Acute myocardial infarction and renal dysfunction due to chronic extreme anemia (hemoglobin 2.5 g/dL) in immune thrombocytopenia

Mark Muenchrath, MA , Katyayini Aribindi, MD , Mark Farnie, MD, and Adrian DaSilva-DeAbreu, MD, MSc

Department of Internal Medicine, McGovern Medical School, The University of Texas Health Science Center at Houston, Houston, Texas

ABSTRACT

Immune thrombocytopenic purpura (ITP) is an acquired thrombocytopenia where autoantibodies are generated against platelet antigens. Primary ITP is often idiopathic, whereas secondary ITP has many potential causes, including drug induced, infection related (human immunodeficiency virus, hepatitis C), leukemias, or autoimmune such as systemic lupus erythematosus. ITP is a common cause of thrombocytopenia in asymptomatic individuals, where evidence of bleeding may be minor or absent. Chronic silent bleeding leading to extreme anemia in patients with ITP is rare, and evidence of multiorgan damage is even rarer; hence the relevance of this case report. Here we describe a case of primary ITP with severe chronic blood loss leading to profound anemia causing renal failure and a type II non-ST elevation myocardial infarction. Our patient underwent extensive workup for the etiology of both thrombocytopenia and anemia and was eventually treated with packed red blood cell and platelet transfusions, along with intravenous steroids and immunoglobulin therapy.

KEYWORDS Acute myocardial infarction; immune thrombocytopenic purpura; renal failure; severe anemia

Bleeding in immune thrombocytopenic purpura (ITP) occurs in 66% of patients on presentation and is usually “platelet-type” bleeding, presenting as petechiae; nonblanchable, flat, erythematous, discrete lesions; or a collection of petechiae called purpura, which are classically nonpalpable in thrombocytopenia.^{1–4} Severe bleeding in ITP can be related to mucosal bleeding: either intracranial hemorrhage or continuous epistaxis or hemorrhage from gastrointestinal loss.⁵ Though studies allude to severe bleeding due to ITP, few use a quantifiable scale such as the common terminology criteria for adverse events or Buchanan or Blanchette score of severe bleeding, and most do not discuss multiorgan involvement.^{5–7} Here we report an unusual case of severe chronic blood loss most likely from a gastrointestinal source secondary to primary ITP, leading to multiorgan failure.

CASE REPORT

A 49-year-old black man with no known past medical history presented to the emergency department complaining

of dull periumbilical pain, progressive malaise, exertional dyspnea, and poor appetite for 7 weeks. He had an episode of epistaxis that was difficult to control and two episodes of nonbloody, nonbilious emesis. Vital signs and physical exam were unremarkable except for mild tachycardia, tachypnea, and scleral and mucosal pallor. Laboratory tests showed a hemoglobin level of 2.5 g/dL, platelet count of 1 K/ μ L, lactate dehydrogenase of 453 U/L (normal: 86–246 U/L), haptoglobin of 156 mg/dL (normal: 32–214 mg/dL), creatinine of 2.8 mg/dL, blood urea nitrogen of 40 mg/dL, and troponin I of 0.310 ng/mL (normal: 0.00–0.045 ng/dL). The electrocardiogram showed sinus tachycardia without evidence of ischemia or left ventricular hypertrophy (LVH) (*Figure 1*).

Chest x-ray and computed tomography of the abdomen and pelvis did not demonstrate evidence of hemorrhage. A single fecal occult blood test was negative, but this test has poor sensitivity for gastrointestinal bleeds.⁸ Further studies showed a low vitamin B12 level (191 pg/mL; normal: 211–911 pg/mL) with an elevated methylmalonic acid level (608 nmol/L; normal: 0–378 nmol/L), low serum iron (13

Corresponding author: Adrian DaSilva-DeAbreu, MD, MSc, Department of Internal Medicine, McGovern Medical School, The University of Texas Health Science Center at Houston, 6431 Fannin Street, Suite MSB 1.134, Houston, TX 77030 (e-mail: adrianjdasilva@gmail.com)
Color versions of one or more of the figures in this article can be found online at www.tandfonline.com/ubmc.

Received May 21, 2018; Revised July 8, 2018; Accepted July 9, 2018.

Figure 1. Electrocardiogram showing sinus tachycardia in the setting of a demand ischemia (type II non-ST elevation myocardial infarction).

