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CASE REPORT

INTERMEDIATE

CLINICAL CASE

Management of High-Grade Coronary Artery Disease and Concomitant Glanzmann Thrombasthenia

Katie P. Truong, MD,[a] Jessica J. Zhang, MD,[a] Marwah Shahid, MD,[b] Aditya Goud, MD,[b] Michael Rosove, MD,[c] Jesse Currier, MD,[d] Kamran Shamsa, MD,[b] Rushi V. Parikh, MD[b]

ABSTRACT

In the present case report, we describe the management of severe coronary artery disease in a patient with Glanzmann thrombasthenia. To the best of our knowledge, there are no established guidelines for revascularization in this setting, and we pose novel discussion points regarding the nuanced care of this patient. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2021;3:1625–1629) © 2021 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 69-year-old man with hypertension, hyperlipidemia, and Glanzmann thrombasthenia (GT) was hospitalized for rectal bleeding. He received desmopressin and platelets, and was started on an intravenous proton pump inhibitor; subsequent colonoscopy revealed 2 diverticular bleeds, which were successfully clipped leading to hemostasis. However, during this episode of lower gastrointestinal bleeding, he also experienced substernal chest tightness radiating to the jaws bilaterally during ambulation that resolved with rest. He reported 3 similar episodes of chest pain in the past decade, the most recent 2 weeks earlier. The patient had stable vital signs and an unremarkable cardiopulmonary exam.

LEARNING OBJECTIVES

- The clinician will understand the pathophysiology of GT.
- The clinician will understand the implications of GT on coronary revascularization.
- The clinician will understand the impact of antiplatelet therapy in the setting of GT.

PAST MEDICAL HISTORY

The patient was diagnosed with GT in his youth. Platelet aggregation studies demonstrated absence of aggregation with adenosine diphosphate (ADP), epinephrine, and arachidonic acid, but mild reactivity to collagen. His disease course has been complicated by gastrointestinal bleeding related to hemorrhoids, diverticulosis, and *Helicobacter pylori* infection requiring blood transfusions, as well as renal lithotripsy necessitating transfusion support, desmopressin, and aminocaproic acid.

From the [a]Department of Medicine, David Geffen School of Medicine at UCLA, Los Angeles, California, USA; [b]Division of Cardiology, David Geffen School of Medicine at UCLA, Los Angeles, California, USA; [c]Division of Hematology and Oncology, David Geffen School of Medicine at UCLA, Los Angeles, California, USA; and the [d]Division of Cardiology, Department of Veterans Affairs Medical Center, Los Angeles, California, USA.

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ABBREVIATIONS AND ACRONYMS

ADP = adenosine diphosphate

CABG = coronary artery bypass grafting

CAD = coronary artery disease

CCTA = coronary computed tomography angiography

DAPT = dual antiplatelet therapy

DES = drug-eluting stent

GT = Glanzmann thrombasthenia

LAD = left anterior descending coronary artery

LIMA = left internal mammary artery

PCI = percutaneous coronary intervention

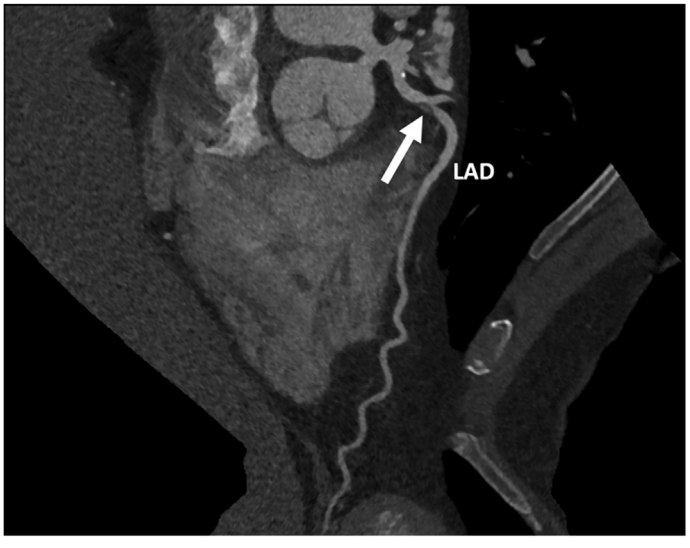
DIFFERENTIAL DIAGNOSIS

Although the differential diagnosis of chest pain is broad, the patient's typical angina was most consistent with cardiac ischemia due to obstructive coronary artery disease (CAD). Other potential considerations included coronary vasospasm, dissection, and embolism.

