Idiopathic no more: A rare cause of late presentation thrombocytopenia

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Disclosure Information	Authors and Co-authors have no relevant financial relationships to declare.
Supplemental Video	Supplemental Video
Category	Medicine & Medical Subspecialties

Abstract

Introduction:

Myriad quantitative and qualitative platelet disorders are recognized in the medical literature. However, in the majority of cases patients are labelled as immune thrombocytopenic purpura (ITP), when the basic tests are unrevealing. Here, we present you a case report of a mislabelled immune-thrombocytopenic-purpura (ITP), which on further investigation revealed the diagnosis of possible two rare genetic functional platelet disorders with the presence of novel genetic mutations.

Case Presentation:

History: A 74 year old female with a lifelong history of multiple hospitalizations due to recurrent bleeding manifestations in the form of menorrhagia and upper GI bleed secondary to small-bowel arterio-venous malformations with a labelled diagnosis of refractory ITP, who was treated with chronic steroids, IVIG, and splenectomy at the age of 72 admitted to our hospital for melena and symptomatic anemia.

Physical Examination: negative for petechiae, purpura, cardiac murmurs, signs of liver failure, but non-bleeding external hemorrhoids were noted.

Differential Diagnosis: Acute GI bleed from AVMs, acute flare of ITP, DIC, and underlying undiagnosed functional platelet disorder.

Diagnostic work-up: hemoglobin 7, platelets 36K, with normal MCV, INR, PTT, iron profile, haptoglobin, LDH, fibrinogen, bleeding time, liver and renal function tests. Peripheral smear showed low platelet counts, but no megakaryocytes or schistocytes were noted. USG abdomen revealed cirrhotic changes most likely secondary to hepatitis C. Upper GI endoscopy revealed small bowel AVMs. Colonoscopy revealed non-bleeding hemorrhoids with no angiodysplasia. Von-Willebrand multimer panel revealed elevated Von-Willebrand antigen (VWA) of 514%, elevated ristocetin cofactor assay of 507% with normal VonWillebrand multimer pattern and distribution bands. Platelet function genetic testing revealed homozygous frameshift mutation in chromosome 17 leading to GP1BA protein truncation, heterozygous insertion variant mutation in exon 2 of GP1BA, and heterozygous missense mutation in thromboxane A2 gene, and mutation of glycoprotein 6.

Final Diagnosis:

Elevated VWA and normal multimer pattern in the setting of thrombocytopenia seen in our patient is consistent with Type 2B Von-Willebrand disease. Platelet Functional Analyzer further consolidates the diagnosis of Type 2B Von-Willebrand disease and potentiates the diagnosis of suspected Bernard-Soulier disease given patient's longstanding history of associated arterio-venous malformations.

Management:

Patient was stabilized with blood transfusions, platelet transfusions, and aminocaproic acid injections. Desmopressin is contraindicated as there is no quantitative defect in the VWA and multimers. Despite no specific therapy available for these diseases, treatment with IVIG, steroids, and desmopressin can be avoided to reduce their complications as no benefit is proven in these diseases.

Learning Objectives

Upon completion of this lecture, learned should be better prepared to evaluate the underlying cause of thrombocytopenia