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Letter to the Editor

Walking a Thin Line

To the Editor:

We congratulate Christophel-Plathier et al. for successfully managing complex coagulation issues in a patient with combined Bernard-Soulier syndrome and storage pool disease who underwent a replacement of ascending aorta and coronary artery bypass grafting during cardiopulmonary bypass.[1] We would like to provide additional comments on the pathophysiology and clinical management of Bernard-Soulier syndrome and storage pool disease.

First, prophylactic platelet transfusion was deemed important in this case that involved heparin anticoagulation for bypass, given the patient's history of numerous bleeding events after noncardiac surgeries. The authors documented the presence of grayish giant platelets in the blood smear, reduced glycoprotein Ib-V-IX complex, and severely reduced release from alpha and dense granules. A reduced formation of coated platelets (**Co**llagen **A**nd **T**hrombin-activated platelets) on flow cytometry signifies the following: (1) platelets express less surface phosphatidylserine, which is a catalytic surface for thrombin generation; and (2) the platelet surface retains low amounts of procoagulant proteins including fibrinogen, factor V, and von Willebrand factors due to alpha-granule defects. The lack of glycoprotein Ib-V-IX complex or von Willebrand factors results in reduced prothrombin conversion to thrombin on platelets.[2] Therefore, hemostatic defects in Bernard-Soulier syndrome and storage pool disease involve both primary and secondary hemostasis.

Second, their surgery was performed under normothermia, which presumably mitigated the severity of thrombocytopenia and coagulopathy after bypass.[3] Nevertheless, microvascular bleeding continued after platelet transfusion, and a subsequent contact-activated INTEM test demonstrated a grossly abnormal clotting time (CT, 348 s [normal 161-204 s]) and low 5-minute clot amplitude (A5, 30 mm [normal 33-52 mm]). HEPTEM (heparinase) CT also was prolonged (311 s). Thus, thrombocytopenia and coagulation factor deficiency were suspected despite normal fibrin polymerization (FIBTEM-A5, 13 mm). Prolongation of INTEM-CT previously was reported in congenital factor V deficiency.[4] In the current patient,[1] alpha-granules were depleted, and the lack of platelet-derived factor V most likely contributed to prolonged INTEM-CT. The expected factor V recovery from 2 units of fresh frozen plasma is low (<5%),[5] and 4-factor prothrombin complex concentrate does not contain a therapeutic amount of factor V. Incomplete recovery of INTEM-CT (208 s), and moderate postoperative blood loss (1.35 L in 24 h) highlighted the major challenges in managing coagulopathy in this setting.

Finally, the authors used tranexamic acid for antifibrinolytic therapy during bypass, and then resumed thromboprophylaxis using unfractionated heparin (10,000 units over 24 h), and oral tranexamic acid after surgery. It is important to emphasize that platelet alpha-granules contain plasminogen activator inhibitor-1, which antagonizes local plasminogen activator.[6] A profibrinolytic state is expected in the presence of thrombocytopenia and storage pool disease, which certainly justifies the authors' use of tranexamic acid.

Declaration of Competing Interest

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Kofi Vandyck, MD[*]
Casey Windrix, MD[*]
Elyse C. Wyatt, BSc[†]
Kenichi A. Tanaka, MD, MSc[*,#]
[*]*Department of Anesthesiology, University of Oklahoma Health Sciences Center, Oklahoma City OK*
[†]*University of Oklahoma College of Medicine, Oklahoma City OK*

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