harker LA. Bleeding complications associated with cardiopulmonary bypass. *Blood* 1990;76(9):1680–1697
- 11 Komp DM, Nolan SP, Carpenter MA. Open-heart surgery in a patient with von Willebrand's disease. *J Thorac Cardiovasc Surg* 1970;59(2):225–230
- 12 Aris A, Pisciotta AV, Hussey CV, Gale H, Lepley D. Open-heart surgery in von Willebrand's disease. *J Thorac Cardiovasc Surg* 1975;69(2):183–187