Figure 2. (a) Peripheral blood smear showing normocytic normochromic anemia with severe thrombocytopenia. Red blood cell morphology was not grossly abnormal; there were no signs of megaloblastic changes. (b) Bone marrow aspirate showing erythroid hyperplasia without megaloblastic features and increased erythrocytes with maturation. Iron stains were performed but were inadequate for evaluation of iron storage due to lack of particles. Megakaryocytes were noted as present with unremarkable morphology.

ug/dL; normal: 65–175 ug/dL), low ferritin (6.3 mg/mL; normal: 26–388 ng/mL), elevated reticulocyte count (5.3%; normal: 0.5%–1.8%), and low mean corpuscular volume (78; normal: 80–100). Screening for infectious and autoimmune causes was unremarkable. Peripheral blood smear demonstrated normocytic, normochromic anemia with severe thrombocytopenia (*Figure 2a*). A bone marrow biopsy showed erythroid hyperplasia (61%) with no significant blasts or megaloblastic features, indicating that the anemia and thrombocytopenia likely had two separate etiologies (*Figure 2b*), as opposed to a primary bone marrow process, such as myelodysplasia.

The patient's anemia was a combination of iron deficiency due to chronic slow blood loss secondary to severe thrombocytopenia complicated with B12 deficiency. Based on the lack of megaloblastic features on the peripheral blood smear, we may infer that the B12 deficiency may have developed relatively recently compared to the slow blood loss from severe thrombocytopenia. He was treated with packed red blood cells and platelet transfusions, intravenous iron

dextran, and oral cyanocobalamin. Though the hemoglobin steadily increased to 8.6 g/dL, the platelet count remained 1 K/ μ L until treatment with intravenous immunoglobulin and dexamethasone eventually brought it up to 55 K/ μ L. The patient was asymptomatic at discharge.

DISCUSSION

ITP can cause profound hematological abnormalities without the classic initial presentation of apparent bleeding and purpura.⁹ In this case, the patient had severe anemia, attributed to sustained slow bleeding secondary to profound thrombocytopenia, causing multiorgan failure: myocardial demand ischemia, renal failure, and fatigue. Though his symptoms and troponin down-trended once the hemoglobin reached 8 g/dL, his renal dysfunction did not improve during hospitalization, meaning that his chronic anemic state led to irreversible kidney injury.

ITP-associated severe hemorrhage is generally broken down into intracranial or nonintracranial hemorrhage

bleeding (gastrointestinal, menstruation, or hematuria); both are uncommon. A systematic review of prospective clinical studies of severe bleeding in primary ITP showed that 1.4% of patients had intracranial hemorrhage and 9.6% of patients had a nonintracranial source but with significant variability due to patient populations and reporting methods, including the use of established bleeding severity scales.⁵ Individual studies showed some predictors of severe bleeding, such as degree of thrombocytopenia, previous minor bleeding, and chronic ITP (defined as >12 months prior to presentation with severe bleeding), but these factors are inconsistent.⁵ Bleeding severity in ITP cannot be correlated to other causes of low platelet counts, because circulating platelets in ITP have greater hemostatic effectiveness than platelets in bone marrow suppressive conditions. Thus, ITP-associated bleeding is often less severe at similar numbers than thrombocytopenia due to other causes.¹⁰

ITP is not usually associated with white or red blood cell line abnormalities. Though the initial insult was ITP causing severe thrombocytopenia, the patient developed a chronic slow blood loss anemia severe enough that his renal function could not fully recover despite treatment of both the anemia and thrombocytopenia. Though anemia in chronic kidney disease (CKD) is well studied, severe anemia causing renal failure is not. However, our hypothesis remains that prolonged severe anemia caused reduced oxygen delivery to the renal tubules, leading to increased ischemia, apoptosis and necrosis, and permanent damage to the kidneys. Regarding the patient's type II non-ST elevation myocardial infarction, demand ischemia is a well-noted sequela of severe blood loss. However, anemia is also a risk factor for development of LVH in both dialysis and non dialysis patients with CKD and has been identified as an independent risk factor for LVH in dialysis patients with CKD.^{11–14} The mechanism for LVH in CKD is likely due to reduced oxygen delivery to the myocardium, leading to necrosis and apoptosis of myocytes and an increase in cardiac output and oxidative stress, causing a compensatory increase in myocardium size.^{11–16} We propose a similar mechanism as a cause of the patient's now chronic renal insufficiency. Regardless, our patient presented with severe anemia due to ITP-induced thrombocytopenia, resulting in multiorgan failure and likely irreversible damage to the kidneys, further revealing the relationship between chronic severe anemia and its effects on the cardiac and renal systems.

