Thrombocytopenia

Eun-Ju Lee, MD[a], Alfred Ian Lee, MD, PhD[b,*]

KEYWORDS

- Thrombocytopenia • Immune thrombocytopenia
- Heparin-induced thrombocytopenia • Thrombotic thrombocytopenia purpura
- Atypical hemolytic uremic syndrome

KEY POINTS

- Major causes of isolated thrombocytopenia include immune thrombocytopenia, drug-induced thrombocytopenia, disseminated intravascular coagulation, heparin-induced thrombocytopenia, gestational thrombocytopenia, and inherited thrombocytopenias.
- Patients with mild, chronic, isolated thrombocytopenia often maintain a platelet count in the range of 100 to 150 $\times$ 10^9/L, whereas some develop immune thrombocytopenia with or without a concomitant autoimmune disease.
- Immune thrombocytopenia is a diagnosis of exclusion and requires evaluation for secondary causes of thrombocytopenia.
- Diagnosis and management of heparin-induced thrombocytopenia rely on an assessment of pretest probability of having this disease.
- Microangiopathic hemolytic anemia and schistocytes are defining features of thrombotic microangiopathies.

INTRODUCTION

Platelets are derived from megakaryocytes whose production and maturation in the bone marrow are regulated by thrombopoietin.[1] Platelets play important roles not only in thrombosis and wound repair but also in inflammation, immunity, and cancer biology.[2] Normal platelet values range from 150 to 450 $\times$ 10^9/L. There is some debate as to whether patients with platelet counts in the range 100 $\times$ 10^9/L to 150 $\times$ 10^9/L should be designated as having true versus borderline thrombocytopenia[3]; data suggest that most of these patients remain asymptomatic and maintain their platelet counts in this range, whereas a smaller percentage develop immune thrombocytopenia (ITP) with or without a concomitant autoimmune disease.[4]

Disclosure: The authors have nothing to disclose.
[a] Division of Hematology, Weill Cornell Medical College, New York, NY, USA; [b] Section of Hematology, Yale Cancer Center, Yale University School of Medicine, 333 Cedar Street, Box 208021, New Haven, CT 06520, USA
* Corresponding author.
E-mail address: alfred.lee@yale.edu

Prim Care Clin Office Pract 43 (2016) 543–557
http://dx.doi.org/10.1016/j.pop.2016.07.008
primarycare.theclinics.com

A major clinical consequence of thrombocytopenia is bleeding caused by impaired primary hemostasis and platelet plug formation. Mucocutaneous bleeding usually occurs when platelet counts decrease to less than the range of 20×10^9/L to 30×10^9/L. Severe bleeding, including intracranial hemorrhage, occurs with platelet counts of less than 10×10^9/L to 20×10^9/L.[5–7]

Thrombocytopenia is a common problem, affecting 40% to 50% of patients in medical and surgical intensive care units.[8–10] In the outpatient setting, primary care physicians are generally comfortable managing patients with at least modest thrombocytopenia (eg, platelet count 80×10^9/L) without referral to a hematologist, so an understanding of the major mechanisms of thrombocytopenia is essential for practicing internists.[11] However, the evaluation of thrombocytopenia can be challenging, because hematologists confronted with the same case of thrombocytopenia frequently disagree on the underlying diagnosis.[12]

The major underlying mechanisms of thrombocytopenia include pseudothrombocytopenia, splenic sequestration, marrow underproduction, and peripheral destruction (**Box 1**). Clues from a patient's history (including medication exposures, alcohol intake, diet, travel, recent illnesses, and transfusions), physical examination (eg, petechiae, mucosal bleeding, splenomegaly, lymphadenopathy, and skeletal abnormalities), family history, and other laboratory studies may refine the differential diagnosis. Of central importance is the peripheral blood smear to evaluate both for the presence of platelet clumps, indicating pseudothrombocytopenia (**Fig. 1**), and for other abnormal cell morphologies, such as schistocytes, large or giant platelets, or immature or dysplastic cells.

This article presents 4 clinical cases as examples of our diagnostic approach to patients with thrombocytopenia.

Case 1

A 20-year-old male college student presented to his university urgent care clinic 3 weeks ago with fever, chills, sore throat, and headache. He was diagnosed with an upper respiratory tract infection. He now returns with epistaxis and gum bleeding. He does not take any medications, vitamins, or herbal supplements. He denies alcohol or recreational drug use. He consumes a broad diet. There is no known family history of cytopenias or other blood disorders. Physical examination reveals wet purpura in the oral cavity, mild crusted blood in the nares, and petechiae on both legs, with no lymphadenopathy or hepatosplenomegaly. Laboratory studies show a white blood cell (WBC) count of 4,400/μL, hemoglobin level 14.4 g/dL, platelet count 1×10^9/L, and preserved coagulation studies (prothrombin time [PT], International Normalized Ratio [INR], and partial thromboplastin time [PTT]). The peripheral blood smear is shown in **Fig. 2**. What is the patient's diagnosis, and how should he be treated?

Petechiae and mucocutaneous bleeding can be seen with platelet disorders, mild coagulation factor deficiencies, or connective tissue disorders. This patient's severe thrombocytopenia and normal coagulation parameters suggest a platelet disorder. Given that the WBC count and hemoglobin are preserved, the evaluation should focus on causes of isolated thrombocytopenia, namely ITP, drug-induced ITP (DITP), disseminated intravascular coagulation (DIC), heparin-induced thrombocytopenia (HIT), gestational thrombocytopenia, and inherited thrombocytopenias.[13] The finding of large or giant platelets on the blood smear suggests either a component of peripheral destruction leading to megakaryocyte hyperplasia in the bone marrow or a platelet structural defect as may be seen in inherited thrombocytopenias; the negative family history points away from the latter. Lack of medication or drug exposure or herbal use renders DITP and HIT unlikely. The absence of systemic symptoms or schistocytes