Cardiovascular Interventions in Thrombocytopenic Cancer Patients

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In 2008, there were an estimated 12.4 million cancer diagnoses and 7.6 million cancer deaths around the world. The estimated number of new cancer cases in the United States for 2010 was 1,529,560, of which approximately 140,000 involved patients with diagnoses of leukemia, lymphoma, and myeloma.[1] Most of those patients will become thrombocytopenic during cancer treatment. Although platelets play an important contributory role in the development of acute coronary syndrome, the decrease of platelets (thrombocytopenia) does not protect cancer patients from ischemic events. Very little clinical information is currently available to aid in the management of acute coronary syndromes in thrombocytopenic patients. Sarkiss and colleagues[2] have shown that withholding aspirin from thrombocytopenic cancer patients with acute coronary syndrome can lead to much worse outcomes.

The distinction between platelet function in hemostasis and thrombosis is poorly understood, but it is best considered within the context of Virchow's triad; moreover, the dynamic interaction between these 3 factors (endothelial injury, venous stasis, and hypercoagulability) differs in accordance with the specific vascular compartment under consideration. For example, there is both theoretical[3] and clinical[2] evidence that thrombosis in mid-sized coronary arteries develops unimpeded by moderately severe thrombocytopenia and impaired mucocutaneous hemostasis. How can this be explained?

Platelet number may be less important in thrombosis than in hemostasis when one considers differences between rheologic factors in the mid-sized arteries and the microvasculature. In the vicinity of a ruptured atherosclerotic plaque, pathologic blood flow (which results in very high wall shear stress) promotes platelet adhesion but washes away all other cellular and soluble components of the blood. Arterial thrombosis is therefore adhesion limited. In contrast, a paracrine platelet-derived vascular endothelial growth factor (VEGF) system regulates hemostasis in the low-flow, post-capillary venular system through its effects on vascular permeability, which are strikingly decreased in the absence of this platelet-derived VEGF.[4] Microvascular hemostasis is therefore both adhesion and diffusion limited, leading one to hypothesize that thrombocytopenia diminishes hemostasis more than it does thrombosis. If this hypothesis were to be validated, it would have profound implications for how acute coronary syndromes are managed in cancer patients with thrombocytopenia; and it would introduce new approaches to managing bleeding in thrombocytopenic patients, separate from administering platelet transfusions.

Clinicians should take different approaches to patients with the "chronic" thrombocytopenia that is frequently found in cancer survivors (that is, after stem-cell transplantation or after taxane- or gemcitabine-based chemotherapy) and those with the "acute" thrombocytopenia that is interpreted as a marker of severity in the setting of sepsis, bleeding, heparin-induced thrombocytopenia (HIT), or glycoprotein IIb/IIIa-induced thrombocytopenia. Limited previous clinical experience suggests that platelet function and not platelet count is the determinant factor.[5] There are no clinical data regarding platelet transfusion and acute coronary syndromes in thrombocytopenic patients.

Case Series

Patients and Methods. Thrombocytopenia has been a contraindication for interventional cardiology procedures due to the increased risk of bleeding. Starting in September 2008, we treated cancer patients who presented with abnormal cardiovascular stress tests or acute coronary syndromes in a systematic fashion according to current cardiovascular guidelines, independent of their platelet counts (excluding patients with sepsis or active bleeding). We identified a total of 30 patients with chronic thrombocytopenia, defined as absolute platelet count <100,000/mm^3 (mean platelet count, 49,000/mm^3; lowest platelet count, 9,000/mm^3). These patients underwent cardiac catheterization and appropriate coronary artery disease treatment.

In all 30 patients, access was obtained using a micropuncture kit and the modified Seldinger technique, with radial access preferred unless the patient had an abnormal result from a modified Allen test or a pulse oximetry test, or had a history of bypass surgery. All patients received anticoagulant agents (unfractionated heparin or bivalirudin) in order to maintain an activated clotting time of greater than 250 sec during the procedure. All patients who underwent radial access received a loading dose of 3,000 U of unfractionated heparin. It appears that lower doses (usually a 66 U/kg bolus, maximum 5,000 U) of unfractionated heparin are required to achieve therapeutic intraprocedural activated clotting time.[6] All patients who needed coronary stenting (guided by fractional flow reserve) received dual antiplatelet therapy (aspirin and clopidogrel).[2] No patient needed or received glycoprotein IIb/IIIa inhibitors. The preferred stents were bare-metal stents, unless the patient was diabetic and the vessel diameter was less than 2.5 mm, in which case a drug-eluting stent was used.

Results. In all patients who had thrombocytopenia, the procedures were completed without major bleeding complications. No platelet transfusions were administered before or during the procedures.

Conclusions. In this 1st consecutive case series of patients with thrombocytopenia who underwent endovascular procedures, we attribute our initial success to meticulous access procedures and to careful hemostasis. On the basis of this clinical experience, we conclude that thrombocytopenic cancer patients can safely undergo cardiovascular interventions. The complications are insubstantial. Yet to be defined is the absolute lowest limit of the platelet count at which interventions should be performed; our case series has moved the boundary from 100,000 to 10,000 platelets per mm^3. Larger studies will also have to determine the appropriate length of dual antiplatelet therapy and whether stent characteristics (bare-metal vs drug-eluting) affect outcomes.

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