INVESTIGATIONS

The patient's electrocardiogram at the time of chest pain and serial troponin I levels were unremarkable. An inpatient exercise stress echocardiogram showed stress-induced segmental wall motion abnormalities in the left anterior descending coronary artery (LAD) territory after 7 minutes of exercise (8.5 METs). Given his high bleeding risk and initial stable symptoms, coronary computed tomography angiography (CCTA) was favored over invasive coronary angiography for further risk assessment. CCTA revealed a focal plaque in the proximal-mid LAD resulting in severe stenosis (**Figure 1**). Over the next several months, the patient experienced increasing anginal frequency and intensity despite initiation of amlodipine and escalating doses of isosorbide mononitrate. Given his high-risk CCTA findings and refractory angina, the patient underwent transradial angiography to definitively assess his coronary anatomy. Angiography demonstrated 90% stenosis of the proximal LAD involving the bifurcation of the first diagonal branch (**Figure 2,** Video 1).

FIGURE 1 Coronary Computed Tomography Angiography



Coronary computed tomography angiography showed severe stenosis of the proximal left anterior descending artery (LAD) **(arrow)**.

MANAGEMENT

After careful multidisciplinary discussions with hematology and cardiothoracic surgery colleagues, we recommended that the patient pursue percutaneous coronary intervention (PCI) over robotic coronary artery bypass grafting (CABG). In light of his residual platelet aggregability to collagen and the plan for a 2-stent PCI strategy, we chose an antiplatelet strategy of short-term dual antiplatelet therapy (DAPT) with aspirin and clopidogrel for 1 month followed by clopidogrel monotherapy indefinitely, barring significant bleeding. Of note, clopidogrel responsiveness testing was deferred because it cannot be reliably assayed in the absence of platelet aggregation. He underwent successful intravascular ultrasound-guided LAD-diagonal bifurcation PCI with the use of a double kissing crush technique with placement of a 4.0 × 20 mm Synergy drug-eluting stent (DES) in the LAD (post-dilated to 5.5 mm proximally) and a 3.0 × 16 mm Synergy DES in the diagonal artery (**Figure 3,** Video 2).

