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EDITORIAL COMMENT

Management of Bleeding Disorder During Dual Antiplatelet Therapy

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Dual antiplatelet therapy (DAPT) is a cornerstone of the management of acute coronary syndromes (ACS) reducing the thrombotic risk, particularly in patients who undergo percutaneous coronary interventions (PCIs).[1] In recent years, there has been increasing focus on the bleeding risk associated with DAPT. Additionally, new strategies have emerged to help minimize the risk for bleeding in patients who are at high risk for hemorrhage.

In this issue of *JACC: Case Reports*, Yao et al[2] present the case of a patient who developed acquired hemophilia A (AHA) during treatment with prasugrel following recurrent ACS and repeated PCI. The patient presented with progressive subcutaneous bleeding, anemia, and an isolated prolongation of activated partial thromboplastin time (aPTT), ultimately leading to the diagnosis of AHA due to factor VIII inhibitors. Discontinuation of antiplatelet therapy and initiation of corticosteroid treatment resulted in remission, and subsequent coronary artery bypass grafting was performed to achieve durable revascularization while avoiding prolonged DAPT.

AHA is an extremely rare autoimmune disorder characterized by the development of autoantibodies against coagulation factor VIII.[3] Its incidence is estimated at approximately 1 to 1.5 cases per million individuals annually, and the condition is associated with significant morbidity and mortality because of severe bleeding. In many cases, the disorder occurs in association with autoimmune diseases, malignancies, pregnancy, or exposure to medications. Drug-induced AHA represents a minority of cases but has been linked to several agents, including antibiotics, interferons, and antithrombotic drugs (eg, clopidogrel, ticagrelor, and prasugrel).[3]

One of the key messages highlighted by this case concerns the potential for diagnostic delay when bleeding develops in patients receiving antiplatelet therapy. In routine clinical practice, hemorrhagic complications after PCI are often attributed to DAPT. However, the presence of unexplained bleeding accompanied by isolated prolongation of aPTT should immediately raise suspicion for an acquired coagulation disorder. The diagnostic pathway is relatively straightforward: Failure of aPTT correction suggests the presence of an inhibitor, which should prompt measurement of factor VIII activity and confirmation with a Bethesda assay to detect anti-factor VIII antibodies.[3] Early recognition is vital as prompt hematologic evaluation and initiation of appropriate therapy may be lifesaving (**Figure 1**).

The case also underscores a broader and increasingly relevant issue in cardiovascular medicine: the management of coronary artery disease in patients with bleeding disorders.[4] Although congenital hemophilia and AHA have different pathophysiologic mechanisms, both conditions pose a similar challenge: balancing thrombosis and bleeding risk after coronary revascularization. Importantly, patients with acquired coagulation disorders may also be considered functionally comparable to those classified as high bleeding risk according to contemporary definitions, reinforcing the need for tailored revascularization and antithrombotic strategies.[4] Several considerations may help guide clinical decision-making in this challenging scenario.

First, close collaboration between cardiologists and hematologists is essential to tailor both antithrombotic therapy and revascularization strategies according to the individual bleeding profile. In such situations, the traditional “heart team” should

