Evaluation and Management of Congenital Bleeding Disorders

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KEYWORDS

• Congenital • Bleeding • Hemophilia • von Willebrand • Factor • Coagulopathy
• Platelet dysfunction

KEY POINTS

- Patients presenting to the emergency department with acute bleeding and a history of clotting or platelet disorder present a unique challenge to the emergency physician.
- The severity of bleeding presentation is based on mechanism as well as factor levels: patients with factor levels greater than 5% can respond to most minor hemostatic challenges, whereas those with factor levels less than 1% bleed with minor trauma or even spontaneously.
- Treatment should be initiated in consultation with the patient's hematologist using medications and specific factor replacement except in rare, life-threatening, resource-poor situations, when cryoprecipitate or activated prothrombin complex may be considerations.

INTRODUCTION

Patients presenting to the emergency department (ED) with acute bleeding and a history of clotting or platelet disorder present a unique challenge to the emergency physician (EP). Adults often already carry a diagnosis of either hemophilia A, hemophilia B, or von Willebrand disease (VWD), but many children may be undiagnosed and some milder variants of these diseases can go unrecognized until life-threatening bleeding occurs. This article is intended to familiarize EPs with the presentations and management of common congenital bleeding disorders to allow rapid and accurate treatment of these conditions.

PHYSIOLOGY AND PATHOPHYSIOLOGY

Hemostasis is a complex response by the body to maintain blood in a fluid state in normal vessels while quickly generating a localized response at the site of vascular

This article originally appeared in Emergency Medicine Clinics of North America, Volume 32, Issue 3, August 2014.
Disclosure: None.
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Hematol Oncol Clin N Am 31 (2017) 1105–1122
http://dx.doi.org/10.1016/j.hoc.2017.08.011 **hemonc.theclinics.com**

injury. It requires the coordinated function of the vascular endothelium, platelets, and clotting factors. There must also be balance between formation and lysis of clot to prevent overwhelming response to localized damage. The absent, diminished, or dysfunctional activity of any of the numerous components of the body's hemostatic response can lead to coagulopathy, morbidity, and sometimes fatal events. Because they are so vast and varied, it is best to separate the abnormalities of clotting into those associated with the vasculature, those associated with platelets, and those associated with the coagulation pathway. A basic understanding of normal endothelial, platelet, and coagulation pathway function is necessary to understand the variety of ways hemostasis can go awry.

Vasculature

The vascular lining is composed of endothelial cells supported by a basement membrane, connective tissue, and smooth muscle. In its uninjured state the endothelium secretes antiplatelet, anticoagulant, and fibrinolytic substances to maintain liquid blood flow. When directly injured or activated (by bacterial endotoxins, for example) the endothelium takes on procoagulant properties important for proper clot formation. Damaged endothelial cells:

1. Release von Willebrand factor (VWF), which allows platelet binding
2. Synthesize tissue factor, which activates the coagulation cascade (discussed later)
3. Bind activated coagulation factors IXa and Xa, which increase the activity of the coagulation cascade

Dysfunction of the endothelial lining is often acquired or infectious. Examples include cutaneous drug reactions, scurvy, and meningococcemia. Congenital causes of endothelial abnormality include connective tissue disorders like Ehlers-Danlos syndrome and hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu syndrome), an autosomal dominant disorder characterized by tortuous thin-walled vessels that predispose to bleeding, particularly of the mucous membranes. With the exception of some cases of hereditary telangiectasias, these disorders of the vasculature rarely cause life-threatening bleeding and the focus of this article is largely on congenital platelet and coagulation disorders.

Platelets

Platelets are thin membrane-bound discs that contain granules filled with procoagulant factors and surface receptors that assist in clot formation and aggregation. When platelets encounter damaged endothelium, contact with the exposed endothelial extracellular matrix initiates the following reactions (**Fig. 1**):

1. Adhesion: platelets do not attach directly to the damaged endothelium but instead to VWF, which bridges between the platelet's receptors and the exposed endothelial extracellular matrix (ECM) collagen. Without these strong bridges, platelets would not be able to withstand the shear forces of circulating blood, particularly in the microcirculation.
2. Secretion: once they have attached to VWF the granules within platelets are released. The released factors include chemotaxins for platelet aggregation and cofactors for the intrinsic clotting pathway (discussed later). Adenosine diphosphate (ADP) and thromboxane A_2 (TxA_2) are two of the most important substances.
3. Aggregation: the actions of ADP and TxA_2 attract more platelets, creating the platelet plug. They also initiate the intrinsic clotting cascade, and tissue factor released from the endothelium activates the extrinsic pathway. These factors