

Congenital Disorders of Platelet Function and Number



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KEYWORDS

- Congenital platelet disorder • Thrombocytopenia • Platelet function
- Thrombasthenia

KEY POINTS

- New research and diagnostic tools continue to expand understanding of the genetic and molecular causes of disorders of platelet number and function.
- Congenital disorders of both platelet number and function have been associated with multiple hematologic and clinical manifestations, including auditory, musculoskeletal, cardiac, immunologic, and oncologic complications and disease.
- Delineation of the molecular cause of the platelet disorder can aid the practitioner in the early detection and prevention of disorder-associated manifestations and guide appropriate treatment and anticipatory care for the patient and family.

CLINICAL MANIFESTATIONS OF PLATELET-RELATED BLEEDING

Bleeding associated with platelet disorders primarily involves the skin and mucous membranes. The distribution and other characteristics of petechiae and bruising can be helpful in distinguishing bleeding related to platelet disorders from other causes, such as vasculitic disease or nonaccidental injury. For example, the lesions associated with Henoch-Schönlein purpura, a vasculitic disease, are raised and primarily involve dependent surfaces and the lower extremities. Unusual or regular patterns of skin lesions (eg, handprint, linear) may suggest the possibility of nonaccidental injury.

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Mucosal surfaces that can be involved in platelet-related bleeding include the nasal membranes; oral cavity; gastrointestinal hemorrhage; hematuria; and, in young women, menorrhagia. (See discussion of heavy menstrual bleeding in Kathryn E. Dickerson and colleagues' article, "[Abnormal Uterine Bleeding in Young Women with Blood Disorders](#)," in this issue.) Platelet dysfunction should also be considered in the presence of increased bleeding following dental extraction, tonsillectomy, or other surgical procedures.

Differential Diagnosis of Platelet-Related Bleeding

A careful medical history, physical examination, and evaluation of the platelet count and smear can rapidly narrow the diagnostic possibilities in the setting of platelet-related bleeding. History should be obtained regarding medication usage, particularly aspirin or nonsteroidal antiinflammatory drugs. Detailed evaluation of the family and past medical history may provide clues about whether the bleeding disorder is acquired or congenital. Careful evaluation of the peripheral blood smear and blood count, as well as assessment of hepatosplenomegaly and lymphadenopathy, may reveal the need for further evaluation for the presence of myeloproliferative disease, malignancy, or aplastic anemia.

Differentiation of immune thrombocytopenic purpura (ITP) from a congenital platelet disorder can sometimes be problematic. The persistence of neonatal thrombocytopenia or a low platelet count despite the use of several standard therapies (eg, intravenous immunoglobulin, steroids) for ITP should prompt consideration of a congenital cause for the thrombocytopenia. Patients with ITP typically have minimal bleeding until their platelet count decreases to below 10,000 to 20,000/ μL . Bleeding observed at platelet counts greater than 30,000/ μL suggests the presence of an underlying platelet dysfunction.

Many congenital platelet disorders are associated with other diseases, unique physical characteristics, or findings on the peripheral blood smear. These additional characteristics can assist in narrowing the differential diagnosis. For example, thrombocytopenia in the presence of auditory or renal dysfunction suggests an MYH-9-related thrombocytopenia, and the presence of skeletal abnormalities may lead to the diagnosis of thrombocytopenia with absent radii or amegakaryocytic thrombocytopenia with radioulnar synostosis.

Diagnostic Evaluation of Platelet-Related Bleeding

Initial laboratory evaluation of individuals with platelet-related bleeding should include a complete blood count with differential and von Willebrand factor (vWF) studies (including activity and antigen) to rule out this primary cause of mucocutaneous bleeding. (See Christopher J. Ng and Jorge Di Paola's article, "[Von Willebrand disease: Diagnostic Strategies and Treatment Options](#)," in this issue.) Utilization of a platelet function analyzer can identify individuals with severe defect in platelet number or function; however, this test has poor sensitivity and specificity for less severe defects of platelet function.¹ Standard evaluation of platelet dysfunction should include evaluation of platelet aggregation to multiple platelet agonists. Aggregation studies are often performed in concert with luminometry studies that evaluate for the presence and functional release of platelet-dense granules. Finally, electron microscopy, genetic testing, and other specialized studies (see later discussion) can be used to identify a definitive syndrome or molecular cause for a dysfunction in platelet count or number.

Estimation of platelet size can assist in narrowing the differential diagnosis in patients with a suspected inherited thrombocytopenia. Light microscopy can further

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