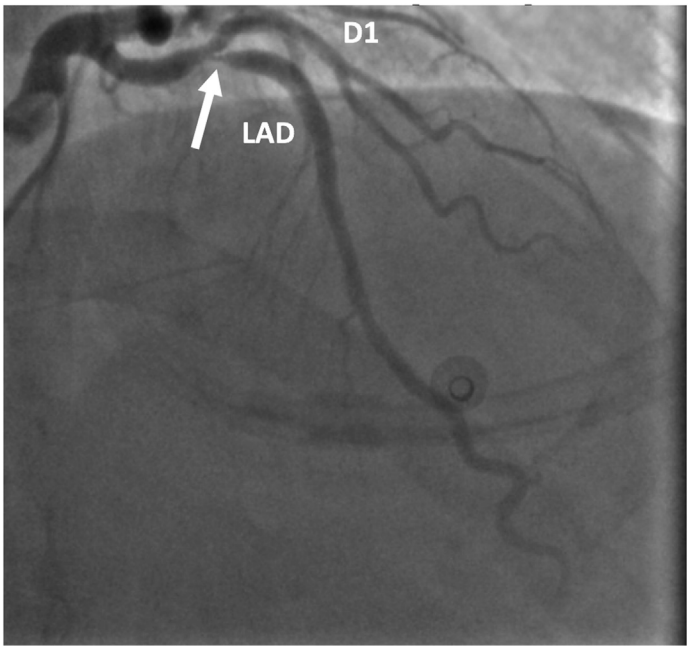
DISCUSSION

This is a complex case of CAD in the setting of GT, requiring consideration of risks and benefits of strategies for revascularization and antiplatelet therapy. GT is an inherited platelet disorder that is characterized by spontaneous bleeding with phenotypic variability ranging from minimal bruising to potentially fatal hemorrhaging. In the present case, the patient had multiple medical issues complicated by bleeding that required blood transfusions. GT is caused by autosomal recessive inheritance of quantitative or qualitative deficiencies of functional αIIbβ3 integrin coded by *ITGA2B* or *ITGB3* genes for αIIb and β3, respectively. As a result, platelets may be stimulated, but the platelet glycoprotein IIb/IIIa receptor is unable to bind fibrinogen to cross-link platelets. Thus, platelet aggregation is impaired (1,2) (**Figure 4**). In platelet aggregation studies, there is lack of response to collagen, epinephrine, arachidonic acid, and ADP stimulation. Indeed, this pathway has been used to develop integrin-blocking drugs that inhibit arterial thrombosis, such as glycoprotein IIb/IIIa inhibitors. Although the final common pathway in platelet aggregation is impaired, patients with GT may still develop atherosclerotic disease (3).

Traditionally, DAPT is the criterion standard for prevention of stent thrombosis and in-stent restenosis after PCI (4). The most recent American Heart Association/American College of Cardiology guidelines recommend DAPT ideally at least 3 months after DES placement in patients with stable ischemic heart disease and high bleeding risk. The use of antiplatelet therapy is not well studied in the GT population, and the potential higher risk of bleeding in the setting of GT posed a challenging dilemma regarding revascularization of his high-grade disease. The strategies of PCI versus robotic CABG with a left internal mammary artery (LIMA) graft to the LAD were deliberated extensively. Although minimally invasive, robotic LIMA-LAD had seemingly prohibitive up-front perioperative bleeding risk in addition to the need for at least short-term single antiplatelet therapy after the surgery. In contrast, PCI with DES placement represented a less invasive but more complex approach to achieve complete revascularization and carried a possibly higher postprocedural bleeding risk in the setting of short-term DAPT. We found only 3 published case reports of patients with GT who underwent CABG (5-7). These patients required significant blood product administration during surgery and 2 of the 3 patients had postoperative bleeding complications (5,6). However, to the best of our knowledge, there are no published reports of PCI in the setting of GT. Ultimately, the consensus was that PCI was the most prudent option, and the patient underwent successful PCI as described.

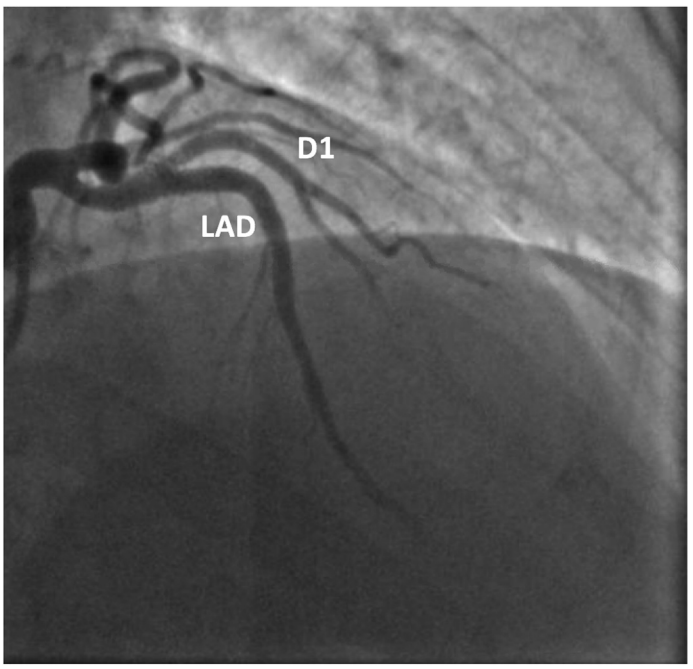
This case raised a few key, nuanced points regarding type and duration of antiplatelet therapy in the setting of PCI and concomitant GT. First, it is unclear if the mechanism of GT alone provides sufficient antiplatelet activity and whether antiplatelet therapy leads to significantly increased bleeding risk. The mechanism of GT prevents platelet aggregation—the final step in platelet-related thrombosis—while oral antiplatelet therapy affects platelet activation via the previously described mechanisms. Therefore, we thought that short-term DAPT would reduce the risk of platelet activation at the stent site and only minimally affect the patient's overall bleeding risk. Second, in the event of an active bleed requiring platelet transfusion, donor platelets possess functional glycoprotein IIb/IIIa receptors and thus exponentially increase the risk of stent thrombosis. Therefore, unlike our case, if a patient is not maintained on chronic oral antiplatelet therapy, initiation of oral or intravenous antiplatelet therapy should be considered to prevent stent thrombosis at the time of platelet transfusion.