ORCID

Mark Muenchrath <http://orcid.org/0000-0001-9169-6514>
 Katyayini Aribindi <http://orcid.org/0000-0002-8945-0571>

1. Neylon AJ, Saunders PW, Howard MR, Proctor SJ, Taylor PR; Northern Region Haematology Group. Clinically significant newly presenting autoimmune thrombocytopenic purpura in adults: a prospective study of a population-based cohort of 245 patients. *Br J Haematol*. 2003;122(6):966–974. doi:10.1046/j.1365-2141.2003.04547.x.
2. Provan D, Stasi R, Newland AC, et al. International consensus report on the investigation and management of primary immune thrombocytopenia. *Blood*. 2010;115(2):168–186. doi:10.1182/blood-2009-06-225565.
3. Arnold DM, Nazy I, Clare R, et al. Misdiagnosis of primary immune thrombocytopenia and frequency of bleeding: lessons from the McMaster ITP Registry. *Blood Adv*. 2017;1(25):2414–2420. doi:10.1182/bloodadvances.2017010942.
4. Moulis G, Palmaro A, Montastruc JL, Godeau B, Lapeyre-Mestre M, Sailler L. Epidemiology of incident immune thrombocytopenia: a nationwide population-based study in France. *Blood*. 2014;124(22):3308–3315. doi:10.1182/blood-2014-05-578336.
5. Neunert C, Noroozi N, Norman G, et al. Severe bleeding events in adults and children with primary immune thrombocytopenia: a systematic review. *J Thromb Haemost*. 2015;13(3):457–464. doi:10.1111/jth.12813.
6. Kuter DJ, Rummel M, Boccia R, et al. Romiplostim or standard of care in patients with immune thrombocytopenia. *N Engl J Med*. 2010;363(20):1889–1899. doi:10.1056/NEJMoa1002625.
7. Gudbrandsdottir S, Birgens HS, Frederiksen H, et al. Rituximab and dexamethasone vs dexamethasone monotherapy in newly diagnosed patients with primary immune thrombocytopenia. *Blood*. 2013;121(11):1976–1981. doi:10.1182/blood-2012-09-455691.
8. Collins JF, Lieberman DA, Durbin TE, Weiss DG; Veterans Affairs Cooperative Study Group. Accuracy of screening for fecal occult blood on a single stool sample obtained by digital rectal examination: a comparison with recommended sampling practice. *Ann Intern Med*. 2005;142(2):81–85. doi:10.7326/0003-4819-142-2-200501180-00006.
9. Feudjo-Tepie MA, Le Roux G, Beach KJ, Bennett D, Robinson NJ. Comorbidities of idiopathic thrombocytopenic purpura: a population-based study. *Adv Hematol*. 2009;2009:1. doi:10.1155/2009/963506.
10. Peng J, Friese P, Heilmann E, George JN, Burstein SA, Dale GL. Aged platelets have an impaired response to thrombin as quantitated by P-selectin expression. *Blood*. 1994;83(1):161–166.
11. Astor BC, Arnett DK, Brown A, Coresh J. Association of kidney function and hemoglobin with left ventricular morphology among African Americans: the Atherosclerosis Risk in Communities (ARIC) study. *Am J Kidney Dis*. 2004;43(5):836–845. doi:10.1053/j.ajkd.2003.12.047.
12. Foley RN, Parfrey PS, Harnett JD, Kent GM, Murray DC, Barre PE. The impact of anemia on cardiomyopathy, morbidity, and mortality in end-stage renal disease. *Am J Kidney Dis*. 1996;28(1):53–61.
13. Harnett JD, Kent GM, Foley RN, Parfrey PS. Cardiac function and hematocrit level. *Am J Kidney Dis*. 1995;25(4 Suppl 1):S3–S7.
14. Parfrey PS, Foley RN. The clinical epidemiology of cardiac disease in chronic renal failure. *J Am Soc Nephrol*. 1999;10(7):1606–1615.
15. Frank H, Heusser K, Hoffken B, Huber P, Schmieder RE, Schobel HP. Effect of erythropoietin on cardiovascular prognosis parameters in hemodialysis patients. *Kidney Int*. 2004;66(2):832–840. doi:10.1111/j.1523-1755.2004.00810.x.
16. London GM. Left ventricular alterations and end-stage renal disease. *Nephrol Dial Transplant*. 2002;17(Suppl 1):29–36. doi:10.1093/ndt/17.suppl_1.29.