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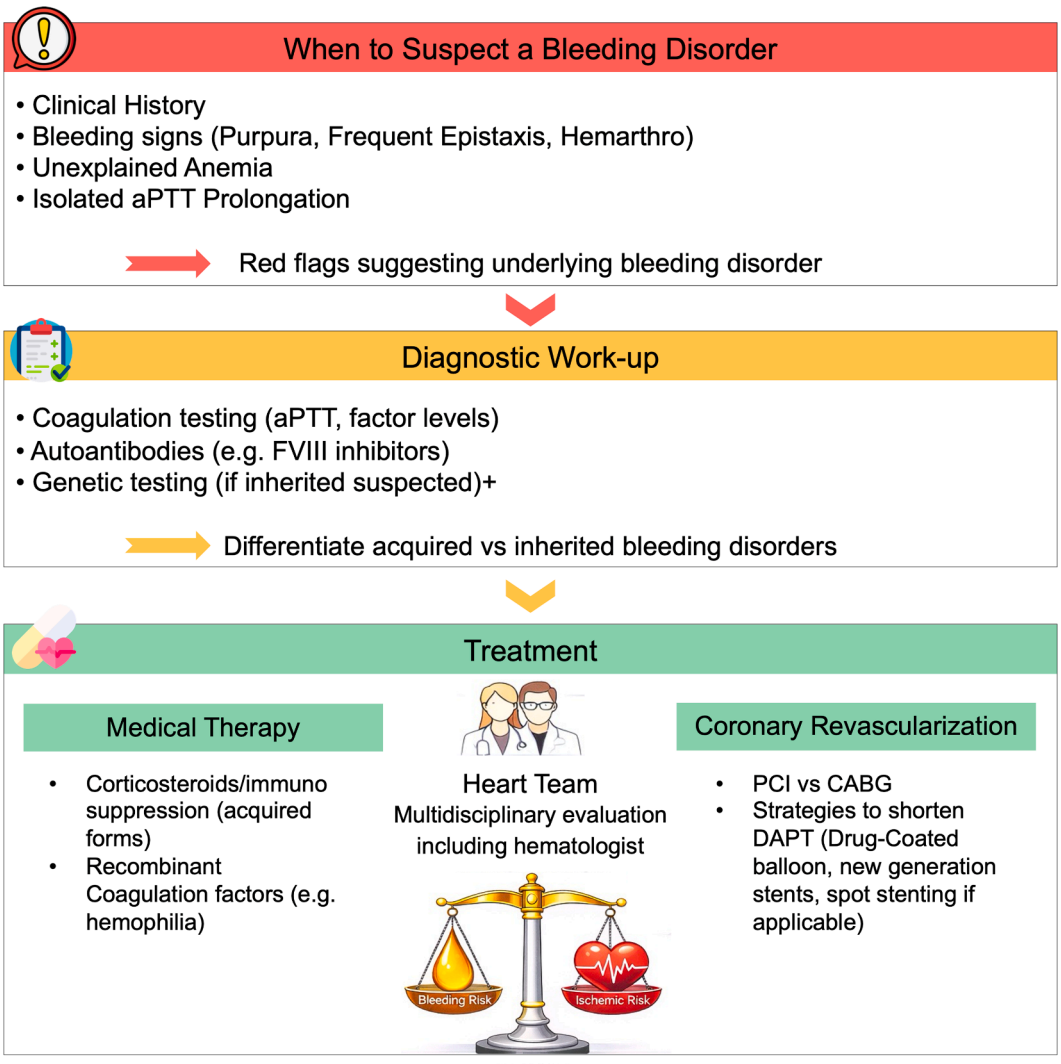
FIGURE 1 Diagnostic Work-Up for Patient With Suspected Bleeding Disorder



Unexplained bleeding associated with isolated prolongation of activated partial thromboplastin time (aPTT) should prompt clinicians to consider rare underlying conditions, including acquired hemophilia A. Balancing ischemic and bleeding risk requires a multidisciplinary approach and the adoption of tailored treatment strategies. CABG = coronary artery bypass grafting; DAPT = dual antiplatelet therapy; FVIII = factor VIII; PCI = percutaneous coronary intervention.

include hematology expertise to appropriately balance ischemic and hemorrhagic risks.[4]

Second, the choice of the revascularization modality itself (percutaneous versus surgical) may become part of the bleeding-risk mitigation strategy. In the case described by Yao et al,[2] after PCI failure, potentially related to early DAPT discontinuation, the authors opted for coronary artery bypass grafting to achieve durable revascularization while maintaining lifelong single antiplatelet therapy. This decision highlights an important clinical principle: When prolonged DAPT is undesirable or contraindicated, the selection of the revascularization strategy may itself represent a tool to reduce bleeding risk.

Third, several interventional strategies are currently available to minimize the need for prolonged DAPT and are of great value for patients with extreme bleeding risk. For example, the use of new-generation drug-eluting stents or drug-coated balloons allows very short DAPT duration also in

the setting of ACS.[4,5] Nevertheless, despite advances in interventional cardiology and antithrombotic therapy, important knowledge gaps remain. Patients with bleeding disorders are typically excluded from major randomized clinical trials of PCI and antithrombotic therapy, leaving clinicians to rely largely on case reports, small observational studies, and expert consensus documents.[6] This lack of evidence may also contribute to therapeutic conservatism because patients perceived to be at very high bleeding risk are sometimes less likely to undergo invasive revascularization despite potential clinical benefit. Future research and collaborative registries will therefore be essential to better define optimal therapeutic strategies in this growing and clinically complex population. Pharmacovigilance studies may help identify previously unrecognized associations between cardiovascular medications and immune-mediated coagulopathies such as AHA. In addition, prospective registries may provide valuable insights into optimal revascularization strategies and antithrombotic regimens in patients at high risk for bleeding.

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