FIGURE 2 Diagnostic Coronary Angiogram



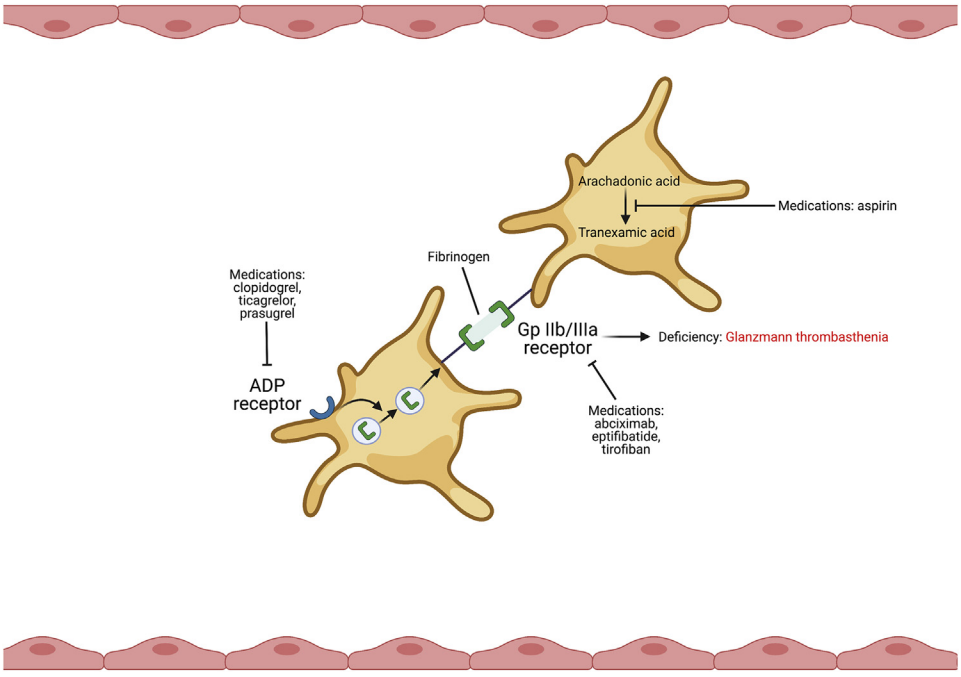
The right anterior oblique cranial view visualizes the left anterior descending (LAD) artery and diagonal branch (D1). The **arrow** indicates an area of 90% stenosis in the proximal LAD.

FIGURE 3 Coronary Angiogram After Stent Placement



Coronary angiogram after double kissing crush bifurcation percutaneous coronary intervention of the left anterior descending (LAD) and diagonal (D1) arteries shows patent stents and resolution of the prior high-grade LAD stenosis.

FIGURE 4 Platelet Aggregation Mechanism of Action



The platelet aggregation pathway involves activation of the glycoprotein (Gp) IIb/IIIa receptor, which leads to irreversible binding of platelets together. Glanzmann thrombasthenia is caused by a deficiency of this receptor, and medications such as abciximab block this receptor. Figure created with Biorender.com. ADP = adenosine diphosphate.

FOLLOW-UP

At 3-month follow-up, the patient had no further angina and denied any bleeding issues. He completed 1 month of DAPT and has been maintained on clopidogrel monotherapy.

CONCLUSIONS

This unique case highlights the complex and nuanced management of CAD in patients with platelet disorders such as GT, for which there are currently no established guidelines. Short-term DAPT appears to be a reasonably safe option for patients with GT undergoing PCI.

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ADDRESS FOR CORRESPONDENCE: Dr Rushi V. Parikh, Division of Cardiology, University of California-Los Angeles, 100 Medical Plaza, Suite 630 West, Los Angeles, California 90095, USA. E-mail: rparikh@mednet.ucla.edu. Twitter: @rushiparikh11.

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KEY WORDS coronary artery disease, dual antiplatelet therapy, Glanzmann thrombasthenia, percutaneous coronary intervention

APPENDIX For supplemental videos, please see the online version of this paper.